



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/HMA Action plan on availability for veterinary vaccines

Progress and developments in 2016

EMA Veterinary Medicines Info Day 16-17 March 2017, London

Presented by Dr Faye Ioannou – 16 March 2017

An agency of the European Union





Overview of presentation

- Background to the veterinary vaccine availability action plan
- Developments in 2016 and progress tracking
- Analysis of industry recommendations
- Stakeholders focus group on field efficacy trials
- Next steps
- Key message

EMA/HMA action plan on Availability for veterinary vaccines

- Joint EMA/HMA Workshop 25th March 2015 to improve the availability of veterinary vaccines → 6 recommendations → 13 step action plan
- Action plan to bring together activities from several different initiatives into a single coherent plan to ensure that:
 - resources of the Network as a whole are used to best effect taking into account the recommendations from the EMA/HMA workshop in March 2015
 - efficient and effective cooperation between all of those involved in ensuring the availability of vaccines within the EU (including marketing authorisation holders, regulatory authorities and the European Commission)

EMA/HMA action plan on Availability for veterinary vaccines

Actions and progress tracking

1. Integrate appropriate elements of action plan into the EU Medicines Agencies Network Strategy to 2020 and the linked multi-annual work plans of the EMA and HMA.
2. Set up a steering group to oversee and monitor progress against the action plan comprised of representatives from HMA and EMA. The EC and EDQM invited as observers. Industry observers invited to participate in relevant topics.
3. Review the list of issues identified by industry
4. Explore possibilities for public private partnerships under Horizon 2020
5. Develop guidance on standards for manufacture of autogenous vaccines
6. Identify training opportunities in the area of veterinary vaccines in co-operation with the Network Training Centre (NTC)
7. Set up a webpage to promote communication on veterinary vaccine availability initiative



EMA/HMA action plan on Availability for veterinary vaccines

Actions and progress tracking

8. Create a group of CVMP members to identify, prioritise and make public CVMP plans and activities in the area of veterinary vaccine availability
9. CVMP-IWP Party to identify training opportunities for 2016 and 2017 in cooperation with Joint EMA/HMA Network Training Centre
10. Provide support to development of new vaccines and associated technology through existing mechanisms such as scientific advice, innovations task force (ITF)
11. Finalise review of MUMS guidelines and publish
12. CVMP/IWP to reflect on existing measures to promote availability of vaccines for epizootic diseases (FMD, BT, AI) and if new, or review of existing, guidance is required (e.g. multi-strain dossier guideline)



EMA/HMA action plan on Availability for veterinary vaccines

Actions and progress tracking

13. CVMP/IWP to reflect on ways to take into account the different types of vaccines (e.g. live/inactivated vaccine, food producing/companion animals) and different situations for authorisation (e.g. normal vs. exceptional situations) as part of guidance on the benefit-risk assessment of veterinary medicinal products.
14. Using appropriate channels, input technical considerations on requirements for vaccines into the process for review of the legal framework for veterinary medicines

green = completed; blue = on-going; black = planned



Developments in 2016

- Recommendations were placed within the context of a wider HMA Network Strategy and **an EMA/HMA action plan on Availability for veterinary vaccines** to ensure efficient and effective cooperation between all of those involved in ensuring the availability of vaccines within the EU was drafted. The plan was adopted in the HMA February 2016 meeting in Amsterdam.
- **A Steering Group (SG) on Joint EMA/HMA Action Plan on Availability of Veterinary Vaccines** was created to provide strategic oversight on the implementation of the action plan. The Terms of Reference(ToR) of the Steering Group were adopted in February 2016 HMA meeting in Amsterdam.
- A **CVMP ad hoc group on veterinary vaccine availability (CADDVA)** was created and the ToR were endorsed by CVMP in its March 2016 meeting.

Developments in 2016

- A **webpage** on veterinary availability to improve communication was launched by EMA/HMA in August 2016 ([Availability of veterinary vaccines](#))
- An **analysis of industry recommendations** with input by CADDVA and SG was adopted by CVMP and HMA in its November 2016 meeting.
- A meeting with industry to communicate analysis outcome and establish **communication strategy** was held in December 2016.
- The main priority from the analysis agreed is the need for a **Stakeholders focus group on field efficacy trials**, which has been included in the CVMP and IWP plans for 2017 and is now foreseen for June 2017.
- **Communication strategy agreed**: bi-annual meetings between SG and stakeholder groups + ad-hoc meetings on specific topics.

