Australian Government

Australian Pesticides and Veterinary Medicines Authority

Guideline on manufacturing site transfer requirements for immunobiological products

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INTRODUCTION

This document provides information on data requirements for manufacturing site transfers of veterinary immunobiological products (live and inactivated).

The guideline supplements and revises the tailored guidance material for manufacturing site transfer for immunobiologicals.

This guideline aims to provide clarity and consistency on data requirements for manufacturing site transfers of primary and secondary manufacturing steps for registered immunobiological products.

1 DEFINITIONS OF SITE TRANSFERS

Manufacturing site transfers for immunobiologicals can be broadly classified as:

1. site transfer of an immunobiological product from a local (Australian) manufacturing site to another local manufacturing site
2. site transfer of an immunobiological product from an overseas manufacturing site to another overseas manufacturing site
3. site transfer of an immunobiological product from a local manufacturing site to an overseas manufacturing site
4. site transfer of an immunobiological product from an overseas manufacturing site to a local manufacturing site.

For the purposes of this guidance for variation applications for registered immunobiological products, manufacturing site changes are classified into the following:

a) site transfer of primary* manufacturing steps for immunobiologicals

b) site transfer of secondary* manufacturing steps for immunobiologicals

c) administrative changes—name or address change without any physical relocation.

*Primary and secondary manufacturing steps are defined as follows:

A primary step includes all steps in the manufacturing process that result in direct contact with the veterinary chemical product. For immunobiological products, this would include production from the master seed(s) through to the final product filled into the primary container.

Secondary manufacturing steps are defined as those manufacturing steps that do not result in direct contact with the veterinary chemical product:

- labelling or relabelling or secondary/supplementary labelling
- secondary packaging
- storage
- release for supply
- analysis testing.

Primary and secondary manufacturing categories are not defined under the APVMA code of Good Manufacturing Practice (GMP). Therefore, the manufacturing steps described in this guidance should be used only for the purposes of submitting manufacturing site transfer applications for registered immunobiologicals.

For immunobiologicals, a manufacturing site transfer is defined as the transfer of some or all manufacturing operations and/or in process (IP) and final product (FP) testing. Examples of such transfers include:

1.1 Primary manufacturing steps for immunobiologicals

- site transfer of some or all manufacturing steps for a registered product (from master seed through to final filled product in the primary container)
- site transfer of some or all manufacturing steps for an active constituent (from master seed through to final bulk antigen)
- site transfer of any intermediate manufacturing step (bulk antigen or final formulation prior to filling or freeze-drying)
- change of site for formulation and filling operations for a registered product.

1.2 Secondary manufacturing steps for immunobiologicals

- a change to the site for labelling, re-packaging, storage and release
- change of site of analysis/QC testing for In-Process (IP) and Finish Product (FP) tests for a registered product and/or active constituent.

2 TYPES OF VARIATIONS FOR SITE TRANSFERS

2.1 Transfer of a primary manufacturing site for immunobiologicals

Primary manufacturing site transfers for immunobiologicals can potentially affect the quality, safety and efficacy profile of a registered product. Therefore, this requires the submission of data to support the transfer and a technical assessment to ensure it meets APVMA standards. Thus, primary manufacturing transfers from/to a local or overseas site will be assessed under an Item 14 application.

Where the proposed transfer affects an active constituent, in addition to an Item 14 application for the transfer of the product, APVMA legislation requires the submission of application to cover the transfer of an active ingredient. An Item 17 or an Item 18 application will be required for each antigen associated with a product transfer under Item 14.

If undertaking a site transfer for the final product and active, it is necessary to submit an Item 14 for the product and an Item 18 for the active. The Item 18 will include a separate data list cross-referencing the data package included in the Item 14.

Alternatively, you have the option to submit concurrently an Item 17, with a chemistry package, with an Item 14 if the ambition is to register a new source with the relevant particulars to be included in the record.

