EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Regulatory Update

EMA Veterinary Medicines Info Day May 2022

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Update on regulatory topics recently finalised or still under development:

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- Grouping of I-scope VRAs (the ex line-extensions)
- QRD template v.9 and VRA G.I.18
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- Article 107(3) prophylaxis indications for existing antimicrobials
- Data protection Articles 38(3) and 40(5)
- Indefinite validity of centralised MAs
- Union interest referrals (Article 82)

Duplicate MAs in the centralised procedure

- No explicit provisions within Regulation (EU) 2019/6
- EMA will continue to request pre-submission info on whether an MAA is a duplicate, i.e. 'same applicant' + 'same product', according to the previously established definitions.
- Basis for eligibility to centralised procedure (CP) may differ slightly depending on actual legal basis of the MAA i.e. a duplicate can be submitted as full MAA (Article 8), an auto-generic MAA (Article 18) or a self-informed consent MAA (Article 21) but duplicates are always eligible to CP, i.e. 'automatic access'.
- No longer a requirement to obtain prior consent from EC for the duplicate.
- In view of Article 77(2), please note the requirement to have same PhV master file for VMPs falling within above definition of 'same' veterinary medicinal product.

Grouping of variations requiring assessment (VRAs)

Clarification on EMA's published post-authorisation Q&A on VRAs

- VRA Q&A No. 5 discourages grouping of I-scope* VRAs with non-I scope* VRAs due to relatively short timetable for I-scope VRAs (these are the ex line-extensions).
  - E.g. not feasible to introduce ASMF changes within an unrelated I-scope VRA and such changes should be submitted separately, and not simultaneously with the I-scope VRA.
  - If in doubt what can be included within your I-scope VRA, please contact us (vet.applications@ema.europa.eu).
- However, in cases where MAH intends in any case to simultaneously submit an I-scope VRA with a non-I scope VRA, particularly where the **simultaneous VRAs all affect the product information**, please discuss the possibility of grouping with EMA in the normal pre-submission phase via vet.applications@ema.europa.eu

* * With reference to CMDv/EMA classification guidance for VRAs (EMA/CMDv/7381/2021)

QRD template v.9 and VRA G.I.18

- Regulation with transitional rules for packaging & labelling expected by early June.
  - Provisions in line with previous DG SANTE statement on Article 152(2) of Reg. 2019/6;
- Regulatory mechanism to align SPC, labelling & package leaflet (product information or 'PI') with requirements of Regulation 2019/6 is to **transfer the PI to QRD template v.9** and submit this for approval via VRA G.I.18.
- EMA has developed a single page document with advice to MAHs before submission of the VRA G.I.18 – will be sent to each MAH when they notify us of intention to submit & retrospectively to MAHs who already notified us.
- For centralised products, not possible to transfer PI to QRD v.9 within another ongoing/planned VRA – a VRA G.I.18 must be submitted for each product .
  - Preference to group VRA G.I.18 with more substantial efficacy/safety variation but try to avoid grouping with an I-scope variation due to relatively short timetable for these.

QRD template v.9 and VRA G.I.18

- EMA exploring possibility of fee incentive for VRA G.I.18 due to a number of enquiries, only for pharmaceuticals due to current higher fee
  - ➢ this process will take at least until summer & no guarantee or retrospective application.
- Any review of classification (prescription status) vis-à-vis Article 34 will be handled outside of VRA G.I.18 when respective CVMP guidance is finalised.
- If MAHs request to align PI with revised CVMP SPC GLs on antimicrobials or antiparasitics during VRA G.I.18, EMA can agree to it but will not make it mandatory at that time.
- No need for critical expert report for VRA G.I.18 but can be provided if needed (e.g. in case of alignment with abovementioned SPC GLs and MAH wishes to present arguments).
- Please note the new QRD **combined label-leaflet template v.9** – for use when there is no PL and all info must appear on outer packaging.

