

The Director General

Maisons-Alfort, 30 May 2023

OPINION

of the French Agency for Food, Environmental and Occupational Health & Safety

on the "Assessment of the risks to human health and the environment, and recommendations for their control, from the administration of external antiparasitic veterinary medicinal products in the form of dips, showers and sprays on ruminant livestock farms"

ANSES undertakes independent and pluralistic scientific expert assessments.

ANSES primarily ensures environmental, occupational and food safety as well as assessing the potential health risks they may entail.

It also contributes to the protection of the health and welfare of animals, the protection of plant health and the evaluation of the nutritional characteristics of food.

It provides the competent authorities with all necessary information concerning these risks as well as the requisite expertise and scientific and technical support for drafting legislative and statutory provisions and implementing risk management strategies (Article L.1313-1 of the French Public Health Code).

Its opinions are published on its website. This opinion is a translation of the original French version. In the event of any discrepancy or ambiguity the French language text dated 30 May 2023 shall prevail.

On 21 December 2018, ANSES issued an internal request to assess the risks to human health and the environment of external antiparasitic (EAP) veterinary medicinal products in the form of dips, showers and sprays (DSSs) used on ruminant livestock farms, and to make recommendations for their control.

1. BACKGROUND AND PURPOSE OF THE REQUEST

To combat the many parasitic diseases that can affect ruminants, veterinarians prescribe EAPs in forms such as dips, showers and sprays (DSSs). The active substances in these veterinary medicines mainly belong to the organophosphate and pyrethroid classes. These treatments generate exposure to antiparasitic emulsions, with potential risks to professionals (through inhalation, splashes, etc.) and the environment (through run-off, spraying, etc.).

When marketing authorisation (MA) is sought for a veterinary medicinal product, a user risk assessment is conducted to determine whether there is a potential risk for any of the exposure scenarios identified and to recommend risk management measures if necessary. An environmental risk assessment is also carried out in accordance with the guidelines in force at the time of the MA application. This includes, if necessary, advice on effluent management to be included in the summary of product characteristics (SPC). However, because the five MAs for all the EAP DSSs intended for ruminants were obtained many years ago, these medicines have not been assessed according to the recommendations of the guidelines currently in force concerning the risks to users and the environment. The conditions of use of the EAP DSSs available on the market do not specify, for example, how residual product and effluents should be managed by users. The SPCs for these medicines only state the practices to be avoided. Moreover, the SPCs' imprecise recommendations on preventing health risks for professionals and environmental impacts, mainly regarding effluent disposal, are leading users to ask questions (for example, livestock farmers are asking French departmental directorates about the management of residual dip). Lastly, the lack of effectiveness observed with regard to certain myiasis (e.g. *Wohlfahrtia magnifica*) has led to uses in the field that do not follow the recommendations in the SPCs (over-concentration, mixtures of different compounds, local application, etc.).

As a result of this, ANSES issued an internal request to draft a report to establish procedures for using EAP DSSs in such a way as to minimise their impact on exposed professionals and the environment, mainly by recommending alternative methods where possible, and by making specific recommendations on effluent management. The scope of the expert appraisal was to cover the following in particular:

- 1) Work and worker exposure situations concerning EAPs applied in sheep farming, addressed in volume 3 of the collective expert appraisal report relating to internal request No. 2011-SA-0192, updated with a literature review and supplemented by hearings or other case studies;
- 2) A survey of information on the professional context and changes to this information (health situation, herd management), as well as use practices (methods of administration by animal owners, use of recommended or non-recommended spraying equipment, effluent management, etc.);
- 3) A risk assessment based on a cross-disciplinary, integrated expert appraisal of the risks associated with:
 - a. exposure of professionals administering veterinary medicines. Appropriate recommendations for workers (possibility of substitution, including changes to administration practices, collective or individual means of protection);
 - b. environmental impact assessment of administration practices;

- 4) Drafting of recommendations on the use and disposal of effluents generated by this type of veterinary medicine.

2. ORGANISATION OF THE EXPERT APPRAISAL

The expert appraisal was carried out in accordance with French Standard NF X 50-110 "Quality in Expert Appraisals – General requirements of Competence for Expert Appraisals (May 2003)".

