



# AgVetLink

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## SPECIAL ISSUE FOR MANUFACTURERS

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### LABELS REMINDER

1 July 2007 is the deadline for HSNO compliance and for updating old labels that say "Approved under the Animal Remedies Act..." We advise that these labels will be illegal in the marketplace from 1 July 2007. Further manufacture, sale or use of labels with this regulatory statement will be in breach of the ACVM Act.

### From the Director

*Frequently asked questions relating to good manufacturing practice (GMP) and an emerging pattern of common deficiencies showing up in GMP inspections have prompted the ACVM Group to put together this special issue of AgVetLink for manufacturers. In it, we provide answers to the most common questions we receive and point out areas where GMP inspectors regularly note deficiencies.*

*Please note that the articles relate to GMP requirements but product registration requirements may also apply.*

*We hope you will find the information useful. If you have further questions or comments, see the contact details on page 4.*



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Director  
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**AgVetLink** is produced at least six times annually by the New Zealand Food Safety Authority's Agricultural Compounds and Veterinary Medicines Group. The newsletter is of special relevance to those interested or involved in all aspects of agricultural compounds and veterinary medicines. It contains regular updates on implementation of legislation, notifications, new standards and policies, consultation, international agreements, and other information.

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Disclaimer: This publication is intended only as a guide. It is not a legal interpretation of the legislation discussed.

## Questions & Answers

### Notification of Changes

#### Q1: What if I change premises or processes?

Approved manufacturers of veterinary medicines and vertebrate toxic agents must notify the ACVM Group of any changes to their premises, plant or processes that is different from the manufacturing information provided at the time of the registration. Such changes are likely to require an application to make a change to the registered trade name product (TNP) to be lodged and approved *prior* to the change being implemented.

#### Q2: We have only changed the firm we use to pack our product. Do we have to notify the ACVM Group about this change?

Yes, notifiable changes include changes to contract labellers, packers and quality control laboratories. This will also result in the need to lodge an application to change/add the manufacturer(s) of the TNP.

#### Q3: When should we notify changes?

Notification should be made *before* changes are implemented. If in doubt, ask. The proposed changes may not result in an additional inspection but will be placed on the manufacturing file to ensure information held by the ACVM Group is current at all times. The regulator and the auditors do not like surprises!

#### Q4: We have leased a manufacturing site that was GMP approved for the previous tenant. Is the GMP approval still valid?

The approval and GMP certificate links an organisation with a specific site for the manufacture of specific categories (types) of products. If a manufacturer vacates a site, the approval automatically lapses. Another manufacturer cannot move into a vacated site and assume GMP compliance because the previous tenant had approval.

#### Q5: We are GMP approved but we are moving to a new manufacturing site. What do we need to do to keep our approval?

Any new site has to be inspected and approved before any product can be released for sale from the site. This approval must be for both the site (GMP approval) and for the product (product registration).

#### Q6: What do we have to do if we want to extend the range of products we manufacture?

Manufacturers must apply for an extension to their GMP certificate if they intend to extend the types of products they manufacture. This includes both an additional category and dose form of product (liquid/powder/cream etc.). If you are just adding another product in the *same* category, another approval is not required.

### Inspection Programme

#### Q7: What is the purpose of GMP inspections?

Inspections of manufacturers of registered veterinary medicines are carried out to confirm that the registered veterinary medicines are being manufactured in accordance with the information and processes that were notified at the time of registration and in appropriate facilities. Users of veterinary medicines and vertebrate toxic agents expect them to be safe, effective and of high quality. To achieve this, products must be manufactured consistently, by a specified and approved process by appropriately trained staff to meet the registered specification – that is using Good Manufacturing Practices (GMP). Manufacturing a product in accordance to the *ACVM Standard for Good Manufacturing Practice* is a condition of registration of particular TNPs registered under the ACVM Act 1997.

#### Q8: What is the basis of the inspection?

The basis of the inspection is the assessment of a manufacturer's level of compliance for the range of products manufactured with the *ACVM Standard for Good Manufacturing Practice* and, where appropriate, the *ACVM Guideline for Good Manufacturing Practice* for manufacture of specific categories of products.

Products vary in complexity from high risk veterinary pharmaceuticals to low risk dietary products. The scope and intensity of the inspections are matched to the risk levels of the products being manufactured.

### Recognition of overseas manufacturers

The ACVM Group will recognise overseas manufacturers for their GMP status rather than grant an approval in the form of a GMP certificate. This recognition will be based on evidence of GMP compliance from another regulatory authority where there is a MRA (EC) or a MOU (Australia). For those countries where certificates from the local authorities are not accepted (e.g. China), GMP certificates issued by recognised inspection authorities (e.g. FDA) will be accepted.

The GMP certificate supplied should be current. It should quote the date of the last audit as well as the steps of manufacture (all manufacturing steps or quality control testing only) and the types of products inspected.

