HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

# Guide to
# Batch-Specific Requests for Human Medicines

Batch-specific requests (BSR) are accepted for critical medicines which hold a marketing authorisation (MA) issued by the Health Products Regulatory Authority (HPRA) or by the European Commission, to bring a batch of product into compliance with its marketing authorisation to ensure maintenance of supply. In some instances, a BSR may be accepted for non-critical nationally authorised (including herbal and homeopathic products) products to correct a quality defect or to bring a batch into compliance with its registered MA dossier. MA holders are strongly discouraged from applying for a BSR when batch(es) are not in line with the product's finished product specifications. However, in exceptional circumstances the BSR process may be used for batches with non-critical deviations with respect to the finished product specifications.

The BSR procedure may also be used in situations where an extension to the required implementation time for an approved variation or the extension of implementation of changes to labels/leaflet agreed during renewal is required. In such instances, where the variation has been approved and the MA holder is unable to meet the required implementation timeline, an extension may be sought via submission of a BSR.

If the applicant is someone other than the MA holder, a specific letter of consent from the MA holder is required.

When a BSR is intended to assure the continued supply of a product, it is normally limited to the number of packs or batches required to supply the market for no longer than three months. More than one batch of product can be specified on a BSR application. If the BSR is intended to correct a quality defect (to bring a product in line with the registered dossier), this three-month restriction does not apply, i.e. ~~the BSR has indefinite validity.~~ the BSR is approved to the end of shelf-life of the affected batch(es).

Applications involving labels and leaflet changes must be accompanied by copies of the approved and proposed full colour mock ups with all differences highlighted for review.

If insertion of the approved leaflet is required or, in exceptional circumstances, over-labelling of the packaging, this must be carried out by an authorised manufacturer who is specifically authorised to carry out such manufacturing operations. A copy of the manufacturer's and import authorisation (MIA) held by the site proposed to perform this packaging or over-labelling activity should be submitted.

If over-labelling is required, it must not obliterate any of the required original text; if placed to cover incorrect text, the over-label should not permit the underlying text to be visible. The over-label must have permanent adhesive.

The MA holder may be required to send a Healthcare Professional Communication/Caution-in-Use (CIU) letter to the professions, or it may be necessary for such a letter to accompany each unit of the batch affected. See Appendix 1 for a sample template.

If the HPRA has approved a BSR application for the rubber-banding of documentation (e.g. a package leaflet (PL) or a CIU letter) to the outer pack of the product, or the insertion of product into a sleeve/plastic bag, etc., with additional information (such as the PL or CIU letter) in it, the rubber-banding or insertion operation does not need to be carried out by an authorised manufacturer under GMP, as the packs are not being opened or reassembled. However, such an operation should be performed under the supervision and oversight of the Responsible Person at an authorised wholesaler, and a formal reconciliation of the PLs or CIU letters should be carried out once the operation is completed.

A written report on the operation should be prepared and retained at the manufacturing or wholesaler site for review at a subsequent inspection. Where applicable, sample labels should be included with the report.

BSRs should not be submitted for batches with an unexpected deviation during manufacture or distribution; in these cases, the Qualified Person (QP) should deal with the deviation in line with Section 3 of Annex 16 to the 'European Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use', which also provides useful guidance to determine if the batch can still be considered to meet the requirements of the MA and of GMP and be certified for release.

BSRs may be categorised by the applicant as urgent. The HPRA will endeavour to have a rapid turn-around time for urgent BSRs. Instances where a BSR could be classified as urgent are:

1 Where there is no alternative product on the market;
2 Where the product meets the criteria for criticality as set down in the EMA paper 'Criteria for Classification of Critical Medicinal Products for Human and Veterinary Use' EMA/24304/2016.

Non-urgent BSRs include applications for products not judged as critical to the Irish market. The HPRA will endeavour to commence assessment of these applications within five working days of receipt.

The signed BSR application form should be accompanied by a covering letter and the 'Fee Application Form for Human Products' (fee code 381 for each marketing authorisation involved). The BSR application and fee forms are available from the HPRA website. If the BSR has been discussed with an assessor or a Market Compliance staff member at the HPRA prior to its submission, please indicate this on the form.

The application should be submitted by email to HPRA Receipts and Validation at submissions@hpra.ie.

**HPRA**

~~**17 OCTOBER 2024**~~

**25 MARCH 2025**

**APPENDIX 1 SAMPLE BATCH-SPECIFIC REQUEST CAUTION-IN-USE LETTER**

**<IMPORTANT INFORMATION FOR HEALTHCARE PROFESSIONALS AND PATIENTS>**
**<CAUTION IN USE Notification>**

To: Pharmacists and < >

Date < >

**Supply of <name of the medicinal product, strength and pharmaceutical form>**
**– <PA number>**
**Batch/LOT <Number>, Expiry date: <date>**

## <This letter must always remain with the pack until the point of administration/dispensing>

I am writing to you in connection with the supply of the above referenced product, <name of the medicinal product, strength and pharmaceutical form>, <PA number>.

We are unable to supply Irish licensed packs at the moment and have obtained approval from the HPRA for the temporary supply of the corresponding product from the <name of the country> market to fulfil the urgent medical need for the product. These packs are labelled with <the name of the product if different from the Irish authorised product name>, Batch/Lot No. <number>, with an expiry date of <date>. The pharmaceutical composition of the product is the same, but there are differences in the labelling of the carton.

<List the differences (only critical/important, e.g. product name if different) – carton only.>

**<Important note to Pharmacists/Healthcare professionals:>**

<Please replace the package leaflet (PL) supplied within the pack with the Irish package leaflet attached with this letter at the time of dispensing.>

<For further details on the product, please refer to the attached approved Irish package leaflet appended to this letter for your information.>

<For further details on the product, please refer to the approved Irish summary of product characteristics (SmPC) and package leaflet, which are available on the HPRA website: www.hpra.ie.>

**This information must be shared with those who will be administering the product.**

Some healthcare professionals may note the above differences and may bring these to your attention. If this happens, please explain that the pack they have received is <insert Member State name> stock (Batch Number <insert batch number>) and that it has been approved by the HPRA for use in Ireland as a temporary measure.

**Please ensure all relevant staff <and patients> are made aware of the content of this letter and that the information is communicated to the patients.**

**Reporting of suspected adverse reactions:**

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to HPRA Pharmacovigilance though the HPRA website.

Adverse events should also be reported to <MAH address in IE, telephone number>.

If you have any questions, please contact:

<Name of the contact person

Phone:

Fax:

Email: >

Yours faithfully,

<Name>