



Veterinary Medicinal Products in Europe: Summary of Regulatory Updates in 2018

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1 Cyton Biosciences

1.1 About Cyton

Cyton is a full-service consultancy providing specialist support in regulatory affairs and multi-disciplinary product development for the animal health industry. We have offices in Bristol, UK and Mannheim, Germany.

Cyton's expertise covers veterinary medicines (pharmaceuticals and immunologicals / vaccines), feed additives and borderline products. Our extensive experience covers all major species (dogs, cats, cattle, sheep, pigs, chickens, salmon) and a huge range of minor species (including horses, turkeys, rabbits and foxes).

Our team includes experts in chemistry, manufacturing and controls (CMC) for your quality projects, toxicologists for your safety projects and veterinarians for your clinical projects. In addition, with our separate, dedicated regulatory procedures team, you can be sure that all of your regulatory submissions will run smoothly.

1.2 Regulatory Intelligence

As a leading consultancy for veterinary medicines regulatory affairs in Europe, Cyton invests heavily in keeping our expertise up to date. To help our clients remain informed, we also regularly write in industry publications such as AnimalPharm, Regulatory Rapporteur and the International Animal Health Journal.

As well as Cyton's news feeds on our website, on Twitter and on LinkedIn, we work with TOPRA to provide their monthly VetMed Update service. This is a summary of the regulatory updates for veterinary medicines in Europe, sent out by email to all TOPRA members who are involved in the animal health sector.

Cyton's commitment to regulatory intelligence gives us a complete picture of everything which is happening both at the European Medicines Agency and all the national regulators across Europe.

1.3 About this report

Just in case you missed anything important, this summary document provides an overview of the major developments in regulatory affairs for veterinary medicines which were published by the European regulatory network in 2018.

2 Regulatory updates 2018

2.1 Quality (Chemistry, Manufacturing and Controls – CMC)

2.1.1 New guidance adopted

- New Q & A page for classification of changes for veterinary medicines was published ([Link](#)).
- Updated guidelines on chemistry of active substances for veterinary medicinal products ([Link](#)).
- Revised guideline on the active substance master file (ASMF) procedure, which seeks to clarify the responsibilities of the marketing authorisation holder in the provision of information related to active substances ([Link](#)).
- The training presentations on the Active Substance Master File (ASMF) work sharing procedure can now be found on the HMA website ([Link](#)).
- Combined CMDv / CMDh Q & A on the QP Declaration ([Link](#)).
- Q & A on EU GMP guide annexes: Supplementary requirements: Annex 16 ([Link](#)).
- Q & A pages on Pharmaceutical quality system ([Link](#)).
- Q & A pages on Good Distribution Practice ([Link](#)).
- Q & A pages on active substance registration ([Link](#)).

2.1.2 Draft guidance out for consultation

- VICH GL58 on stability testing of new veterinary drug substances and medicinal products in climatic zones III and IV ([Link](#)).
- Reflection paper on risk management requirements for elemental impurities in VMPs ([Link](#)).
- Quality of water for pharmaceutical use ([Link](#)).
- Guideline on Manufacture of the finished dosage form ([Link](#)).
- Outcome of the public consultation on Q & As on the implementation of risk-based prevention of cross contamination in production and 'Guideline on setting health based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities' ([Link](#)).

2.2 Safety

2.2.1 General safety guidance

- Concept paper for the revision of the guideline on safety and residue data requirements for pharmaceutical VMPs intended for MUMS/limited market has been published ([Link](#)).

2.2.2 User safety

- User safety of topically administered VMPs, together with overview of comments ([Link](#)).

2.2.3 Consumer safety and Maximum Residue Limits (MRLs)

- Approach towards harmonisation of withdrawal periods ([Link](#)).
- VICH GL57: draft guideline for the studies to evaluate the metabolism and residue kinetics of veterinary drugs in food-producing species: marker residue depletion studies to establish product withdrawal periods in aquatic species ([Link](#)).
- VICH GL56: studies to evaluate the metabolism and residue kinetics of veterinary drugs in food-producing species: study design recommendations for residue studies in honey for establishing MRLs and withdrawal periods ([Link](#)).
- The last of three measures have been adopted to formalise new rules to replace the current Volume 8 guidance on MRLs ([Link](#)). The three measures introduced are as follows:
 - Regulation (EU) 2017/12 (Jan 17), changing the structure of the documentation to be included in the MRL application dossier
 - Regulation (EU) 2017/880 (May 17), which aims to increase the availability of veterinary medicines
 - Regulation (EU) 2018/782 (May 18), describing the methodology to be used in the scientific risk assessment and establishment of risk management recommendations
- Updated Q & As: When is a MRL required? What is the procedure for establishment of MRLs? ([Link](#)).

2.2.4 Environmental Risk Assessment (ERA) / Environmental Impact Assessment (EIA)

- Q & A on the implementation of the CVMP guideline on environmental impact assessment for VMPs in support of the VICH GL6 (Phase I) and GL38 (Phase II) have been published ([Link](#)).
- Guideline on assessing the environmental and human health risks of veterinary medicinal products in groundwater, together with overview of comments have been published ([Link](#)).
- Draft reflection paper on AMR in the environment ([Link](#)).