QRD template v.9 and VRA G.I.18

- Until any centralised list of national collection systems is available please **disregard the following guidance** in annotated QRD template v.9, SPC, section 5.5. on disposal:

  *[**For CP only**: the list of national collection systems should be completed in section 12 of the package leaflet only.]*

- EMA & CMDv are exploring possibility of centralised lists of national systems which could be linked from respective sections of the QRD template for:
  - national collection (disposal) systems mentioned in Article 117,
  - national reporting systems for adverse events.
- Updated Q&A on describing adverse events in SPC/PL: EMA/CVMP/150343/2016-rev.1
- PL section 16 with consolidated set of 'contact details' is complex… please carefully follow *green text* in annotated template.
- Nothing has changed for distributors in the PI – if they are not the named local representative in the PL, then distributors cannot be named on the label/PL.

Article 34 classification (prescription) status

- CVMP guidance is under development, which will include public consultation.
- In addition to Article 34, please be aware of the dossier requirement in the revised Annex II to Regulation 2019/6, Section I.2.1:

"*With regard to Part 1B, point 5.1, in connection to Article 35(1), point (l), an application proposing classification of a veterinary medicinal product as "not subject to veterinary prescription"* ***shall include a critical review*** *of the product characteristics in order to justify the suitability of such classification taking into consideration target and non-target animal safety, public health as well as environmental safety, as outlined in the criteria given in Article 34(3), points (a) to (g).*"

Article 34 classification (prescription) status

In case an applicant is requesting non-prescription classification of a VMP, either for initial authorisation or post-authorisation:

- Tick the box for non-prescription in section 2.3 in the eAF for initial MAAs;
- For post-authorisation switches of prescription status, for centralised products use the dedicated VRA with classification G.I.6;
- Include justification (for initial MAA or variation) of non-POM classification according to Annex II, Section I.2.1 requirements – suggest to include this, at least for now, in the critical expert report, or as a separate, clearly labelled document in Part 1 of the dossier.
- In case of uncertainty, please contact us via vet.applications@ema.europa.eu

Article 107(3) Prophylaxis claims for existing antimicrobials

- Public consultation on CVMP reflection paper on prophylactic use ended 29/04/22 – finalisation intended by July, potentially a focus group meeting before finalisation.
- Low number of impacted centralised products (<10).
- EMA intending to proactively contact the affected MAHs to outline the proposed approach.
- MAHs likely to be asked to take regulatory action on this before end of 2022, i.e. within a variation application.
- Liaison with CMDv for a consistent approach.

Unlimited MA validity

- EMA has already contacted all MAHs of already-authorised concerned products (i.e. MAs still with a 5-year validity date) to seek confirmation that the MAHs would like unlimited MA validity.
- For any ongoing centralised MA applications still running under the transitional provisions of Regulation 2019/6, the EMA will continue to request confirmation of the MAH's wish for unlimited MA validity.
- These confirmations are sent by EMA to EC in order to update the Commission Decision granting the MA and to remove the validity date either:
  - when adopting a Commission Decision on a VRA under Regulation (EU) 2019/6;
  - as a standalone update of the Commission Decision if no VRA before MA expiry,
- No further action required from MAHs and all MAs will be updated in due course.
- Q&A on EMA website to be updated shortly with this information.

Data protection: global marketing authorisation (GMA)

GMA under previous legislation: Directive 2001/82/EC, Article 5(1):

"*When a veterinary medicinal product has been granted an initial authorisation in accordance with the first subparagraph, any additional species, strengths, pharmaceutical forms, administration routes, presentations, as well as any variations and extensions* (EMA note: covers e.g. new indications)*, shall also be granted an authorisation in accordance with the first subparagraph or be included in the initial marketing authorisation. All these marketing authorisations shall be considered as belonging to the same global marketing authorisation, in particular for the purpose of the application of Article 13(1).*"

Data protection: global marketing authorisation (GMA)

GMA under Regulation (EU) 2019/6, Article 38(3):

"*A marketing authorisation or a variation to the terms of a marketing authorisation differing from the marketing authorisation previously granted to the same marketing authorisation holder* ***only with regard to target species, strengths, pharmaceutical forms, administration routes or presentations*** *shall be regarded as the same marketing authorisation as the one previously granted to the same marketing authorisation holder for the purpose of applying the rules of the protection of technical documentation* ***[emphasis added]***."

Current understanding is that the narrower wording of Article 38(3) compared to Article 5(1) of Directive 2001/82/EC **excludes new indications added post-authorisation from the GMA**.