ANSES entrusted examination of this request to the Expert Committee on "Animal Health and Welfare" (CES SABA). The Agency also mandated a dedicated working group on "EAP DSSs" for this expert appraisal.

The methodological and scientific aspects of this group's work were regularly submitted to the CES SABA. The report produced by the working group takes account of the observations and additional information provided by the CES members.

ANSES analyses interests declared by experts before they are appointed and throughout their work, in order to prevent risks of conflicts of interest in relation to the points addressed in expert appraisals.

The experts' declarations of interests are made public via the website: <https://dpi.sante.gouv.fr/>.

To answer all the questions in the internal request, the experts divided their work into three phases:

- 1) **Identify literature data and information on the professional context and changes to this information** (health situation, herd management), **as well as use practices** (methods of administration by animal owners, use of recommended or non-recommended spraying equipment, effluent management, etc.). For the part relating to users, background information on work and worker exposure situations concerning the uses of EAPs applied in sheep farming, which were addressed in volume 3 of the collective expert appraisal report relating to internal request No. 2011-SA-0192, has been summarised in this document. These data were updated with a literature review and supplemented by hearings. For the part relating to the environment, a literature review was carried out and supplemented by hearings.
- 2) **Assess the risks.** This part was to be based on a cross-disciplinary, integrated expert appraisal of the risks associated with the exposure of professionals applying veterinary medicines and exposure of the environment in connection with administration practices. In the absence of sufficient data and with no models available for veterinary EAP DSSs used on ruminant livestock farms, it was not possible to complete the exposure assessment and risk characterisation in this report. The recommendations were drafted on the basis of the information available in the literature, supplemented by hearings and the experts' knowledge of the field.

- 3) **Draft the recommendations** presented in the report in three parts. The first part sets out recommendations for ruminant livestock farms. The second part is aimed at exposed professionals. The third part concerns the environment, and makes recommendations on use and disposal of effluents generated by this type of veterinary medicine. These recommendations have been ranked according to the estimated time needed to implement them. A summary of the recommendations to be included in the SPCs is also proposed.

3. ANALYSIS AND CONCLUSIONS OF THE CES AND THE WG

3.1. Literature data and background information

The first part of the report covers the data available in the literature, supplemented by hearings and the experts' knowledge of the field. This part is divided into three chapters: a presentation of the context, the consequences for human beings of the use of EAPs, and the consequences for the environment.

3.1.1. Context

The professional context (health situation with regard to the diseases concerned, herd management), as well as EAP use practices (methods of administration by animal owners, use of spraying equipment whether recommended or not, effluent management, etc.), are changing rapidly. Numerous factors are behind the changes in "host-parasite-environment" systems, requiring animal health stakeholders to be extremely vigilant. Since the 2000s, the emergence, re-emergence and geographical spread of pathogens vectored by parasitic arthropods have been observed among ruminants in mainland France and Corsica. The presence of these various pathogens and the diseases they can cause has major consequences (loss of production, increased zoonotic risk, etc.). This trend seems to be largely favourable to certain external parasitic diseases (ovine psoroptic mange, myiasis) and vector-borne diseases, for which one of the main methods of prevention and treatment remains the use of EAPs.

As there is continuous and regular change in ruminant farming conditions and practices, the means of control and prevention constantly need to be adapted to new situations.

Currently, given the difficulties in treating certain parasitic diseases (psoroptic mange, myiasis, etc.), pyrethroids, organophosphates (OPs) and growth inhibitors are widely used in the field, whether for dips, showers or sprays (Table 1). Dipping, an ancient method of treating external parasites, is nevertheless very well suited to sheep and remains the method of choice for treating psoroptic mange. Showers are also common on sheep farms, as was confirmed by the hearings. For cattle in metropolitan France, spraying¹ is the only method of applying EAPs among those considered by the internal request.

