Repacking & Over Labelling Medicines / Vaccines in Pharmacy Stores

Standard Operating Procedure.

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Engagement & Consultation

Key Individuals/Groups Involved in <u>Developing</u> this Document.

Role / Designation
Nikki Mathers, Senior Pharmacy Technician, Immunisation/Vaccination, Therapies & Pharmacy Stores

Circulated to the following for Consultation

Date	Role / Designation
04/03/2024	Chief Pharmacist
04/03/2024	Medicines Management Pharmacy Technician

1 Introduction

Powys Teaching Health Board (PTHB) is committed to the safe and secure handling of medicines and vaccines to protect patients and staff.

This SOP describes the processes of repacking and over labelling operations that can be carried out in accordance with the principles of Good Manufacturing Practice (GMP) in hospital pharmacies that do not hold a Specials Manufacturing licence from the Medicines and Healthcare products Regulatory Agency (MHRA). Such activities can be carried out under the professional exemption from licensing, provided they are undertaken by or under the supervision of a pharmacist[1]

Repacking medicines/vaccines in PTHB pharmacy stores is sometimes necessary to facilitate vaccination to specific groups of eligible patients where smaller quantities of vaccine are required i.e. to support the District Nurse (DN) Teams Covid vaccination programme to housebound citizens. In this instance, and to assist the DNs, vials of Covid vaccine can be packed down into smaller quantities i.e. packed down into packs of one single multidose vial. This avoids having to unnecessarily supply original packs (OP) of vaccines, ensures minimum vaccine waste at the end of vaccination sessions, saves time in having to arrange vaccine return to pharmacy stores and avoids the need to rotate and manage stock that has been out of the fridge.

Over labelling medicines/vaccines in PTHB pharmacy stores is sometimes necessary when manufacturers issue product expiry extensions or when a product requires dosage instructions to be added to the OP i.e. Paxlovid.

It is mandatory for all staff members involved in the process of repacking and over labelling medicines and vaccines to always follow this standard operating procedure.

This process is following compliance with current legislative requirements and good practice guidance.

For access to any documents/paperwork referred to in this SOP email Nikki Mathers via info.medicinesmanagement.powys@wales.nhs.uk/

[1] Guidance-on-Overlabelling-Repacking.pdf (sps.nhs.uk)

2. Objective

- To clearly describe the professional standards for repacking and over labelling in NHS pharmacies.
- To clearly describe the process for repacking medicines/vaccines in pharmacy stores.
- To clearly describe the process for over labelling medicines/vaccines in pharmacy stores.
- To clearly describe the process for product release.

3. Definitions

- **PTHB –** Powys Teaching Health Board

- **GPhC –** The General Pharmaceutical Council regulate pharmacist, pharmacy technicians and pharmacies in Great Britain.

- **GMP** – Good Manufacturing Practice is the minimum standard that a medicines manufacturer must meet in their production processes.

- **MHRA** – The Medicines and Healthcare Products Regulatory Agency regulates medicines, medical devices, and blood components for transfusion in the UK.

- **OP –** An Original Pack is a medicine/vaccine supplied in the manufacturers original outer packaging.

- **PIL -** Patient Information Leaflets are written by pharmaceutical companies and are summaries of the product characteristics. PILs are included in medicines/vaccines original packs.

- **Quarantine**-To separate/isolate affected stock from supply chain which must be clearly labelled with 'Quarantined – do not use' and dated.

- **Cold chain** – is the system of transporting and storing medicines within the recommended temperature range of +2°C to +8°C from the place of manufacturer to the point of administration to a patient.

- **Temperature deviation/excursion** – any incident where the temperature is outside of the recommended range of +2°C to +8°C.

- **Medicine** – a substance used for treating, preventing, or diagnosing disease, for contraception, inducing anaesthesia or modifying normal physiological function.

- **Vaccine** – a suspension of attenuated or killed microorganisms (viruses, bacteria, or rickettsia) or of antigenic proteins derived from them, administered for prevention, amelioration or treatment of infectious disease.

