Manufacturing of veterinary medicinal products: some controls for industry and regulatory authorities

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Improved Market Access for Authorised Veterinary Medicines - The Asian Perspective

Organising Committee:
Session overview

Session content

► Some controls on manufacturers
  • Approval and inspection

► Some controls at manufacturers’ level
  • Quality control and product release

► Some controls for regulatory agencies
  • Inspection programmes and qualification, training and impartiality of inspectors

Controls on VMP manufacture

VMPs are subject to a number of controls:

- Product related controls e.g. product authorisation
- Manufacturing site controls
- Other controls and surveillance
- Often similar approaches as for human medicines

Frequently similar approaches are adopted for both human medicine and VMP manufacture
Potential controls on VMP manufacturers

Some controls may include:

- “Desktop assessment” of site information
  - Blueprints, procedures, records, etc.
- Official testing of VMPs by regulatory authorities
- Inspection of VMP manufacturing sites

Inspections may be used in combination with other controls
Some general expectations of manufacturers which may be verified during inspections

- A formal quality management system (QMS)
- Sufficient numbers of appropriately trained staff
- Suitable premises and equipment
- Adequate documentation in place
- Secure retention of accurate records

Some general expectations of manufacturers which may be verified during inspections, continued

- Suitable, defined production processes
- Appropriate quality control testing throughout manufacture
- Formal product release mechanisms
- Systems to address complaints, quality defects and product recall
Overall expectation

- All the systems in place ensure quality is built into a VMP as this cannot be tested into the product once manufactured.
Manufacturing requirements / standards to be applied during inspections

Requirements or manufacturing standards applied should be:

- Formal / defined
- Based on good science
  - risks applying to a particular dosage form
- Transparent / published


Manufacturing requirements / standards to be applied during inspections

Requirements or manufacturing standards applied should be:

- Formal / defined
- Based on good science / risks applying to a particular dosage form
- Transparent / published – freely available to manufacturers
Manufacturing requirements / standards to be applied during inspections, continued

Requirements or manufacturing standards applied should be:

- Local requirements / standards
- International Good Manufacturing Practice (GMP) standards
  - e.g. EU GMP, PIC/S GMP, WHO GMP
Industry / Manufacturer controls on finished VMPs

Prior to being placed onto the market a VMP is usually quarantined until a number of controls have been applied:

► All QC testing has been completed with a satisfactory outcome
► Formal release of the VMP batch following independent review and approval, e.g. by a member of the Quality Assurance team or the Qualified Person (EU requirement)
Industry / Manufacturer controls on finished VMPs, continued

Some information to be reviewed prior to product release:

- Batch production and packaging records
- In process and finished product quality control testing results,
- Associated documentation,
  - e.g. deviation / investigation reports, complaints, adverse event data, environmental monitoring data, trend reports

Formal review prior to product release should confirm:

- The VMP batch complies with its product licence / authorisation
- All QC testing results are within specification
- Appropriate requirements / standards (e.g. GMP) were applied during manufacture
Industry controls on VMP manufacture – some questions for discussion

In your territory:

► How is a VMP manufacturer defined / which activities (e.g. active substance, intermediate, finished product manufacture) are within scope?
► Are VMP manufacturers subject to formal approval / regulation?
► If so, what requirements are in place for holding an approval?


Notes
Industry controls on VMP manufacture – some questions for discussion, continued

In your territory:

► What measures are in place to ensure that manufacturing requirements are met?
► If an inspection system is in place in compliance against formal standards checked?
► If so which standards are applied, e.g. local, EU GMP, PIC/S GMP, WHO GMP?

PIC/S: Pharmaceutical Inspection Cooperation Scheme


Notes
Industry controls on VMP manufacture – some questions for discussion, continued

In your territory:

► Which manufacturing activities are subject to a approval and / or inspection (e.g. active substance, intermediate and finished product manufacture, QC testing, VMP release)?

► Is greater emphasis placed on quality assurance throughout the manufacturing process or QC testing at the end?

► How is it ensured that any QC samples are representative of the VMP batch as a whole?

Industry controls on VMP manufacture – some **questions** for discussion, continued

In your territory:

- Is it expected that manufactures’ have a formal VMP batch release system?
- If so what requirements are in place?
- Are designated personnel responsible for batch release at the manufacturer?
- If so, what arrangements are in place to avoid conflicts of interest and is their role formally defined?


