EGGVP
European Group for Generic Veterinary Products

Position Paper

Brussels, 30 June 2014

Review of Legislation for Veterinary Medicinal Products
Version 3

Directive 2004/28 entered into force on 1st May 2004, introducing many improvements for the transparent and harmonized authorization of veterinary medicines in the EU. However, a few years after implementation of these rules, the need to revise and address additional issues has been confirmed. EGGVP is aware of the enormous opportunities of improvement given by the ongoing process of the review of legislation and therefore welcomes this initiative.

The current situation where requirements for authorization and marketing of veterinary medicines differ from one Member State to another lacks justification and causes an enormous workload and damage to industry. Further steps towards harmonization are necessary, and for this reason EGGVP proposes that the new legislation is published in the form of a Regulation (not a Directive).

EGGVP is also very pleased with the statements made by the Commissioner John Dalli during his speech on 16th June 2011 at the IFAH-Europe Conference, where commitment and support towards a totally renewed and pragmatic legislation were confirmed. According to EGGVP's position, the new legislation should reach **two fundamental objectives:**

1- Make the system more efficient and balanced:

- The main focus of the review should be aimed at reducing the burden both for the industry and regulators (administrative, financial, as for assessments, etc.). Over the past years, regulators have taken the general approach to align requirements for both human and veterinary medicines. Even if this might be a logical approach, reality shows that the human and the veterinary markets are substantially different (veterinary medicines market represents approximately 4% of human medicines market), and this should be taken into consideration). Not doing so results in an enormous/disproportionate burden for the veterinary industry, which results in administrative expenses estimated at about 13% of total industry turnover; this is inadmissible in any context, but even more taking into account the slow return of investment of veterinary medicines and the current economic scenario. In order to reduce any unnecessary burden - which is also very often not bringing any added value in terms of safety, quality and efficacy - the new veterinary medicines' legislation should be customized to the specific characteristics of this segment of the industry. Here below are some examples (non-exhaustive list) where human guidelines have been copied into veterinary guidelines:

- VICH guideline on bioequivalence
- Guideline on variations
- certain GMP requirements

There are also examples where requirements for veterinary medicines are more stringent than for human medicines:

- Product literature: human leaflets (intended for the user) provide much simpler information compared to veterinary leaflets.

Nevertheless, EGGVP is pleased to confirm that there have been recent developments where the right direction has been taken in order to make a clear (and adequate) difference as per requirements for human and veterinary medicines, e.g.:

- Uncoupled pharmacovigilance requirements: the problem is partially solved after publication of volumes 9A (human) and 9B (veterinary) of EudraLex **-** The rules governing medicinal products in the European Union

2- Make veterinary medicines more available:

Data protection somewhat stimulates investment in new veterinary medicinal products. The establishment of periods of exclusivity should balance the dual objectives of providing continued incentives for investment in the development of new products, while allowing the generic veterinary medicines' industry to enter the market at a point in time where investment from innovators has been recovered.