4. Role / Responsibilities

4.1 Chief Pharmacist

The Chief Pharmacist must:

- Ensure that all staff working to this SOP have undertaken appropriate education and training, in accordance with General Pharmaceutical Council (GPhC) standards.
- Ensure that all repackaging and over labelling activities follow Good Manufacturing Practice (GMP) principles and are performed by or under the supervision of a pharmacist.

4.3 Senior Pharmacy Technician, Vaccination/Immunisation, Therapies & Pharmacy Stores

- The senior pharmacy technician must ensure that all staff read and understand this procedure and have been appropriately trained to meet the requirements of the (GPhC).
- The senior pharmacy technician must ensure that pharmacy stores staff are competent to perform the duties required of them under this SOP.
- The senior pharmacy technician is responsible for ensuring that the repackaging and over labelling limits are not breached.
- The senior pharmacy technician is responsible for arranging regular review to monitor compliance with this procedure, providing advice on pack down, over labelling and batch release processes in line with pharmacy professional standards.

4.2 Other Staff

- All pharmacy staff working to this SOP are responsible for undertaking cold chain training, Good Distribution Practice (GDP) training, adhering to this SOP, maintaining competence, and reporting and reacting to temperature excursions.
- All pharmacy staff working to this SOP must undertake education and training to meet GPhC standards Standards | General Pharmaceutical Council (pharmacyregulation.org)
- All pharmacy staff working to this SOP must be aware of Good Manufacturing Practice (GMP) principles.
- Competency to carry out duties will be assessed initially by trained and competent Pharmacy Stores staff, and reassessed annually, or sooner if necessary.

5. Principles and Professional Standards for Over Labelling and Repacking medicines/vaccines

5.1 Overview

The following principles are established from MHRA guidance (see appendix A).

NHS pharmacy departments may undertake batch repackaging and over labelling subject to the following restrictions:

- The limit for repackaging is a **maximum batch size of 25 packs**.
- The limit for over labelling is a **maximum batch size of 100 packs.**
- There should be a limit of one batch per product per month prepared for stock.
- The repackaging or over labelling activity must follow GMP[2] principles (also see appendix B) and must be performed by or under the supervision of a pharmacist.
- Batch release must be by a pharmacist.
- Batch records must be kept.
- Repackaging or over labelling of medicines for sale or supply outside its corporate body, i.e., to another hospital pharmacy, must be undertaken in a licensed facility which holds a Specials Manufacturing Licence, regardless of the quantities supplied. Presently PTHB does not hold such a licence.

[2] EU Good Manufacturing Practice (see http://ec.europa.eu/health/documents/eudralex/vol-4/index_en.htm)

- Repackaging is a more complex operation than over labelling and is associated with increased risk of errors during preparation. Packing into plain cartons reduces differentiation between products and therefore increases the risk of selection errors. If repackaging is undertaken, steps must be taken to minimise these risks. Wherever possible, preference should be given to over labelling original packs rather than repackaging.
- Worksheets must be completed contemporaneously in indelible ink. Any alteration should have one line crossed through the incorrect information, the correction added, and the alteration should be signed and dated.
- Any deviations or unexpected events should be recorded on the worksheet.

5.2 Professional standards for repackaging and over labelling in NHS pharmacies

The following standards for the quality assurance of repackaging and over labelling of medicines in NHS pharmacies have been developed by the NHS Pharmaceutical Quality Assurance Committee[1], based on the principles of GMP (see appendix B). They aim to support dispensaries in the preparation of small batches of over labelled and repackaged medicines in a safe, accurate and practical way.

- Quality Management
- Facilities
- Personnel
- Documentation & Labels
- Processing
- Product Release

These standards can be accessed here

Shelf lives should be assigned using the following principles:

Product type Suggested shelf life	**Product type Suggested shelf life**
Over labelled packs	Manufacturer's original shelf life
Products sealed enclosed in their original primary container (tablets and capsules in blister strip packaging, ampoules, vials)	Manufacturer's original shelf life
Loose tablets and capsules and liquids with no special storage requirements	Maximum 12 months from the date of repacking

Loose tablets and capsules with a desiccant or liquids with a stated shelf life on opening	Seek advice from manufacturer or Regional QA

6. Process for Repacking

A worksheet using a standard template should be used for all repackaging and over labelling activities (see Appendix C & D for example templates). Worksheets should incorporate the master label for the product being prepared and both the worksheet and the master label must be approved by a pharmacist. All pack downs must take place in the pharmacy stores preparation area.