### Q9: How often do inspections take place?

Regular inspections (at least once every two years but likely to be more often if there are significant non-compliances) of manufacturers of agricultural compounds that are registered under the ACVM Act are required to provide assurance to users of veterinary medicines and vertebrate toxic agents that risks from manufacture are being managed. This frequency is in line with international practice.

### Q10: Who does the inspections?

GMP inspections are carried out by trained inspectors in a third party agency, AgriQuality New Zealand, under contract to the ACVM Group. The costs of the inspection are recovered from the manufacturers by the ACVM Group. Members of NZFSA Verification Agency (VA) staff are undergoing training to perform Category 1 inspections in the future.

### Q11: My product is exempt from registration. Will I be inspected?

Manufacturers of exempt products do not have to be ACVM-approved manufacturers in compliance with the *ACVM Standard for GMP* and they are not subject to regular inspection. Exempt manufacturers must comply with the conditions of exemption in the ACVM Regulations 2001. For some types of exempt products (e.g. topical preparations), there is a condition to manufacture to the principles of good manufacturing. These principles are defined by the manufacturer to ensure that the product is fit for purpose (for the type of the product).

However, all aspects of the ACVM Act are covered by at least 'level 1 responsive compliance'. This means that any allegation or suspicion of non-compliance with the legislation by a manufacturer of exempt products will be investigated and may result in inspection of the manufacturer.

### Q12: Is there an inspection programme for vertebrate toxic agent (VTA) manufacturers?

Manufacturers of vertebrate toxic agents are included in the GMP inspection programme, but the standard used is the *ACVM Standard for Vertebrate Toxic Agents*.

## Inspections

### Common Deficiencies

#### Site master files

Inspectors have noted that not all manufacturing sites visited have complete and current site master files even though this is a requirement under section 2.4.4 of the *ACVM Standard for Good Manufacturing Practice*. Guidelines for the preparation of a comprehensive site master file can be obtained from the ACVM website.

For a small manufacturing operation it is appropriate that the form 'Application for Authorisation to Manufacture Agricultural Compounds and Veterinary Medicines' is kept up to date, and provided to the Inspector or the ACVM Group prior to, or at the time of, the inspection. This form contains the minimum information that is considered acceptable as a site master file for a small or uncomplicated manufacturing operation. For more complex manufacturing operations, the PIC/s guidance document should be used as a template (<http://www.tga.gov.au/docs/pdf/siteinfo.pdf>).

#### Others

Other deficiencies being noted regularly include:

- the lack of secure storage of pre-printed packaging components and lack of reconciliation of the product specific printed items at completion of the pack job
- the lack of any evidence that a line clearance had been performed prior to the start of a new packing operation
- the lack of a formal system to handle reject material that incorporates a secure location and a log for recording its fate.

#### 'Close out' of GMP inspections

GMP certificates may be issued with conditions. These conditions relate to the 'close out' of deficiencies contained in the audit report.

The ACVM Group will impose time frames for the provision of data to support close out of the audit deficiencies. (These will be in three-monthly periods.) Evidence of the company's actions taken to close out a deficiency will also be required. If companies do not adhere to the conditions of the GMP certificate, further regulatory actions may be taken, including further inspections at the company's cost.

### LIST ALL MANUFACTURING SITES

Registrants and applicants must list **all** the manufacturing sites in the manufacturing specifications for a registered trade name product. Manufacture, in relation to any agricultural compound, means to make up, prepare, produce, or process the agricultural compound; and includes the packing (and labelling) of an agricultural compound in a container for the purposes of sale. Therefore any site that carries out **any** of these activities (or any subdivision of these activities, such as quality testing) must be listed in the manufacturing specification.

## Categories of Manufacture

Category	Type of manufacturer	Products
Category 1A	Immunobiological	Vaccines
Category 1B	Sterile Injectables	Sterile pharmaceuticals
Category 2	Non sterile Veterinary Medicines	Tablets/capsules/boluses Creams/ointments Liquids Sprays/aerosols Pastes/powders Medicated Collars
Category 3	Large volume ectoparasiticides	Dips/drenches
Category 4	Plant Compounds	Aerosols Baits Granules Liquids Pastes/Powders Tablets Technical active
Category 5	Repacking/Labelling	Applies only to work carried out on products in their final containers.
Category 6A	Contracted testing organisations	For any type of product or service covered by GMP Standard.
Category 6B	Contracted sterilising organisations	For any type of product or service covered by GMP Standard.
Category 7	Registrants/Distributors of HGP's	Compliance with ACVM Standard for HGP's.
Category 8	Vertebrate Toxic Agents	Baits/Powders/Granules Liquids/Pastes/Gels

*Check the website ([www.nzfsa.govt.nz/acvm](http://www.nzfsa.govt.nz/acvm)) for more information or contact Trish Whitaker ([trish.whitaker@nzfsa.govt.nz](mailto:trish.whitaker@nzfsa.govt.nz)) if you have specific questions.*