Developments in 2016

- Stakeholders Focus group on Lumpy Skin Disease (organised in January 2017)
- A survey for Member States, on the list of exempted vaccines from full authorisation in order to better understand veterinary vaccine needs in EU, to be launched soon
- Ongoing work:
 - CMDv working on autogenous vaccines (*“Recommendations for the Manufacture, Control and Use of Inactivated Autogenous Veterinary Vaccines within the EEA” adopted in February 2017 by CMDv and HMA*).
 - IWP working on revising MUMS guideline & on a Reflection paper on measures to promote availability of vaccines against emergency animal health diseases,
 - IWP to receive shortly request by CADVVA to reflect on ways to take into account the different types of vaccines (e.g. live/inactivated vaccine, food producing/companion animals) and different situations for authorisation (e.g. normal vs. exceptional situations) as part of guidance on the benefit-risk assessment of veterinary medicinal products.



Analysis of recommendations provided by industry in March 2015 on veterinary vaccine requirements – Methodology

- Forty three (43) recommendations were submitted
- Qualitative methodology was followed:
 - Recommendations were grouped in main categories and then split further into subgroups.



1 December 2016
EMA/239617/2016-Draft
Veterinary Medicines Division

Joint EMA/HMA Veterinary Vaccine Availability Action Plan Analysis of industry recommendations

1. Background

A "Joint EMA/HMA Workshop on requirements for the authorisation of veterinary vaccines in the EU" took place on the 25 March 2015. A key question addressed at the meeting was if requirements for marketing authorisation of vaccines in the EU were considered to be proportionate to the benefits and risks of this type of product.

A report of this workshop was published on the EMA website that contains a number of recommendations. These recommendations have been placed within the context of the wider Network Strategy in preparing an action plan (the HMA/EMA action plan on veterinary vaccine availability) with the objective of ensuring efficient and effective cooperation between all of those involved in making vaccines available within the EU (including marketing authorisation holders, regulatory authorities and the European Commission).

To provide strategic oversight on the implementation of the Joint EMA/HMA Action Plan on Availability of Veterinary Vaccines the HMA in its February 2016 meeting established a Steering Group (SG). In March 2016 the CVMP also established the CVMP ad-hoc expert group on veterinary vaccine availability (CAOVVA) to identify, prioritise and monitor the implementation of actions within the Action Plan for



Analysis of recommendations provided by industry in March 2015 on veterinary vaccine requirements – Methodology

- The following criteria were taken into account for assessing the potential impact of each recommendation:
 - The potential increase of the availability of veterinary vaccines if the action were to implemented
 - The type of impact on veterinary vaccine availability (e.g. reduction of time/cost burden, positive impact on 3Rs, etc.)
 - The feasibility of implementing all necessary actions
 - The impact on increasing the level of risk for animal or public health
 - The likelihood of success
- Following the impact analysis a specific action was proposed to address each one of industry's recommendations
- For the purposes of analysis the definition of vaccine availability agreed

Analysis of recommendations provided by industry in March 2015 on veterinary vaccine requirements – Methodology