Process

- Wipe workspace with a Clenil wipe before beginning the repacking process. Ensure the work area is free from clutter and any other medicines, labels, or documentation, to avoid any mix ups. Only one batch pack down to be prepared at any one time.
- Print a copy of the product-related worksheet.
- Prepare the correct number of Patient Information Leaflets (PILs) according to the batch size (for Covid vaccine pack downs, this will not be necessary, as Vaccination Centre (VC) admin staff will issue PILs to people as they arrive at the VC).
- Fill in the date of repacking, the batch size (maximum of 25), the unique pharmacy batch number (this will be a sequential number, following on from the previous pack down batch number) and the expiry date from the OP.
- Complete the assembly section of the worksheet with product details and sign for assembly.
- Print off the required number of labels for the product being repacked plus one extra for the worksheet (all labels can be found in the pharmacy stores stock management system located here: Medicines Management - Pandemic Room documentation - All Documents (sharepoint.com)).
- Add the product batch number (where possible, use the product with same batch number for the pack down), date and time of expiry to each label and attach one label to the worksheet in the space provided on the label section.
- Prepare the correct number of pharmacy labels with the unique pharmacy pack down batch number and expiry date and initial the 'dispensed by' box.
- Attach one pharmacy label to the worksheet in the space provided on the label section, alongside the product label.

- Pre-label all cartons for re-packing. Use a highlighter marker to highlight the expiry date on the label. Place cartons upright with the lids open in a pharmacy tray/basket.
- **Re-packing fridge items** must be carried out in a cold area e.g., the fridge, and must be completed swiftly. Take the pre-labelled cartons to the fridge in the pharmacy tray/basket. Keep the fridge door ajar to remove product from the OP and place into the pack down cartons. Add packing to the carton (i.e., tissue), if necessary, to avoid product movement, e.g., to keep vials upright. Monitor the fridge temperature during the pack down process. Take time out if the fridge temperature raises quickly and only return to the repacking process once the temperature has stabilised **N.B. The temperature must not go above 8ºC.** In the event of a temperature excursion refer to MMP 427 Safe and Secure Management of Refrigerated Medicines/Vaccines, Access here: Medicines Management - 6. SOPs - All Documents (sharepoint.com).
- The PIL (original or copy) should be inserted into a carton with the packed down product or attached to the outside of the primary container using an elastic or cellophane band, in such a way that the label is still readable.
- Complete the remainder of the worksheet detailing pack and label reconciliation.
- Once the worksheet has been completed, place it with the completed batch pack down for a pharmacist check, and to authorise release of the product. Finished product should be quarantined pending release by a pharmacist.
- Add the required batch pack down details to the local stock management system relating to the product that has been packed down e.g., details of product batch number, expiry, unique pharmacy batch number, quantity packed down etc.
- Once the batch pack down has been checked and signed by a pharmacist and the batch released, scan the completed signed worksheet, and save electronically in the dedicated worksheet folder. Once saved electronically, the original copy can be discarded in confidential waste.
- Enter a stock check onto the appropriate documentation i.e., local stock management system to update the number of pack downs in stock and document the expiry date.
- When the batch has been released by a pharmacist, return the product to stock.

7. Process for Over Labelling

Occasionally, some medicines may need over labelling, for example, with dosage instructions or extensions to expiry dates.

Details of expiry extensions will usually be communicated to the NHS via the manufacturer and/or other national agencies. Most expiry extensions are agreed by the MHRA. When over labelling medicines, any communication received from product manufacturers/national agencies, that indicate details of product changes requiring over labelling, must be printed, and attached to the over labelling worksheet.