Setting up a dip, shower or spray site is a complex operation that requires a great deal of rigour. Not only must the treatment be sufficiently effective, but the safety of animals, operators and the environment must also be ensured, by applying precautions including those recommended in the SPCs, at all stages of the operation. However, it appears that the current SPCs do not take account of all the stages for all products, and the hearings revealed cases of misuse on these treatment sites.

¹ The term "spraying" is used when equipment such as a sprayer fitted with a lance and nozzle is used

Table 1: Compounds of interest for the internal request and associated marketing authorisations

Name of medicine	Active substance	Chemical class	Mode of administration	Target species
BUTOX 50 POUR MILLE®	Deltamethrin	Pyrethroid	Spray	Cattle Sheep
CLIK®	Dicyclanil	Larval growth inhibitor	Spray (gun + spray nozzle)	Sheep
CLIKZIN 1.25% POUR-ON SUSPENSION FOR SHEEP®			Spray (gun + spray nozzle)	Sheep
ECTOFLY 12.5 MG/ML POUR-ON SOLUTION FOR SHEEP®	Cypermethrin	Pyrethroid	Spray (gun + spray nozzle)	Sheep
SEBACIL 50% SOLUTION®	Phoxim	OP	Dip/Spray	Cattle Goats Equines Sheep Pigs

The only medicinal product currently available for dipping was authorised in 1985. BUTOX 50®, which had previously also been authorised for dips, was authorised in 1986. The other products were authorised between 2002 and 2012. In France, sales of EAP DSSs accounted for a third of the market for ruminant EAPs in 2018.

3.1.2. Potential consequences for humans of using EAP DSSs

In this part, the work and worker exposure situations concerning the uses of EAPs applied in sheep farming, which were addressed in volume 3 of the collective expert appraisal report relating to internal request No. 2011-SA-0192 "Occupational exposure to pesticides in agriculture", have been repeated and summarised. This information was updated following a literature review, and supplemented by the hearings conducted by the working group.

The data collected suggest that dermal absorption is the main route of human exposure. Furthermore, in addition to exposure due to work situations during or after treatment, undesired exposure events (falling into the dipping tank, etc.) are also a major source of contamination.

The different types of personal protective equipment (PPE) and the different application methods have an impact on the level of exposure to EAP active substances. The effectiveness of the PPE depends on its specific characteristics, how the EAP is applied and how the PPE is used by workers. The data and the hearings suggest that EAP users are reluctant to equip themselves with PPE. Moreover, it seems that in the field, when it is actually used, this PPE can to some extent give workers a false sense of security. In addition, the effectiveness of this PPE has not been tested for EAPs under conditions of use in dips, showers and sprays.

The available data show that people employed in agriculture (salaried or self-employed farm workers) have a higher incidence of pesticide-related occupational diseases than people employed in non-agricultural industries². With regard to the products considered in this internal request, poisoning by organophosphates leads to neurological syndromes with acute or

² Calvert, Geoffrey M, David K Plate, Rupali Das, Rachel Rosales, Omar Shafey, Catherine Thomsen, Dorilee Male, John Beckman, Ernest Arvizu and Michelle Lackovic. 2004. "Acute occupational pesticide-related illness in the US, 1998–1999: Surveillance findings from the SENSOR-pesticides program." *American Journal of Industrial Medicine* 45 (1): 14-23.

chronic effects, such as acute cholinergic crisis³, intermediate syndrome⁴, induced delayed polyneuropathy⁴, chronic neuropsychiatric disorders⁵, anxiety and depression⁶, and even cancers⁴⁷ such as non-Hodgkin's malignant lymphomas. Organophosphate compounds are also considered to be endocrine disruptors⁸.

Acute toxic effects are known to occur among sheep farmers exposed to organophosphates when dipping their sheep. Although the results of the studies carried out are sometimes contradictory, long-term health effects appear to occur in certain professionals working on sheep-dipping sites and exposed to concentrated solutions of organophosphates in the course of their working lives⁹.

Inhalation, dermal or oral exposure to pyrethroids – or a combination of these routes – can cause respiratory, neurological and gastrointestinal symptoms, as well as haematological and immune diseases.

3.1.3. Potential consequences for the environment of using EAP DSSs

This part presents all the possibilities for environmental exposure.