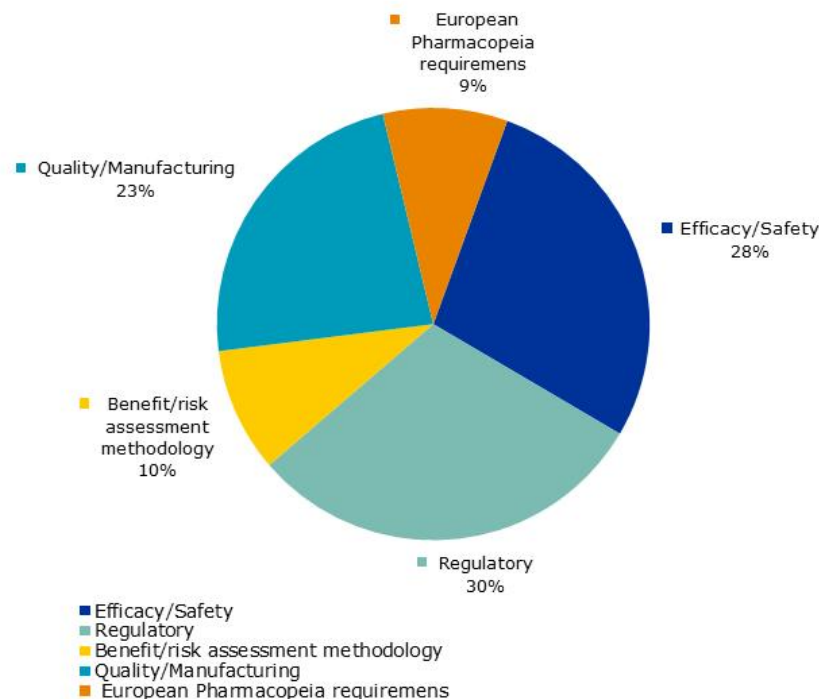
Definition of availability, as agreed by CADVVA:

Timely and adequate access to the market of suitable new and/or improved veterinary vaccines, to improve the health and welfare of animals, increase production of livestock in a cost-effective manner and prevent animal-to-human transmission from both domestic animals and wildlife, as well as to significantly impact on public health through reductions in the use of antibiotics and other veterinary pharmaceuticals and their residues in the human food chain

The availability of existing veterinary vaccines was also recognised as a concern in some EU markets but was not considered appropriate for the scope of this group.



Analysis of recommendations provided by industry in March 2015 on veterinary vaccine requirements – Methodology



Main actions proposed by SG to address industry's recommendations in the analysis report

- **Role of efficacy field trials** - Problem statement: conduct of field efficacy trials often too challenging when compared with the added value of the produced data in the context of final dossier, Proposed action: Stakeholders focus group on field efficacy trials in 2017
- **Role of serology** - Problem statement: accepting serology more readily in EU as marker of efficacy , Proposal: Industry to provide a clearer problem statement with examples to be reviewed by CVMP/IWP against current guidance and decide whether space for flexibility and need to follow up with focus group
- **Use of PhV data** - Problem statement: use of PhV as valid field data; Proposal: Industry to provide refined problem statement with more detailed arguments and examples; CADDVA/SG to decide on further follow up
- **SPC simplification** - Proposal: Industry invited to provide specific concerns and examples in the form of concept paper - SG to evaluate and decide follow up

Main actions proposed by SG to address industry's recommendations in the analysis report

Recommendations related to European Pharmacopeia

Problem statement :

- subjecting some “Development” sections of Ph. Eur. monographs to evaluation that are considered excessive or confusing
- specific sterility issues
- reduced stability data (up to shelf life and not +3)

EDQM (Group 15V), appropriate body to implement issues directly relating to their area of competence. Proposed actions:

- i. IWP/CVMP to review industry concerns and recommend whether it would support a meeting with EDQM
- ii. SG to organise a meeting with EDQM
- iii. EDQM/industry to agree further follow up



Overview of actions proposed and responsible actor

Responsible Actor	Action
Steering Group	The SG is expected to prioritise and coordinate the implementation of all proposed actions, monitoring and tracking their progress. The SG is also expected to take the lead in organising any focus groups that have been agreed to be organised i.e. efficacy field trials and in deciding on appropriate participants for such groups. SG is also expected to lead in to organising a high level meeting with EDQM to discuss industry's concerns and CVMP's position and in communicating with industry the progress of the agreed priorities and actions.
EMA	EMA has been allocated a number of actions, namely related to the following: • coordinating with the Network Training Centre on training of assessors to improve better flexibility on alternative approaches, • revision of template and guidance of scientific overview and LoQ for immunological products, • training on 3Rs. • Investigate and clarify the reasons why the Vaccine Antigen Master file concept was not successful for human products.
CVMP (CADVVA/IWP)	The CVMP and at first instance CADVVA (the CVMP ad hoc group on veterinary vaccine availability) is invited to work on a number of issues and involve IWP as considered most appropriate. It is expected that IWP will be directly involved on all quality issues. In this context recommendations for CVMP actions relate to: • proposal to review industry's problem statements on serology as a surrogate marker of efficacy and proposals on the validity of PhV data when used in the context of an authorisation, • safety and efficacy laboratory studies - GLP issues - , • proposal to review industry's proposals on SPC simplification • training of assessors. • Difference in efficacy demonstration for companion vs small animal vaccines - reflect how to take into account in B/R guideline. • Possible extrapolation of inactivation kinetics: IWP to reflect how best to address. • Stability issues: IWP to reflect how best to address. • Vaccine antigen master file and Vector vaccine platform: review industry's proposed use and recommend whether to initiate guideline drafting. Include drafting of guideline in IWP work plan. • Extraneous agents testing: IWP is providing already input at the VICH paper on extraneous testing,