Process

- Wipe workspace with Clenil wipe before beginning the over labelling process. Ensure the work area is free from clutter and any other medicines, labels, or documentation to avoid any mix ups.
- Only one over labelling batch to be prepared at any one time.
- Print a copy of the product-related worksheet.
- Fill in the date of over labelling, the batch size (maximum of 100), the unique pharmacy batch number (this will be a sequential number, following on from the previous over labelling batch number) and the expiry date and time from the OP.
- Complete the assembly section of the worksheet with product details and sign for assembly.
- Print off the required number of labels for the product being over labelled, plus one extra for the worksheet (all labels can be found in the pharmacy stores electronic folder located here: Medicines Management - Pandemic Room documentation - All Documents (sharepoint.com)).
- Ensure that the product batch number, date, time and the expiry date/new expiry (where applicable) have been added to each label and attach one label to the worksheet in the space provided on the label section.
- Prepare the correct number of pharmacy labels with the unique pharmacy pack down batch number and new expiry date/new expiry date (where applicable) and initial the 'dispensed by' box.
- Attach one pharmacy label to the worksheet in the space provided on the label section, alongside the product label.
- Label each pack, ensuring that important information on the OP is not obscured (flag-labelling may be necessary). Use a highlighter marker to highlight the expiry date on the over label and place packs in a pharmacy tray/basket.
- The over label must not interfere with any FMD (Falsified medicines Directive[3]) features of the original pack.

[3] https://www.gov.uk/guidance/implementing-the-falsified-medicines-directive-safety-features

- **Re-labelling fridge items** must be carried out in a cold area e.g., the fridge, and must be completed swiftly. Keep the fridge door ajar to re-label packs. Monitor the fridge temperature during the re-labelling process. Take time out if the fridge temperature rises quickly and only return to the repacking process once the temperature has stabilised **N.B. The temperature must not go above 8^{0}C.**
  In the event of a temperature excursion refer to MMP 427 Safe and Secure Management of Refrigerated Medicines/Vaccines, Access here: Medicines Management - 6. SOPs - All Documents (sharepoint.com)
- Complete the remainder of the worksheet detailing pack and label reconciliation.
- Once the worksheet has been completed, place this with the completed relabeled batch for a pharmacist check, and to authorise release of the product. Finished product should be quarantined pending release by a pharmacist.
- Add the required relabeled batch details to the local stock management system for the product that has been relabeled e.g., details of product batch number, expiry (including new expiry date, where applicable), unique pharmacy batch number, quantity packed down etc.
- Once relabeled packs have been checked and signed by a pharmacist and the batch has been authorised for release, scan the completed signed worksheet, and save electronically in the dedicated worksheet folder. Once saved electronically, the original copy can be discarded in confidential waste.
- Enter a stock check onto the appropriate documentation i.e., local stock management system for any medication/vaccine that has been over labeled.
- When the batch has been released by a pharmacist, return the product to stock.

8. Product Release

A formal recorded decision of batch release should be taken by a pharmacist.

The release check should include:

- Checking the label against master label

- Visual inspection of each finished product, including label positioning.

- Checking that the batch has been prepared by suitably trained staff and that the pharmacy dispensing label has been initialed.
- Checking that the worksheet has been accurately completed.
- Evaluating any recorded deviations.

For repackaged items, checks should include:

- Quantity and identity are correct.
- PIL is present and correct (exception – Covid vaccine)

Records of all products repackaged and over labelled must be retained for five years after release or for one year after the product's expiry, whichever is the longer, for audit and management purposes.

9. Monitoring Compliance / Audit / Review

Compliance with this SOP will be audited during annual pharmacy audits.

This SOP will be reviewed every three years or earlier should changes to legislation or to practice indicate otherwise.

10. References

NHS Pharmaceutical Quality Assurance Committee 2020. Guidance on repackaging and over labelleing small batches of medicines in pharmacy departments. Edition 2 October 2020 https://www.sps.nhs.uk/wp-content/uploads/2020/11/Guidance-on-Overlabelling-Repacking.pdf (accessed 04/03/2024)

Appendix A

Regulatory Background and Definitions

MHRA guidance

In 1992 the MHRA (at that time called the MCA) issued a document called "Guidance to the NHS on the Licensing Requirements of the Medicines Act 1968"[4].