There are few publications summarising the available analytical data on environmental contamination by residues of ruminant EAP treatments. British and Australian studies have reported environmental contamination accidents, mainly in water courses.

The management of dipping water (several hundred litres for each site), drainage from showers and run-off from the skin of treated animals, direct release into pastures via urine and faeces, and the presence of residues of these insecticides and acaricides in effluents, which are themselves spread on agricultural soils, all contribute to environmental contamination.

Physico-chemical and ecotoxicological data show that the active substances in question persist for varying lengths of time in soil, water and sediment. It should be pointed out that metabolites can sometimes be more persistent than the parent substance itself.

Terrestrial arthropods, aquatic invertebrates and aquatic vertebrates are all highly susceptible to pyrethroids, more so than terrestrial vertebrates. For example, phoxim has moderate to high acute toxicity in terrestrial vertebrates and moderate toxicity in *Apis mellifera* and earthworms (*Eisenia foetida*), but high chronic toxicity in aquatic vertebrates and a noticeable effect on soil

³ Jamal, G. A., S. Hansen, F. Apartopoulos, A. Peden, M. Abdul-Aziz and J. P. Ballantyne. 2001. "Peripheral nerve dysfunction in farmers using organophosphate sheep dip." *Journal of Nutritional and Environmental Medicine* 11 (1): 9-22. <https://doi.org/10.1080/13590840020030221>

⁴ Jaga, Kushik and Chandrabhan Dharmani. 2003. "Sources of exposure to and public health implications of organophosphate pesticides." *Revista panamericana de salud pública* 14: 171-185

⁵ Jayasinghe, S. S., K. D. Pathirana and N. A. Buckley. 2012. "Effects of Acute Organophosphorus Poisoning on Function of Peripheral Nerves: A Cohort Study." *PLoS One* 7 (11). <https://doi.org/10.1371/journal.pone.0049405>

⁶ Judge, Sarah J, Claire Y Savy, Matthew Campbell, Rebecca Dodds, Larissa Kruger Gomes, Grace Laws, Anna Watson, Peter G Blain, Christopher M Morris and Sarah E Gartside. 2016. "Mechanism for the acute effects of organophosphate pesticides on the adult 5-HT system." *Chemico-biological interactions* 245: 82-89

⁷ INSERM. 2021. *Pesticides et effets sur la santé. Nouvelles données [Pesticides and health effects. New data]* (Montrouge). <https://www.inserm.fr/wp-content/uploads/2021-07/inserm-expertisecollective-pesticides2021-rapportcomplet-0.pdf>.

⁸ Diamanti-Kandarakis, E., J. P. Bourguignon, L. C. Giudice, R. Hauser, G. S. Prins, A. M. Soto, R. T. Zoeller and A. C. Gore. 2009. "Endocrine-Disrupting Chemicals: An Endocrine Society Scientific Statement." *Endocr Rev* 30 (4): 293-342. <https://doi.org/10.1210/er.2009-0002>

⁹ Ross, S. J. M., I. C. McManus, V. Harrison and O. Mason. 2013. "Neurobehavioral problems following low-level exposure to organophosphate pesticides: a systematic and meta-analytic review." *Crit Rev Toxicol* 43 (1): 21-44

microbial activity. Dicyclanil has low toxicity in terrestrial vertebrates, more marked toxicity in terrestrial or aquatic arthropods (effect due to the targeted action on certain development stages) and low toxicity in aquatic vertebrates.

While the impact of EAPs on coprophagous entomofauna has been considered since the 1990s, no specific studies have ever been conducted on the risk to certain species such as pollinators (wild and domestic). The discussions carried out as part of this work led to the conclusion that studies on this issue are needed.

3.2. Risk assessment

As the WG's work was not intended to generate data directly, and in the absence of sufficient data and available models for veterinary EAPs in the form of DSSs used on ruminant livestock farms, it was not possible to complete the exposure assessment and risk characterisation in this report. Only the information available in the literature, supplemented by the hearings and the experts' knowledge of the field, was used to draw up the recommendations. Under these conditions, it was not possible to carry out a cross-disciplinary, integrated expert appraisal of the human and environmental risks associated with the exposure of professionals applying veterinary medicines and exposure of the environment in connection with administration practices.