Pre-Application Advice (PAA) can be used to determine the optimum route and data requirements for specific transfers. The acceptance of International data is another option that could be considered to facilitate manufacturing site transfers.

Data requirements for transfer of a primary manufacturing site

A transfer of primary manufacturing site for immunobiologicals for both overseas and local sites will fall under an Item 14 variation.

For a primary manufacturing site transfers we would advise that the variation should be specific for the site transfer and not include other variations to the particulars of the registered product or label. For site transfers of primary manufacture, a chemistry data package is required demonstrating physicochemical equivalence between the existing site and new site of manufacture.

Additional safety and efficacy data to support the transfer of primary manufacture will only be requested for immunobiologicals that are released without a validated potency assay and therefore additional *in vivo* test may be required to support the transfer.

Data requirements applicable for the transfer of primary manufacturing steps from master seed(s) through to antigen and final product:

- results of at least two consecutive antigen batches at the new site according to the registered manufacturing process

- results of at least two consecutive vaccines batches at the new site according to the registered manufacturing process
- transfer validation reports for critical manufacturing steps eg centrifugation, purification, filtration or other evidence demonstrating production equivalence
- validation reports of IP and FP tests eg potency tests (eg ELISAs, serological tests, and sterility tests) unless the test is a pharmacopeia standard
- a manufacturing flow chart for the new manufacturing site
- evidence of satisfactory GMP compliance for the new QC site
- a commitment to undertake stability studies on the final product

For inactivated antigens/products additional requirements:

- inactivation kinetics at industrial scale at the new site
- inactivation test validation
- inactivation tests results for at least two consecutive antigen batches.

Note: In all cases involving the import of immunobiological from an overseas site of manufacture, an import permit from the Department of Agriculture and Water Resources will be a condition of approval of the site change application if not accompanying the application.

2.2 Transfer of a secondary manufacturing site for immunobiologicals.

The transfer of the secondary manufacturing steps (labelling, repackaging, storage or release) does not require technical assessment.

The transfer to a local site for secondary production should be carried out under an Item 13A. A GMP certificate does not need to be submitted in the application, as this information is already available to APVMA.

A transfer to an overseas site falls under Schedule 6 of the Agvet Code Regulations and requires an Item 12 application. The variation is to allow a minor change and no data of a technical nature is required.

The following information should be included in the Item 12 application:

- evidence of Good Manufacturing Practice (GMP) for each new manufacturing site that is licenced to perform the required secondary packaging tasks. Further information on how to meet the GMP requirements can be found on our website
- description of the changes of the secondary manufacturing steps.

Transfer of a Quality Control (QC) site

For immunobiologicals, QC site transfers may be classified as technical or non-technical depending on the test and the location of the transfer:

The transfer of biological assays will be considered as technical variations for both local (Australian) and overseas sites and requires an **Item 14** application.

1. site transfer of a local (Australian) manufacturing site to another local manufacturing site requires an Item 13A application where the test is a physical or chemical test
2. transfer of an overseas manufacturing site to another overseas manufacturing site requires:
    - an **Item 12** application where the test is a physical or chemical test
    - an **Item 14** application where the QC test is a biological test eg endotoxin, microbiological, sterility, serological or immunological tests
3. site transfer of a local manufacturing site to an overseas manufacturing site requires:
    - an **Item 12** application where the test is a physical or chemical test
    - an **Item 14** application where the QC test is a biological test eg endotoxin, microbiological, sterility, serological or immunological tests
4. site transfer of an overseas manufacturing site to a local manufacturing site requires an Item 13A. For technical transfers of biological assays (**Item 14**) the following data requirements apply:
    - validation reports for the transfer of the QC assays to the new site
    - confirmation that the specifications for the methods of analysis are identical/equivalent to those approved for the registered product, or a justification for any changes to the specification that does not impact safety and efficacy
    - evidence of satisfactory GMP compliance for the new QC site.

2.3 Name change of a manufacturing site

A variation to the name change of both local and overseas manufacturing sites requires an Item 13A application.