This provided guidance on the application of the licensing provisions in the Medicines Act 1968 and its secondary legislation, in particular those provisions governing the manufacture, preparation and distribution of medicinal products.

At the time of writing, this document had not been withdrawn by the MHRA or superseded.

In addition, the MHRA has published "Questions & Answers for Specials Manufacturers"[5] which clarifies that over labelling and repackaging activities are assembly activities and therefore is a licensable activity unless certain conditions are met.

Definitions

The definition of "assemble" in relation to a medicinal product given in Section 8 of the Human Medicines Regulations 2012[6] is: "includes the various processes of dividing up, packaging and presentation of the product, and "assembly" has a corresponding meaning".

Repackaging

For the purpose of this document, "Repackaging" is synonymous with "breaking bulk", "pre-packing", "repacking" or "packing down".

It is defined as taking the pack of a licensed medicinal product, opening it to repackage the contents and labelling it with directions for use.

Usually, repackaging operations involve the packing down of tablets from original packs into smaller lots, but it can be applied to other forms of medicine such as liquid preparations and may occasionally involve combining medicines to create a larger pack size.

Over labelling

Over labelling is defined as the placing of a label onto the outer (secondary)

[4] Guidance-to-the-NHS-on-the-licensing-requirements-of-the-medicines-act-1968.pdf (devitup.co)
[5] https://www.gov.uk/government/publications/guidance-for-specials-manufacturers
[6] The Human Medicines Regulations 2012 (legislation.gov.uk)

packaging of a licensed medicinal product in a batch process. No other operation is undertaken to manipulate the licensed medicinal product in any other way.

Appendix B

What is GMP?

Good manufacturing practice (GMP) is the minimum standard that a medicines manufacturer must meet in their production processes. Products must:

- be of consistent high quality
- be appropriate to their intended use.
- meet the requirements of the marketing authorisation (MA) or product specification.

GMP covers every aspect of the manufacturing process to guard against any risks that can be catastrophic for products, such as cross-contamination, adulteration, and mislabelling.

The 10 Principles of GMP

- Create Standard Operating Procedures (SOPs)
- Enforce / Implement SOPs and work instruction.
- Document procedures and processes.
- Validate the effectiveness of SOPs.
- Design and use working systems.
- Maintain systems, facilities, and equipment.
- Develop job competence of workers.
- Prevent contamination through cleanliness.
- Prioritize quality and integrate into workflow.
- Conduct GMP audits regularly.

The MHRA and the European Medicines Agency (EMA) have published guidance on GMP and GDP.

- Orange Guide: Rules and Guidance for Pharmaceutical Manufacturers and Distributors 2022
- Green Guide: Rules and Guidance for Pharmaceutical Distributors 2022

Appendix C Batch Pack Down Worksheet Example

Comirnaty®Bivalent▼Original/Omicron BA.4-5 (15/15 micrograms)/dose dispersion for injection COVID-19 mRNA Vaccine (nucleoside modified) 6 dose vials	Health Board: Powys Teaching Health			
• Use this worksheet to record the details of batch repacking activity in all bold-edged boxes • Each packed down batch is assigned a unique pharmacy batch number generated by populating the Pack Down spread sheet (not the manufacturers Batch number!) • Assign expiry date and time to batch by transcribing from stock pack label.	**Date of repacking:**	**Batch size (Max 25):**	**Pharmacy batch number:**	**Expiry date & time:**
			Example: COMBI002	

1. ASSEMBLY						
1.1. Starting materials (all starting material packs should have same BN)						
Manufacturer name	**Manufacturers Batch number:**	**Expiry date & time:**	**No. original packs:**	**No. cartons:**	**Assembled by:**	**Assembly checked by:**
Comirnaty®Bivalent▼Original/Omicron BA.4-5 (Pfizer)						

1.2 Label preparation

- Print sufficient labels for each pack plus one extra for the worksheet. If extra labels need to be printed separately this should be documented • Obtain check before affixing to this worksheet and proceeding with repacking