3.3. Recommendations

This third part, available in Annex 1, includes proposed recommendations tailored to exposed professionals (possibility of substituting EAP DSSs with other veterinary medicines, changing administration practices, collective or individual means of protection), as well as recommendations on herd management and protecting the environment.

The recommendations are divided into three parts, depending on whether they are aimed at ruminant livestock farmers or exposed professionals, or concern the environment. They have been ranked according to the estimated time required to implement them.

A variety of different stakeholders are likely to be involved in implementing these recommendations. The joint involvement of public authorities (DGS¹⁰, DGAL¹¹, DGCCRF¹², DDETSPPs¹³), national (e.g. INRS¹⁴, INSERM¹⁵, ANSES¹⁶) and European (e.g. EMA¹⁷) scientific establishments, professional organisations (GTVs¹⁸, GDSs¹⁹, chambers of agriculture, etc.), pharmaceutical companies placing veterinary medicinal products on the market and, lastly, the various stakeholders in the field (veterinarians, farmers and farmers'

¹⁰ Directorate General for Health

¹¹ Directorate General for Food

¹² Directorate General for Competition, Consumer Affairs and Fraud Control

¹³ Departmental Directorates for Employment, Labour, Solidarity and Population Protection

¹⁴ French National Research and Safety Institute

¹⁵ National Institute of Health and Medical Research

¹⁶ French Agency for Food, Environmental and Occupational Health & Safety, which includes the French Agency for Veterinary Medicinal Products

¹⁷ European Medicines Agency

¹⁸ Veterinary technical groups

¹⁹ Animal health protection groups

groups, occupational physicians and the MSA²⁰, private practitioners and hospital doctors more generally) is essential to the implementation of these recommendations.

In addition, specific recommendations for non-target species are given in the report. Research and development needs and recommendations to be included in the SPCs are also given.

3.4. Conclusions of the WG and the CES

The experts recommend:

- **Implementing all the recommendations** set out in Annex 1 to this opinion;
- Adding some of the proposed recommendations to the **SPCs** of the veterinary medicines concerned, as summarised in the report;
- Targeting **communication** on the proposed recommendations to all stakeholders (livestock farmers, prescribing veterinarians, technicians applying treatments, etc.);
- **Educational initiatives** to raise awareness and provide training (initial and continuing education) for all stakeholders, in order to improve practices. Vigilance will be needed to ensure that all stakeholders have been trained in the new practices and that they are properly implemented in the field;
- Extending the work at a later date to the **French overseas territories**. This is because the fight against parasites, vectors and vector-borne diseases in these regions is on a vastly greater scale, and is sometimes compounded by weather conditions that are particularly favourable to the development of parasites and disease vectors;
- Broadening the debate to include macrocyclic lactones, which can also be used to treat certain external parasitic diseases mentioned in the report. The use of macrocyclic lactones raises a number of questions because of their characteristics, in particular their high toxicity to terrestrial arthropods and aquatic organisms, and their persistence within ecosystems and food chains. In addition, there can be considerable environmental contamination from "pour-on" (or topical) treatments, the route of administration most commonly used in cattle, because large quantities are marketed with high concentrations of the active substance. Lastly, their repeated use leads to the selection of resistant nematode populations;
- Conducting a debate on all veterinary antiparasitics, not only those intended for food-producing animals but also those for pets. Indeed, if the health authorities wish to discuss this issue and take concerted action as part of the "One Health" concept, in order to protect the health of target animals and humans and avoid increasing environmental contamination, it will be necessary to examine current protocols regarding preventive and/or curative antiparasitic treatments for all domestic animals. In this respect, with the aim of making it easier for owners to use veterinary antiparasitics, very broad-spectrum, long-acting, dual-purpose (internal and external)

²⁰ National Health Insurance Fund for Agricultural Workers and Farmers

veterinary antiparasitics containing several active substances are increasingly being placed on the market, whereas the risk of parasite infestation should be assessed before even recommending the appropriate compound or compounds.