2.3 Efficacy

2.3.1 Antimicrobials and antimicrobial resistance (AMR)

- Revised guideline on the SPC for VMPs containing antimicrobial substances ([Link](#)).
- Reflection paper regarding use of aminoglycosides in animals in the EU ([Link](#)).
- Draft revised guideline on the assessment of the risk to public health from AMR due to the use of antimicrobial VMPs in food-producing animals ([Link](#)).
- Draft reflection paper on dose optimisation of established veterinary antibiotics in the context of SPC harmonisation ([Link](#)).
- Reflection paper on off-label use of antimicrobial VMPs ([Link](#)).
- Draft reflection paper on the use of aminopenicillins and their beta-lactamase inhibitor combinations in animals in the European Union: development of resistance and impact on human and animal health. ([Link](#)).

2.3.2 3Rs (replacement, reduction, refinement)

- New EMA webpage regarding the ethical use of animals in medicine testing, including VMPs. ([Link](#)).
- Recommendation to MAHs, highlighting recent measures in the veterinary field to 3Rs measures described in the Ph. Eur. ([Link](#)).
- Guidance for individual laboratories for transfer of quality control methods validated in collaborative trials with a view to implementing 3Rs ([Link](#)).
- Reflection paper providing an overview of the current EU regulatory testing requirements for VMPs and opportunities for implementation of the 3Rs ([Link](#)).

2.3.3 Immunological Veterinary Medicinal Products (IVMPs)

- Draft guideline on the use of adjuvanted veterinary vaccines ([Link](#)).

2.3.4 Ectoparasites

- Draft reflection paper on resistance in ectoparasites ([Link](#)).

2.3.5 Vector Borne Diseases (VBDs)

- Draft guideline on data requirements for VMPs for the prevention of transmission of vector-borne diseases in dogs and cats ([Link](#)).

2.4 Regulatory Procedures

2.4.1 Electronic submissions

- The user guide for the electronic application form has been updated ([Link](#)).
- A webinar was held for SPOR: Substance, product, organisation and referential data (SPOR) impact on veterinary stakeholders – presentations now available ([Link](#)).
- Several new Q & A posts have been added during 2018, covering bibliographic applications and the Active Substance Master File ([Link](#)).
- The VNeS Q&A relating to eSubmission for Veterinary Applications was updated ([Link](#)).

2.4.2 Variations

- The best practice guide for Type II variations has been updated ([Link](#)).
- The "Recommendations for classification of unforeseen variations" were updated for SPC changes to implement PSUR outcomes ([Link](#)).
- A new best practice guide for changing the reference member state was published ([Link](#)).
- The CMDv published initiatives on reduction of administrative burden relating to variations such as an MAH change, product name change and supergrouping ([Link](#)).

2.4.3 Dossier requirements

- A clarification was issued on the acceptability of CTD format and Quality Overall Summaries (QOS) for veterinary submissions ([Link](#)).
- Several new Q & A posts have been added during 2018, covering bibliographic applications and the Active Substance Master File ([Link](#)).

2.4.4 Pharmacovigilance

- Revised recommendation for the basic surveillance of EVVet data for centrally authorised products ([Link](#)).
- Public bulletin on pharmacovigilance for 2017 ([Link](#)).

2.4.5 Labelling

- QR codes in the labelling and/or package leaflet of VMPs authorised via the CP, MRP, DCP and NP ([Link](#)).
- QRD guidance on the use of approved pictograms on the packaging of VMPs authorised via the CP, MRP, DCP and NP ([Link](#)).
- Packaging 'blue-box' requirements and additional information on labelling/package leaflet for VMPs authorised via the CP, MRP, DCP and NP ([Link](#)).
- Updated Guideline on Common Baltic Package and Common Baltic Package procedure for VMPs ([Link](#)).
- Recommendations for labelling and packaging of VMPs now revised giving a comprehensive overview covering multilingual provisions, the use of pictograms and QR codes, acceptable abbreviations, correct use of the blue box and considerations for small packaging ([Link](#)).

2.5 General updates

2.5.1 The new Veterinary Medicines Regulation (VMR)

2018 saw the VMR finally enter trilogue negotiations with the end result that the final text was published in the Official Journal of the European Union on 7th January 2019. 2019 will be an important year for ongoing discussions on the full details of the legislation which will be elaborated in 29 delegated and implementing acts.

2.5.2 Brexit

Preparations for the UK's exit from the EU have continued throughout 2018. Dedicated pages relating to Brexit implications for VMPs have been published by various regulators, to provide stakeholders with as much information as possible to make the necessary preparations.

- EMA general page ([Link](#))
- Presentations from the event "Brexit regulatory preparedness for veterinary medicinal products in the centralised procedure" ([Link](#))
- CMDv ([Link](#))

The UK VMD has prepared a "Stakeholder Engagement" PDF, providing guidance for industry if there is no Brexit deal, which gives a simple overview of all areas of impact for UK authorised products ([Link](#)). More detailed information can be found in the industry guidance for a Brexit "no deal", which is split into three technical notices ([Link](#)):

Registration of VMPs ([Link](#))

- Batch testing of VMPs
- QP batch certification & release of VMPs
- Wholesale Dealer's Authorisations
- Manufacturing Authorisation requirements for imported VMPs from the EU
- Centralised VMP authorisations

Regulation of VMPs ([Link](#))

- MAH - legal presence requirements
- Veterinary 'Generic' MAs – reference products
- MAs for Parallel Import (MAPI)
- Maximum Residue Limits

Access to IT systems ([Link](#))

- Common European Submission Portal (CESP)
- EudraVigilance veterinary (Gateway / Webtrader)
- EudraLink