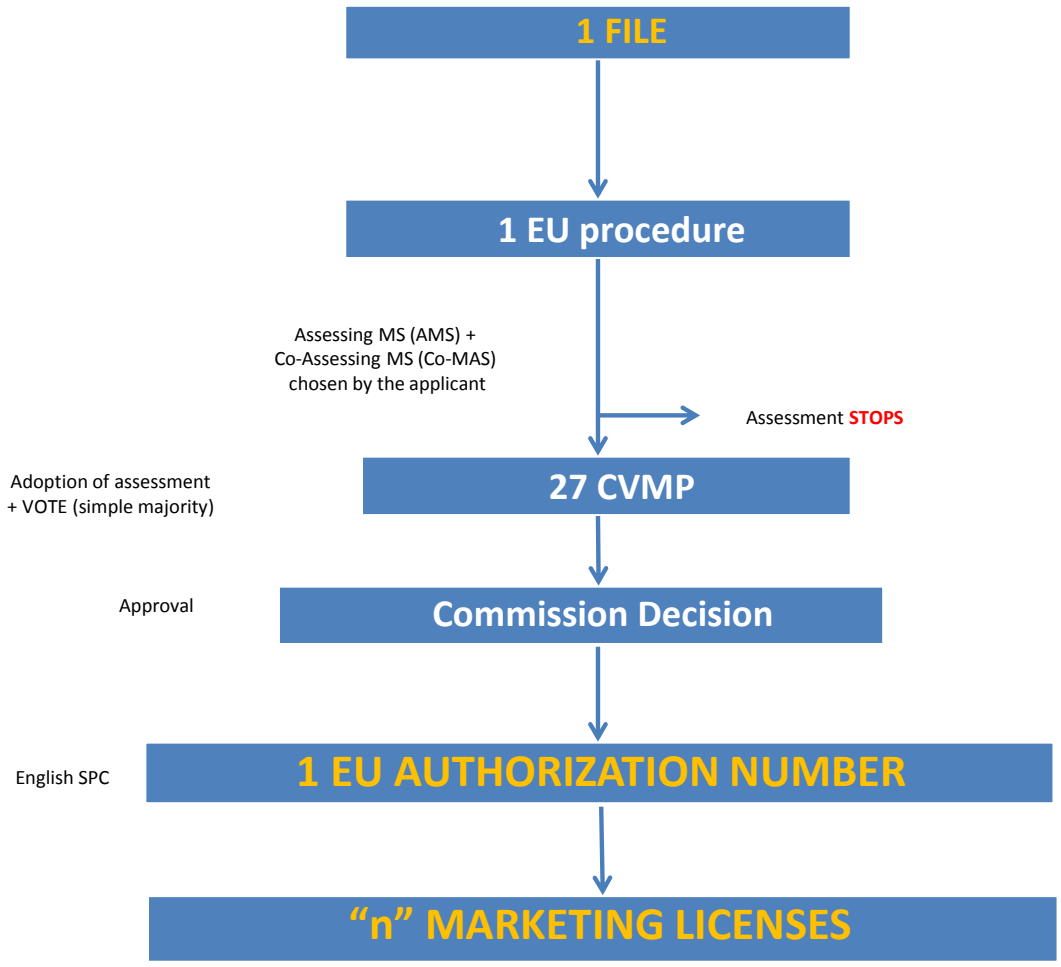
This balance is essential and incentives for the industry bringing generic veterinary medicines into the EU market should also be encouraged. Generic veterinary medicines create an appropriate competitive environment, while increase the range of choices available without compromising the quality, safety and efficacy. This higher availability, provided by the presence of generics on the market, is also fundamental to supply quality safe food to a growing population in many geographic regions where the cost of non-generic medicines might not be affordable. Due to the price competition, safe and tested formulations are available to wider markets that previously may not have been able to afford them.

In order to achieve these two objectives, EGGVP would like to table the following proposals:

I- AUTHORIZATION PROCEDURES

- For new marketing authorizations submitted after entering into force of the new legal framework, EGGVP supports the adoption of a 1-1-1 concept. This way, harmonized SPCs could be obtained throughout the EU and the system would also bring major advantages for products that are not eligible for the centralized procedure today.

  The 1-1-1 model proposed by EGGVP is described below:



As a general principle and in order to increase availability of veterinary medicines in small markets, the fees applicable in the new legislation should be **proportionate** and significantly **lower to the current ones** in the Centralized Procedure (EMA). The fees proposed by EGGVP are:

- Assessment fees
  - Full application (FPA/ NFPA): full fee

  - Generic applications (FPA/ NFPA)*: 30% of the full fee
  - Generic/hybrid applications (FPA/ NFPA): 50% of the full fee
  - Well Established Use applications (FPA/ NFPA): 50% of the full fee
  - MUMs application: 25% of applicable fee
  - SMEs: 25% of applicable fee
- Marketing fees/country
  - Proportionate to the market
  - Maximum 1,000 €

**Food Producing Animals (FPA) / Non Food Producing Animals (NFPA)*

- Alongside the 1-1-1 process for new marketing authorizations, and on a temporary basis (transition scenario), the existing procedures should still be an option.

  The reason for this is that with the 1-1-1 process, especially the small and medium sized companies, with only interests in one or a few individual markets, would be forced to go through an European assessment system. To give these companies a fair chance in the future, the now existing national procedures (to be eventually followed with a MRP procedure) should be kept in place as they are right now. Applications in individual Member States on basis of a national application should still be possible during a transition period for six years after coming into force of the new legislation. Justification for this time frame is that the life cycle of a veterinary medicinal products under the existing procedures is of (5) + (1) years.

  Furthermore, the European generic veterinary industry, which is mainly composed of small and medium sized companies, is very much concerned about the potential fee increases that applications under the 1-1-1 system could lead. EGGVP is afraid that the fees for the expert evaluation will head towards the costs (and work load) for a central registration, with the consequent difficulties to be handled by small and medium sized companies. It should be noted that some products are of interest to a few Member States only, and that the current authorization regimes allow an investment which is proportionate to the number of markets that companies have chosen. In case that fees associated to the 1-1-1 system were not proportionate, companies may not be able to support extra fees if they have no investment return in countries where there is no market for their products. Thus, an increase of fees under the 1-1-1 system would reduce or even prevent marketing possibilities. There should be guarantees that assessment fees linked to the 1-1-1 system will be proportionate. It is also essential that dossier requirements under this system remain balanced and fair; a further increase in requirements would harm the availability of veterinary medicines because it would no longer be possible for industry to sustain the profound investments in new products.