In addition, the experts stress the importance of introducing tools to help reduce antiparasitic inputs for both therapeutic and prophylactic purposes:

- Firstly, by assigning an "EcoScore" to each veterinary antiparasitic in order to improve prescription criteria;
- Secondly, as has already been done by the veterinary profession in the fight against the emergence of antimicrobial resistance ("EcoAntibio plan"), the experts recommend introducing a national and European "EcoAntiparasito" plan to raise awareness among the various users about the urgent need for action.

4. AGENCY CONCLUSIONS AND RECOMMENDATIONS

The French Agency for Food, Environmental and Occupational Health & Safety endorses the conclusions and part of the recommendations of the working group on "EAP DSSs" and the CES SABA concerning the assessment of risks to human health and the environment from administering veterinary EAPs in the form of dips, showers and sprays.

Major changes are currently taking place in the professional context and the practices of livestock farmers in France when using EAPs on ruminants, due to the emergence, re-emergence and geographical spread of pathogens vectored by parasitic arthropods, which have serious consequences.

The veterinary medicines available are relatively limited, with five commercial products using three classes of compounds (pyrethroids, organophosphates and larval growth inhibitors), most of which are covered by MAs obtained many years ago. Most ruminant treatments involve setting up a dip, shower or spray site. These are major operations that call for a great deal of rigour, and precautions that must be applied at every stage, mainly those recommended in the SPCs of the prescribed products. However, the current SPCs for the products used are outdated, having been drawn up when the MAs were granted. These MAs are themselves not very recent, and do not cover all the stages involved. This situation has given rise to many questions from users about the most suitable precautionary measures to take with regard to user and environmental risks. The hearings also revealed frequent cases of misuse on these sites.

There are very limited data available on user exposure to these products and environmental contamination, making it impossible to perform an assessment of the risks to applicators and the environment. However, regarding human exposure, although the results of studies carried out on sheep farmers exposed to organophosphates are sometimes contradictory, they do suggest that long-term health effects could occur in certain professionals working regularly on sheep-dipping sites and exposed to concentrated solutions of organophosphates in the course of their working lives.

With regard to the environment, although few data are available in France on contamination by residues of these EAP treatments, British and Australian studies have reported environmental contamination accidents, mainly in water courses.

Even with these limited data, ANSES notes that the experts have issued many recommendations seeking to reduce and improve the use of these antiparasitic DSSs in ruminants.

These recommendations, set out in Annex 1, primarily concern ways of reducing the use of antiparasitics in livestock farming through biosecurity, a pragmatic diagnostic approach, vaccination, integrated control methods and the monitoring of parasite populations. They then aim to reduce the exposure of professionals, mainly by carrying out studies on practices and PPE, and by working together with manufacturers of shower and spray equipment to improve prevention schemes. Lastly, there are numerous very specific recommendations on how to limit the release of treatment water into the environment, through good practice in the use of these products.

Given the scope of the recommended measures and the variety of stakeholders potentially involved in carrying them out, their effective implementation may require coordinated management and political support. In fact, some of the recommendations may need to be supported at European level, in order to amend current regulations (Annex 1, measure 6.2) and find the necessary funding. The creation of an "EcoAntiparasito" plan to provide political impetus and release the necessary resources for the phased implementation of all these recommendations is therefore justified.

Without waiting for such a plan to be put in place, two types of important measures can be put in place quickly:

- Updating the MAs of the products concerned to include the necessary recommendations in the products' SPCs;
- Efforts to raise awareness and inform veterinarians about this issue, mainly through professional seminars and conferences, and training initiatives through presentations in training curricula.

It should be noted that the WG's recommendations on hazard symbols (Annex1, 6.2) were not adopted by the Agency. Similarly, the presence of an EcoScore on the medicine's leaflet and packaging is not being considered, because European regulations on the authorisation and labelling of veterinary medicinal products (Regulation (EU) 2019/6) currently make it impossible. However, we would encourage this characterisation to be developed for all products.

