



**Veterinary Medicines
Guidance Note**

**Specific Batch
Control Scheme
(Pharmaceutical
Products Only)**

No 24

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**ASSURING THE SAFETY, QUALITY AND EFFICACY
OF VETERINARY MEDICINES**



THESE NOTES ARE ONLY A GENERAL GUIDE AND MUST NOT BE TREATED AS A COMPLETE OR AUTHORITATIVE STATEMENT OF THE LAW ON ANY PARTICULAR CASE

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INTRODUCTION

1. This is one of a series of Veterinary Medicines Guidance (VMG) Notes explaining the requirements under the Veterinary Medicines Regulations ('the Regulations'). The Regulations are revoked and replaced every year, so the references to them should be read as referring to the ones that are currently in force. Therefore, the date and number of the Statutory Instrument are not included in this VMG Note. The VMG Notes will be updated as necessary and the date of the most recent update shown on the front cover.
2. The Regulations set out the UK controls on veterinary medicines, including their manufacture, advertising, marketing, supply and administration. VMG Note 1: *An Introduction to Marketing Controls on Veterinary Medicines* gives basic information about the scope of the Regulations and the requirement for Marketing Authorisations (MAs). This VMG Note describes the Specific Batch Control Scheme for pharmaceutical products.

REQUESTING SPECIFIC BATCH CONTROL

3. Specific Batch Control may be requested in relation to pharmaceutical products authorised by means of an Animal Test Certificate (ATC) or by means of National UK MAs that have not been the subject of a Mutual Recognition procedure. The Scheme does not apply to immunological products.
4. An ATC or MA holder may request the VMD to carry out Specific Batch Control where some element of the product differs in some way from those detailed in the ATC dossier or the MA. Such situations may relate to the quality characteristics of the batch of final product or to a starting material used during manufacture. In this context, starting material includes the active substance, excipient and packaging, which includes the primary packaging, and where they are described in the authorisation, the secondary and tertiary packaging. When making a request, the ATC or MA holder must provide details of the deviation and submit relevant papers including supporting data relating to the batch deviation.
5. The VMD will consider the request and other papers in light of the MA or ATC and form a view based on the documents submitted. The VMD will then inform the MA or ATC holder whether or not it expects to take regulatory action. Such action may be to instigate recall or otherwise prohibit the supply of the product should the batch be released onto, or remain on, the UK market. The VMD will make its decision in light of the quality characteristics reported with the request for Specific Batch Control and accompanying papers.

EXAMPLES

6. The following are examples of situations where, subject to the provisos set out in paragraphs 3 and 8 of this VMG Note, it may be appropriate to consider submitting an application for specific batch control.
- A batch of the finished product marginally fails to meet the agreed release Finished Product Specification (FPS) for one parameter which will not have a negative impact on the stability of the product nor its safety and efficacy.
 - A batch of the active substance has been subjected to an additional purification step and the rework procedure is not described in the MA dossier. The solvents used and their residual levels do not have an adverse impact on the safety of the product or its physico-chemical characteristics or stability. The batch of active substance may be destined for use in the manufacture of several batches of the finished product.
 - The labelling of the finished product is not in strict accordance with the agreed labelling but the differences are minor and will not have any adverse impact on the safe use of the product.
 - Ongoing stability studies for a particular production batch of finished product have identified that a parameter may just fall outside the agreed shelf-life. FPS limits the time the batch reaches the end of its shelf-life but this will not have an adverse impact on safety or efficacy of the product. A justified widening of the shelf-life limits for the relevant parameter is proposed for that specific batch.
 - A conservative extension to the shelf-life of one batch of the finished veterinary medicinal product beyond the approved shelf-life is required in order to avoid a supply problem in the market place. The batch has been retested against the complete FPS within 3 months of its expiry date and there is no evidence of any significant degradation.
7. It is understood that an initiative is being progressed within the European Union to permit Qualified Persons some discretion in certain specific circumstances. Under this initiative and in the following circumstances, a batch of product may be placed on the market without the need for specific batch control.
- The deviation is minor, one-off and unplanned in nature and relates only to the manufacturing process and/or the analytical control methods of either the starting materials or the medicinal product as described in the MA.
 - The active substance and FPS as described in the MA are complied with.
 - An assessment is performed by the manufacturer using the approaches described in ICH Q9, Quality Risk Management, to support a conclusion that

the occurrence is a minor quality deviation that does not affect the safety and efficacy of the product.

- The risk assessment should assess the need for inclusion of the affected batches in the on-going stability programme.
- The Quality Risk Management Programme is integrated into the manufacturer's quality assurance system, notably the documentation system established to comply with GMP, and records are available for inspection by the Competent Authorities.
- All such deviations must be reviewed as part of the annual product quality review.

Inspectors will examine the files logging use of this system to ensure that it is not abused and will take a serious view of any abuse.

HOW TO REQUEST SPECIFIC BATCH CONTROL TO BE UNDERTAKEN

8. An MA or ATC holder must first consider whether it is appropriate to apply for specific batch control of a particular batch. This decision must be reached taking into account the views of the relevant Qualified Person as to the suitability of the batch for its intended use. In addition, consideration should be given as to whether or not sufficient supporting data already exist which would permit a variation application to be progressed instead. Wherever feasible, the submission of a variation application is preferable, as this will apply to all batches of the starting material or finished product. For further information on how to apply for a variation see VMG Note 4: *Marketing Authorisations for Veterinary Medicinal Products – National (IA/IB/II) Variation Procedures*.
9. In the case of a batch of product which is already on the UK market and the Qualified Person considers that a request for specific batch control is not appropriate and that recall of the batch is necessary. In such a case, the VMD Suspected Adverse Reactions Surveillance Scheme (SARSS) should be contacted immediately and details of the nature and extent of the recall should be supplied.
10. For MAs only, if it is considered appropriate to proceed with the release of the relevant batch(es), then in the first place the MA Holder should usually contact the Supervisory Authority. This is the relevant body in the member state where the site of final product release into the EU is located. For veterinary medicines manufactured in the UK, the VMD is the Supervisory Authority. Thus, for a veterinary medicine manufactured and authorised in the UK, a single approach to the VMD in the form of a specific batch control request should be made. Where a veterinary medicine is authorised in the UK but the VMD is not the Supervisory Authority, you should first approach the Supervisory Authority and then submit a request for specific batch control to the VMD.