Responsible Actor	Action
	• Review industry's comments on changes to European Pharmacopoeia monographs and provide CVMP/IWP position on proposed changes.
CMDv	CMDv is invited to consider the recommendations relating to: • autogenous vaccines, • grouping of changes relating to production transfer, • MRP & repeat MRP procedures: investigate what extent problems have been experienced with vaccines going through an MRP and repeat use procedure and how these were resolved.
EDQM(Group 15V)	EDQM (Group 15V), is the appropriate body to implement issues directly relating to their area of competence: • subjecting the development of some sections of Ph. Eur. monographs to evaluation that are considered excessive or confusing, • specific sterility issues raised by industry, • Reduced stability data (up to shelf life and not +3).
Industry	Industry itself is required to provide: • specific problem statement and examples on use of serology as a surrogate marker of efficacy, • proposals and examples on the validity of PhV data when used in the context of authorisation, • proposals and examples on SPC simplification, • proposals and examples on validity of data from non EU countries, • list GMP issues where problems are encountered, • proposals and examples on vaccine antigen master file and vector vaccine platform envisaged implementation, • clear description of the antibiotic residue concerns, • compile necessary evidence dossier and co-ordinate with national representatives to implement changes to European Pharmacopoeia monographs following CVMP/IWP's review (i.e. provide required supporting material for each proposed change).

Stakeholders focus group on field efficacy trials

Scope:

To explore the specific challenges faced by industry in performing field trials to support efficacy claims and how these challenges might be overcome whilst still obtaining adequate assurances of the expected efficacy of a vaccine under field conditions.

Objectives:

- Identify specific challenges faced by industry in performing field trials to support efficacy claims.
- Identify risks and benefits from not including field efficacy data in the dossier of a new vaccine application.
- Identify possible alternative sources of information on expected efficacy of a vaccine under field conditions.
- Identify possible circumstances under which field efficacy studies would not be considered necessary to conclude on efficacy and, by contrast, the circumstances under which field efficacy studies would be required to conclude on efficacy.
- Make recommendations on the need for field efficacy trials to support efficacy claims.

Stakeholders focus group on field efficacy trials

Composition:

The focus group should bring together stakeholders and experts from EU and other regions with a maximum level of attendees of aprox. 40 people.

Regulators: Steering Group, CADDVA, IWP members, USDA/FDA or other region regulators.

Experts: academics from the areas of: veterinary infectious diseases, epidemiology and epidemiological modelling, statisticians, IWP experts

Timing:

A 2 half days meeting is being considered for 22-23 June 2017

Final output:

SG to consider focus group conclusions and decide whether to request to revise the CVMP guidance on field trials



Next steps

- ❖ Follow up recommendations of stakeholders focus group on field efficacy trials for new veterinary vaccines
- ❖ Finalise report from Member States survey on veterinary vaccine needs in EU
- ❖ Implement communication strategy with stakeholders
- ❖ Use the experience of the stakeholders focus group on field efficacy trials to progress other high priorities (e.g serology)
- ❖ Keep progress on ongoing work including European Pharmacopeia recommendations



Key message

- ✓ Availability of veterinary vaccine remains important for EU regulators but mindful of EMA resource constraints there is a need for expectation management



Thank you for your attention

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