ANSES therefore recommends:

- At European level:
 - Pursuing the work begun by ANSES on revising the guidelines for user risk assessments, to include the specific issue of EAPs, and monitoring its progress;
 - Presenting and promoting the WG's work to the European authorities (EMA) to encourage debate on the issue of assessing the environmental risks of EAPs by including exposure models;

- Promoting the WG's work to encourage a debate on the theme of "One substance, one assessment", including the uses of these substances in veterinary medicine.
- At national level:
 - Asking the marketing authorisation holders of the medicines in question to revise the SPCs of the products considered by the internal request;
 - Advising the veterinary profession to draw up a guide to good practice in the use of EAPs, based on the recommendations in this report;
 - Promoting this work in order to pool pharmacovigilance data on veterinary medicines and plant protection products (for prevention in exposed workers);
 - Considering setting up a system for collecting waste and unused veterinary medicines, and including establishment of an "EcoAntiparasito" plan whose main purpose would be to oversee implementation of all the WG's recommendations in terms of livestock farming and prevention of human and environmental exposure. In summary, these recommendations cover:
 - training/information for professionals (farmers, technicians, future professionals, chambers of agriculture, GDSs, cooperatives, etc.) on livestock farming, prevention of human and environmental exposure;
 - dissemination of good practice to veterinarians and farmers in terms of livestock farming, prevention of human and environmental exposure;
 - R&D for livestock farming, prevention of human and environmental exposure;
 - monitoring of emerging and re-emerging diseases in livestock farming.

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ANNEX 1: RECOMMENDATIONS MADE BY THE WG

A short-term time frame is considered to be less than one year, a medium-term time frame less than five years, and a long-term time frame less than ten years. Ongoing vigilance is recommended for certain recommendations, which need to be made permanent.

1) Livestock farms

To limit the use of EAPs, the experts recommend:

1. Paying more attention to biosecurity on farms, in order to **limit exposure of herds to parasites and vectors**. It will be necessary to:

In the short term

- 1.1. Monitor animal purchases to prevent the introduction of new parasites and/or vectors on the farm,
- 1.2. Ensure the hygiene of buildings and the farm surroundings to prevent vectors from breeding on or near the farm,
- 1.3. Regularly maintain and clear undergrowth from grazing areas, particularly those used for susceptible animals, to limit tick population levels,
- 1.4. Take into account the proximity of other herds or animals (neighbours, gatherings, markets) in order to ensure the herd's external biosecurity: for example, by avoiding any possible intrusion by animals from other herds, by installing and regularly maintaining double fences that are sufficiently far apart to avoid any contact, by determining the infectious status of neighbouring herds with regard to certain parasitic or transmitted diseases, by health surveillance before and after gatherings, etc.,
- 1.5. Monitor the parasite load and vector pressure on the farm in order to react as quickly as possible,
- 1.6. Ensure close monitoring of the animals' state of health, regardless of the size of the herd, in order to detect any infestation/infection due to external parasites as early as possible, and rapidly take the appropriate **integrated control** measures(s),
- 1.7. Comply with biosecurity rules everywhere and in all circumstances, mainly in relation to nearby herds and whenever moving animals,

In the medium term

- 1.8. Reserve low-risk pastures for susceptible animals, in order to limit the infestation of certain consignments of animals by vectors and the onset of clinical signs of vector-borne disease,
- 1.9. Ensure that animals have access to shelters in their pastures, natural ones at the very least but preferably specially built ones, to protect them at times when flying vectors are most active during the day. The built shelters should shade the animals and be sufficiently aired and naturally ventilated. It will be important to check that these shelters and their immediate surroundings are maintained, and animal effluents regularly removed from the ground, to ensure that they do not promote the development of certain parasites and vectors,

- 1.10. Prioritise the use of biocontrol methods (plants and plant extracts, parasitoids, predators, pathogens) over chemical control whenever available, in order to reduce the impact on the environment and the risk of acquiring chemical resistance,

In the long term

- 1.11. To enable the development of phytotherapy, it is important to encourage the validation of a list of plants and plant-based substances for which an MRL status will be defined. This would then make a greater number of products available to prescribers (MA/therapeutic "cascade").