Master product label	Stick Actual label for batch (two part)		
_ ……..multidose vials **Comirnaty® Bivalent Original/Omicron BA.4-5** 15/15 micrograms per dose dispersion for injection. COVID-19 mRNA Vaccine (nucleoside modified) For intramuscular Injection Each vial contains 6 doses at 0.3ml per dose Store at 2 to 8ºC. Store in this carton to protect from light. **DO NOT DILUTE PRIOR TO USE** Use within 12 hours of first puncturing the vial - any unused solution must be discarded after this time. BN: …… Expiry: MM/YY Time: HH/MM PTHB. Bronllys Hospital LD3 0LU		**labels printed**	
		Printed by	
		Checked by	

1.3 PIL preparation

- PIL not required and will be supplied for each individual dose given via Covid 19 supply POD

REPACKING	
• Repackaging must be carried out in a cold area. Work as quickly as possible & wear gloves to minimise hand heat • Clear work area to prevent mix-ups with any other product (signature required) • Prepare everything required • Remove vaccine vials at the fridge• • GENTLY handle the vaccine and keep UPRIGHT at all times – DO NOT SHAKE • Remove the vaccine vials from the original container and count out the required amount • Add the required amount of vials to each plain carton and label. • Repeat for each pack	Confirm work area clear Repacked by

Confirm identity and number of original packs Check label and contents of finished packs Complete label and pack reconciliation checks	**Packs**		**Labels**	
	No. Of packs expected		No. printed (G)	
	No. Rejected (E)		Used on worksheet (H)	
	No Released (F)		No. Destroyed (I)	
			Used on product (J)	
			Reconciliation G = H + I + J	
Batch released by Pharmacist (signature)				
Date & Time				

Appendix D Over Label Worksheet Example

Paxlovid 150mg/100mg (Nirmatrelvir 150mg/Ritonivir 100mg)	Health Board: Powys Teaching Health

- Use this worksheet to record the details of batch over labelling activity in all bold-edged boxes
- Each over labelled batch is assigned a unique pharmacy batch number generated by populating the over labelling spread sheet.

Date of repacking:	**Batch size (Max 100):**	**Pharmacy batch number:**	**Expiry date & time:**
		Example: PAXOL003	

1. ASSEMBLY						
1.1. Starting materials (all starting material packs should have same BN)						
Manufacturer name	**Manufacturers Batch number:**	**Expiry date & time:**	**No. original packs:**	**No. packs:**	**Assembled by:**	**Assembly checked by:**
Paxlovid 150mg/100mg (Nirmatrelvir 150mg/Ritonivir 100mg)						

1.2 Label preparation

• Print sufficient labels for each pack plus one extra for the worksheet. If extra labels need to be printed separately this should be documented • Obtain check before affixing to this worksheet and proceeding with repacking

Master product label	Stick Actual label for batch		

PAXLOVID 150mg/100mg Tablets (Nirmatrelvir 150mg/Ritonivir 100mg) **TWO Nirmatrelvir tablets and One Ritonivir tablet to be taken together TWICE daily (every 12 hours) for FIVE days** Swallow whole. Complete the course. Pt Name……. 1 x 30 Date…….. MM Team. PTHB. LD3 0LU 01874 712641 **KEEP OUT OF THE REACH & SIGHT OF CHILDREN**		**labels printed**	
		Printed by	
		Checked by	

1.3 PIL preparation

- PIL will be inside each box

REPACKING	
• Clear work area to prevent mix-ups with any other product (signature required) • Remove required quantity of Paxlovid (Nirmatrelvir 150mg/Ritonivir 100mg) boxes from medicines cupboard • Label each Paxlovid (Nirmatrelvir 150mg/Ritonivir 100mg) box with prepared labels • Label with pharmacy batch pack down number	Confirm work area clear Repacked by

• Confirm identity and number of original packs • Check label and contents of all finished packs • Complete label and pack reconciliation checks	**Packs**		**Labels**	
	No. expected (D)		No. printed (G)	
	No. Rejected (E)		Used on worksheet (H)	
	No Released (F)		No. Destroyed (I)	
	Reconciliation D = E + F		Used on product (J)	
			Reconciliation G = H + I + J	
Batch released by Pharmacist (signature)				
Date & Time				