- For existing authorizations, the 1-1-1 approach would only be reasonable if veterinary medicinal products were authorized under the same conditions and evaluated under the same criteria. As this is not the case, such a system would imply a huge workload to reach harmonisation and would therefore not be suitable for existing medicines. Applying such

an approach for existing veterinary medicines, where target species and indications may have been lost in one Member State whilst the product literature may have remained the same in other Member States, would result in triggering referrals over and over.

- With regard to the non-harmonised SPC's for existing products, EGGVP wishes to repeat its position. Harmonisation of SPC's is supported by EGGVP for generic products only on the strict precondition that such a harmonisation follows the harmonisation of the originator SPC and would **NOT be based on a re-assessment** of old or new material **and NOT leading to the lowest common denominator**. Such a process should entail a pragmatic approach, taking into account existing pharmacovigilance data.

- Finally, EGGVP would like to establish the "**Informed consent application**", valid for generic veterinary medicines as well. The current situation is leading to overloading of medicines' agencies, and imposing a heavy administrative burden, duplications and huge financial investments for industry.

II- DATA PROTECTION

EGGVP is favourable to an extended data protection for specific reasons (such as new indications, new species or new withdrawal periods), as long as the periods of extension are **proportionate** to the investment and **linked to the extent of innovation**. This means that any prolongation should solely be possible for the specific extension of a marketing authorization and not for the product in general. Thus, after the first protection period, generics should be possible but without the new species or indications of the related extension.

- Any extension in data protection should also be equally applied to innovation performed to generic veterinary medicines, and not only to originators.

- EGGVP proposes the following data-protection period (except for products for minor species, where the period should be higher) to be foreseen in the new veterinary medicines legislation:
  - Initial data protection period: 10 (8 + 2) years
  - Additional data protection periods **for each innovation only** (both for originator and generic veterinary medicines), not for the marketing authorization:
    - +3 years for the 1st addition for food producing species
    - +1 year for further extra additions for food producing species
    - +1 year for any addition for non-food producing species
    - +1 year for additional indications
    - +1 year for additional pharmaceutical forms
    - +1 year for new withdrawal period

- There should be no restrictions with respect to time-point of submission, and no link to the MRLs regulations.

- The current global marketing authorization concept should be retained in the new legislation as it is now (linked to API only).

- Competent authorities should inform generic companies in the cases where additional protection periods for certain claims are given to the reference product. Additionally, full SPCs from all Member States should be available to MAHs. Eudrafarm tool is not a practical tool; it includes limited information on the products and is only used by certain Member States.

III- PHARMACOVIGILANCE

Pharmacovigilance represents the highest percentage of administrative burden for veterinary pharmaceutical companies, with a significant impact on all enterprises', including small and medium sized enterprises', daily activities and resources. EGGVP believes that a drastic simplification of pharmacovigilance requirements is not only necessary but possible, as it has been proved that there is room for reducing this burden without compromising neither safety of medicines nor transparency of procedures. Some suggestions to reduce this burden are:

- Keep PSUR obligations to a minimum, in particular for veterinary medicines based on well-established veterinary use, which have been in the market for many years. There is no need to give repeated expert reports unless there is an increase of unknown adverse effects (AE), based on the active substance or the formulation, which can be revealed by evaluating the electronically reported adverse effects. EGGVP is proposing a reduced periodicity for veterinary medicines based on well-established veterinary use as follows:
    - PSUR submission within 3 years following approval, using the occasion of the EU-HDLP (EU-Harmonized Data Lock Points)
    - PSUR submission at 4.5 years, i.e. at the time of renewal application
    - Additional PSURs on request at EU level when signal detection reveals an increase of unknown AE for this product.

- Besides the existing recall system of products with a serious impact on product quality or safety within 24 hours, EGGVP suggests to extend the deadline for reporting known serious AEs to 30 days. The current deadline of 15 days is too short to collect all necessary information; an extension of the deadline to 30 days would result in higher quality reports and a lower incidence of follow-up reports.

- Keep the company's pharmacovigilance system description out of the authorization dossier(s), in order to allow modifications of the system without compromising the validity of the authorization dossier(s). Pharmacovigilance system should be linked to the marketing authorization holder rather than to applications. We suggest that following inspection, the national competent authorities issues a certificate of compliance with the requirements of pharmacovigilance, which can be handled by the MAH to other national authorities on request.

- Promote and implement e-submission procedures: Provision of a modified more practical reporting tool to facilitate electronic submission of AE reports to Eudravigilance data base. Give the possibility to submit electronic periodic safety update reports to all Member States; EGGVP supports all efforts in order to fully eliminate submission of paper copies.