SPECIFIC BATCH CONTROL SCHEME

11. When requesting specific batch control, the MA or ATC holder should submit three copies of the request form and accompanying papers, including supporting data, to the Information Management section of the VMD. Complete batch records are not required.
12. A copy of the request form which should be used can be found on the VMD website: (www.vmd.gov.uk) under Industry Information / Applications Page /Application Forms & Related Checklists. It is important to use the correct form and to complete all sections of it. Where the same issue affects a number of batches, a single form may be used. However, it should be noted that one fee is charged for each batch indicated on a request form.
13. The accompanying papers should include all supporting data and relevant material relating to the finding of a batch deviation. The papers should include copies of the relevant Certificates of Analysis together with the data and/or arguments which justify the suitability of the batch for its intended use. In addition, where appropriate, the papers should address the need for any corrective measures to avoid a future recurrence of the problem. If relevant, they should also indicate any planned variation applications together with a timescale for the submission of these.
14. It is important to note that the relevant batch(es) should remain in quarantine until such time as the VMD has responded substantively to the request for Specific Batch Control to be undertaken.

HANDLING OF REQUESTS

15. On receipt of request forms and accompanying papers at the VMD they will be checked to ensure the correct number of copies has been submitted and that the forms have been completed correctly.
16. Correctly submitted requests are usually only assessed by a quality assessor who may, however, draw upon advice of colleagues from other disciplines in reaching a view on the material submitted. Where the VMD is also the Supervisory Authority, the quality assessor may liaise with the relevant MHRA inspector.
17. If the VMD is satisfied that it can reach a view without the need for questions, we will indicate in writing whether it would expect to take regulatory action. Such action may be to recall or otherwise prohibit the supply of the product should the batch be placed on the market. Any such decision would be based on its consideration of the material provided. In some situations, we may say that we would not expect to take such regulatory action provided that specified steps are taken by the MA or ATC holder when placing the batch on the market.
18. For example, where a product just fails to comply with the FPS limits for a single parameter, which is likely to have some bearing on stability, a reduction in the shelf life of the particular batch may be defined. Another example would be

where a product fails to comply with the FPS for a single parameter, which could, but however is thought unlikely to, have an adverse effect on the stability of the product. Here the specified step may be to establish controlled stability studies on that batch and to inform the VMD immediately of any adverse results or trends.

19. The assessor may decide that further information is required before reaching a view. In this event, they will write to the MA or ATC holder with any questions they may have, seeking a complete response within 10 days of the date of the letter. We will assess the response and indicate in writing whether we would expect to take regulatory action referred to in paragraph 17. Alternatively, if the assessor thinks it appropriate, he/she may send one final further set of questions to the MA or ATC holder for response within 10 days, after which we will make the final assessment and give an indication regarding our anticipated regulatory response should the batch be placed on the market.
20. The VMD's documentation, containing our conclusion on the specific batch control request, be it positive or negative, should be forwarded to the Qualified Person who should ensure that it is included as part of the batch record.
21. Where a positive opinion from the VMD will result in a change to the labelling of a product which has a UK MA, for example where an extended shelf-life is approved, the over-labelling must be conducted at a suitably authorised premise. The premises will usually be the assembly site named on the MA Memorandum for the product. As a minimum the premises must possess a Manufacturing Authorisation that covers the relevant activities.

TIMETABLE FOR SPECIFIC BATCH CONTROL

22. Requests for specific batch control will be the subject of the standard VMD internal timescales for validation and the issue of the final documentation (3 calendar days in each event).
23. The VMD will aim to complete the initial assessment of requests and accompanying papers within 10 calendar days of receipt of a valid application and to assess any responses to questions and reach a final view within 10 calendar days of receipt of a complete and satisfactory response.
24. MA or ATC holders requesting specific batch control may request an accelerated determination, but a justification for this should be provided. Where possible the VMD will accommodate such requests, particularly when an animal welfare issue could arise as a result of non-availability of a particular product.

FEES

25. A single fee applies to a batch even when that batch deviates from the authorisation in more than one respect. Details on the relevant fees can be found in the Regulations, which are available on the VMD website (www.vmd.gov.uk/).
26. The fee should not accompany the request form. The VMD will invoice the applicant on receipt of a properly completed request form and accompanying papers.
27. Whilst this scheme may not be used for those pharmaceutical products which have been the subject of a Mutual Recognition procedure, it may be possible to progress specific batch (Type II) mutual recognition variations. The Reference Member State and relevant Concerned Member State will need to be contacted to establish if this is feasible for a specific product and a specific set of circumstances.

FURTHER INFORMATION

28. Further information is available from the Veterinary Medicines Directorate, Woodham Lane, New Haw, Addlestone, Surrey KT15 3LS - Tel: Reception +44 (0)1932 336911, Direct Line +44 (0)1932 33 + extension number or Fax: +44 (0)1932 336618, as follows:
 - on scientific aspects of specific batch control, please contact one of the VMD's quality assessors on extension 8401, 8403, 8404 or 8405;
 - on administrative aspects, please contact the VMD's Licensing Administration Branch on extension 8498.

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