Data protection: Article 40(5)

- Article 40(5) provides for an additional period of protection of technical documentation underpinning certain specific types of post-authorisation product development, but certain criteria need to be met, e.g. improving the B-R balance of the VMP.
- CVMP draft reflection paper will be released for public consultation in due course.
- Consideration given to merging guidance on Article 40(5) with revised CVMP guidance on benefit-risk but decided against it for now – would delay Article 40(5).
- The main outstanding issues voiced by industry stakeholders were:
  - data protection for new target species and indications via Article 40(5), and
  - acceptance of 'additional benefits' as valid improvements to the B-R balance.

Data protection: Article 40(5)

- Post-authorisation product developments involving a requisite change to the pharmaceutical form, administration route or dosage which equally involve addition of a new indication or target species can, in principle, qualify for the application of Article 40(5), provided that the relevant conditions are met.

- However, a variation that adds a new target species would not automatically qualify for additional data protection under Article 40(5) simply because of an associated change of pharmaceutical form, admin. route or dosage…

- It is fundamental to demonstrate (scientifically) meeting at least one of the two criteria of Article 40(5), i.e. (a) reduction in antimicrobial/antiparasitic resistance or (b) an improvement to the B-R balance *NB Article 40(5)(b) is considered to include a reduction in the **risk** of AMR/APR according to the definition of B-R balance in Article 4(19)*.

Data protection: Article 40(5)

Whilst CVMP reflection paper not yet available and an applicant wishes to claim their right to protection of technical documentation under Article 40(5):

- **Submission of application**

1. Submit variation as normal under the usual legal basis for a VRA (Article 62);
2. Tick the corresponding box for Article 40(5) in the eAF;
3. Provide justification in the dossier as to how the product development covered by Article 40(5) fulfils at least one specific criteria (a) or (b) of Article 40(5) – suggest to include this, at least for now, in the critical expert report, or as a separate, clearly identified document in Part 1 of the dossier.
4. If no justification regarding the claim to Article 40(5) is provided in the dossier, this will be flagged during validation (not a validation blocking issue).
   The applicant will be advised that, without such justification, CVMP will not be able to undertake assessment as regards Article 40(5).

Data protection: Article 40(5)

- **Assessment**
  - CVMP will assess VRA as normal and will additionally assess, in a discrete section of the assessment report, whether the claimed criterion of Article 40(5)(a) or (b) is considered to have been demonstrated based on the applicant's justification.
  - EMA/competent authority does not 'grant' the additional data protection period. As for any other period of data protection, this right derives directly from the Regulation. The EMA/CVMP will only assess whether the scientific criteria of Article 40(5) have been demonstrated.

Article 82 Union interest referral

- Very similar to referrals under Article 35 of Directive 2001/82/EC, but a few new elements introduced, mainly in line with referral procedures for human medicines.
- All product types can be included in the same referral: NAPs, MRP/DCP and CAPs.
- Timetable has been extended to 120 days + additional 60 days.
- 'Urgent' risks to public or animal health or to the environment that result in temporary safety restrictions (Article 129(3) *may* now also referred under Article 82 but this is no longer a mandatory step).
- Article 82 referrals are published on the EMA website under the 'Medicines' section at the start of procedure and stakeholders are invited to provide comments which can be considered in the assessment. Updates and further documents are published throughout the procedure. Example: Procaine benzylpenicillin (EMEA/V/A/145).

Submission of data for referral procedures

- MAHs' active participation in referrals (by submitting responses to CVMP list of questions/outstanding issues) is crucial for the outcome of the procedure.

- Responses should be submitted to EMA using the eSubmission Gateway (mandatory for all veterinary procedural submissions). *NB initial registration process for the Gateway may take up to 20 working days so MAHs not already registered are encouraged to do so ASAP after receiving the 'start of procedure' letter to avoid unnecessary delays in the assessment.*

- The Agency is currently developing guidance in the form of Q&A which will be published on the website in the next few months.

- Any questions on referrals, please contact vet.referrals@ema.europa.eu

It’s possible the regulatory colleagues look at bit like this at the moment…

but to quote Oscar Wilde

‘*Everything is going to be fine in the end… and if it’s not fine, it’s not the end!*’