- Update the Eudravigilance data warehouse to a user-friendly data base and give all MAH access to the collection of electronic Eudravigilance data of the marketing authorisations hold by the MAH.

IV- LABELING AND PACKAGING

General principles

EGGVP believes that **labelling requirements should be simplified** in order to allow a single EU label without translation, and proposes that the **text in the immediate label, outer packaging and leaflet is shortened** in order to better attire the attention of the end-user.

In this sense, EGGVP appreciates the improvements achieved with the **QRD template n. 8** and encourages its associate members to use it, due to the possibility to reduce the amount of text in labels and packages, and therefore to increase the availability of veterinary medicines in the Member States.

A standardised and agreed **catalogue of pictograms** should also be permitted for use on both immediate labels, outer packages and blisters and applied to all species. It should be available to all MAHs in the EU and pictograms should be easily accesible for download from relevant websites (competent authorities and industry associations). Pictograms developed by IFAH-Europe are considered appropriate for this purpose. EGGVP acknowledges and supports the work of IFAH-Europe and CMDv on this issue. The purpose of the pictograms should be to replace the name of species in the label and the mention “Ad us. vet”. MAHs can propose using their own pictograms instead of those in the agreed catalogue. There shall be a procedure in place for the assessment and agreement of additional company pictograms.

EGGVP also proposes to avoid using additional national (“Blue box”) requirements and information.

As per the format, EGGVP proposes alternative substitution of immediate label + outer package + leaflet by a “**combined leaflet-label”** (more interesting for big presentations: 1 L, 5L, 1 kg, 5 kg and 25 kg).

The EGGVP proposals for **mandatory information** in the labelling, package leaflet and combined leaflet-label are hereby detailed.

Any **additional information shall be permitted on a voluntary basis**, if it relates to the use of the veterinary medicinal product or the MAH, and is not inconsistent with the information referred in the package leaflet and/or SPC.

I. LABELLING

Outer package

- Short name of the medicinal product
- Name of the MAH
- Target Species [3]
- Pharmaceutical form [3]
- Content / package size
- Special storage precautions [3]
- MA No
- Batch number (use LOT)
- Expiry date (use EXP)
- Strength [1]
- Statement of the active substance [1]
- Restrictions regarding supply and use
- Read package leaflet [3]
- "Ad us. vet." [3]

Immediate package

- Short name of the medicinal product
- Name of the MAH
- Target species [3]
- Batch Number (use LOT)
- Expiry date (use EXP)
- Strength [1]
- Statement of the active substance [1]
- Content / package size

II. PACKAGE LEAFLET [4][5]

- Short name of the medicinal product
- Name of the MAH
- Target species [3]
- Pharmaceutical form [3]
- Special storage precautions [3]
- Strength [1]
- Statement of the active substance [1]
- Restrictions regarding supply and use
- Indications
- Route (& method) of administration [2] [3]
- Dosage
- Withdrawal period
- Special precautions for disposal
- Special warnings (incl. safety warnings)
- Contraindications
- Adverse reactions
- "Ad us. vet." [3]

III. COMBINED LEAFLET –LABEL [4]

- Short name of the medicinal product
- Name of the MAH
- Target species [3]
- Pharmaceutical form [3]
- Content / package size
- Special storage precautions [3]
- MA Nº
- Batch Number (use LOT)
- Expiry date (use EXP)
- Strength [1]
- Statement of the active substance [1]
- Indications
- Route (& method) of administration [2] [3]
- Dosage
- Withdrawal period
- Special precautions for disposal
- Special warnings (incl. safety warnings)
- Contraindications
- Adverse reactions
- "Ad us. vet." [3]
- Restrictions regarding supply and use

[1] This information, if expressed in single INN or 1 term for all Member States, would still allow labels to be combined for multiple Member States (no local languages would be needed.)

[2] Mandatory – to be included in case this information is not included in the product's name

[3] Consider using pictogram

[4] Allow grouping the following information in a table: Target species, Indications, Route (& method) of administration, Withdrawal period

[5] Information under headings/ sub heading and associated text should only be included if these are relevant. If no information is provided, the section may be omitted from the package leaflet.

IV- ENVIRONMENTAL RISK ASSESSMENT

The current wording of Directive 2004/28 has led generic veterinary medicines into an unfair situation concerning requirements for assessing their impact on the environment.

By definition, generic veterinary medicines **should not be requested** to submit a Safety Package in their applications. Therefore, since it is clear that ERA (Environmental Risk Assessment) is part of the **Safety data from the dossier,** the new veterinary medicines legislation should clearly state that generic veterinary medicines should not be requested to submit an ERA for their authorization.