**Notes**
Industry controls on VMP manufacture – some questions for discussion, continued

In your territory:

▶ Is there a requirement for official (i.e. state / governmental) batch release?
▶ If so are all VMPs within scope or a limited range?
▶ If a limited range, what criteria are used to select products?
▶ What mechanism is applied for official release (e.g. laboratory testing, protocol review)?


Notes
Controls for regulatory agencies

Aspects to be considered

► Inspection programmes

► Inspector qualification, training and impartiality
The inspection system / programme should ensure:

- Adequate surveillance of all VMP manufacturers
- Adequate standards are in place and maintained at the regulatory agency / inspectorate
Inspection programmes, continued

Manufacturers would normally be subject to:

- Initial inspection (new sites), followed by
- Periodic inspections

- Periodic inspections may be repeated on
  - a fixed (e.g. two yearly) basis,
  - a risk based approach (e.g. PIC/S and EU)
Inspection programmes, continued

Criteria for risk based inspection frequency may include:

- Compliance observed at previous inspections
- Complexity of the manufacturing operations
- Size of the operations
- Triggers such as complaints, quality defects, recalls, pharmacovigilance issues
- Intelligence from other regulatory agencies or sources


Inspection programmes, continued

For risk based inspection programmes, criteria affecting re-inspection frequency may include:

- Compliance observed at previous inspections
- Complexity of the manufacturing operations
- Size of the operations
- Triggers such as complaints, quality defects, recalls, pharmacovigilance issues
- Intelligence from other regulatory agencies or sources
The inspection programme may cover:

- Inspections within national boundaries

- Third country inspections
  - These may be alone or in conjunction with the local regulatory agency or another agency

- Inspections may be general, process or product focussed
Inspection programmes would normally be subject to formal systems to ensure:

- Full impartial application equally to all manufacturers
- Appropriate record control, e.g. reports and correspondence kept and confidentiality maintained
- Non-compliance is addressed in a consistent way

Quality management systems (QMS) are expected at regulatory agencies as well as manufacturers!
Adequate measures should be in place to ensure that inspectors are:

- Appropriately qualified
- Suitably trained
- Impartial
An inspector recruitment exercise would normally focus on:

- Appropriate educational qualifications
- Demonstration of key competencies
- Suitable experience
Inspector training programmes should include:

- Induction training
- Documentation training
- On the job training
- External courses as required

Regulatory agency controls: Inspectors, continued

New inspector training programmes would normally include the following aspects:

- Induction training
- Documentation training (legislation, agency procedures, manufacturing standard guidance, etc.)
- On the job training (observing, participating through to leading inspections)
- External courses as required
For qualified inspectors:

- Training requirements / expectations should be defined
- Training needs should be reviewed on a periodic basis and matched to inspectors’ needs
- Training records should be kept
Systems to ensure impartiality of inspectors include:

- Sign up to a code of conduct
- A requirement to declare any interests
- A gifts and hospitality policy
- A formal period of time before an inspector can inspect a company for which they have worked
- Periodic change over of responsibility of sites

Regulatory agency controls: Inspectors, continued

Normally systems will be in place to ensure impartiality of inspectors such as:

- Sign up to a code of conduct
- A requirement to declare any interests
- A gifts and hospitality policy
- A formal period of time before an inspector can inspect a company for which they have worked
- Periodic change over of responsibility of sites (e.g. after 2 or three inspection cycles)
Regulatory agency controls – some questions for discussion

In your territory:

► Is inspection of VMP manufacturers required before approval?
► Once approved are VMP manufacturers subject to periodic re-inspection?
► If so are all manufacturers captured in a formal inspection programme?
► If so how frequently are manufactures re-inspected – is the period set or varied on a risk basis?

Regulatory agency controls – some questions for discussion

In your territory:

► Are inspections and their outcomes documented and records kept?
► If non-compliance is identified, what options are available to deal with this?
► Are inspection programmes coordinated / performed in conjunction with other countries in your region?
► Does your authority recognise the findings of any other inspectorate in your region or elsewhere?

Regulatory agency controls – some questions for discussion

In your territory:

► If a VMP inspection programme is in place, who performs the inspections (governmental agency staff, non-governmental consultants / contractors)?
► What systems are in place to ensure impartiality of inspectors?

Regulatory agency controls – some questions for discussion

In your territory:

► What systems are in place to ensure that inspectors possess the appropriate qualifications, experience and competencies?
► What systems are in place to ensure that inspectors’ knowledge and experience remains current?
► Are there regional training opportunities to allow interaction between inspectors in different territories?

Thank you for your attention