2. Implementing a relevant diagnostic and therapeutic approach. It will be necessary to:

In the short term

- 2.1. Respect the diagnostic approach, which constitutes the veterinary practitioner's core activity, in order to define carefully considered control methods tailored to the parasite and/or vector identified,
- 2.2. Conduct additional examinations to confirm the validity of the suspected diagnosis,
- 2.3. Provide the material resources needed to make the most accurate diagnoses, for example by deploying or promoting the serological diagnostic tool for sheep scab in France,
- 2.4. Maintain awareness among stakeholders in the sectors concerned,
- 2.5. Maintain national and international surveillance,

In the medium term

- 2.6. As part of the mandatory health visits to sheep and cattle farms, suggest different themes for visits: for example, the correct use of EAPs, external parasites (mainly myiasis) or parasites that are vectors of disease,
- 2.7. Remove the active substances of these EAP DSSs from the Ministerial Order of 28 June 2011, so that the medicines containing them are no longer available as part of a livestock health programme through approved producer groups.

3. Most of the recommendations listed below are those typically given in the context of **emerging and re-emerging diseases**. According to ANSES's work (ANSES 2017²¹; Saegerman *et al.* 2019²²), it will be important to:

In the medium term

- 3.1. Conduct a review of the presence of vectors and parasites in France, and set up outbreak and programmed surveillance, in order to 1/ dynamically monitor populations, 2/ monitor potentially emerging species, 3/ obtain a map of insect vector breeding sites, 4/ detect vector-borne pathogens, 5/ monitor the emergence of resistance to insecticides/acaricides in these vectors. In the long term, this monitoring will enable the control measures implemented to be validated and adapted, mainly

²¹ ANSES. 2017. ANSES opinion and report on the risk of introduction of lumpy skin disease into France (Request No. 2016-SA-0120). (Maisons-Alfort: ANSES), 160 p.

²² Saegerman, C., S. Bertagnoli, G. Meyer, J. P. Ganiere, P. Caufour, K. De Clercq, P. Jacquiet, C. Hautefeuille, F. Etoire and J. Casal. 2019. "Risk of introduction of Lumpy Skin Disease into France through imports of cattle." *Transbound Emerg Dis* 66 (2): 957-967. <https://doi.org/10.1111/tbed.13111>.

as part of integrated control, and will limit insecticide treatments to periods when the parasites are active,

- 3.2. Develop dedicated websites (within the epidemiological surveillance platform for animal health, for example), enabling regular monitoring of the epidemiological situation for the most susceptible parasitic and vector-borne diseases,
- 3.3 Conduct reviews of the distribution of vectors, and monitoring to anticipate the arrival of a previously unknown vector.

4. Concerning **vaccination**:

In the short term

- 4.1. Encourage the use of existing vaccines that have proved their value,

In the long term

- 4.2. Given the lack of vaccine tools to date, consider which situations (vector, parasite and vector-borne pathogen) could benefit from them.

5. Introducing integrated control measures in order to use EAPs more precisely. It will be necessary to:

In the short term

- 5.1 Raise the awareness of all stakeholders (farmers, various advisers, veterinarians), so as to obtain an overall view of the health of the farm,
- 5.2. Inform livestock farmers and veterinarians about integrated control measures, in the same way as they are advocated for crops,
- 5.3. Choose the most suitable compound and application method from the outset, depending on the production sector and the available equipment and labour, and the farmer's technical capabilities,
- 5.4. Take action as quickly as possible, in order to control parasites and/or vectors before they reach peak activity (during the growth phase), which would then reduce EAP consumption,
- 5.5. Dipping should be preferred when choosing a topical treatment for psoroptic mange in sheep, as showers and sprays are less effective,

In the medium term

- 5.6. Avoid conflicting messages from the various stakeholders and others involved in livestock farming on the relevance of the actions to be taken,

In the long term

- 5.7. As far as possible, when prescribing, alternate the compounds or classes of compounds to avoid a lack of effectiveness due to the development of resistance,
- 5.8. Biocontrol methods should be preferred when available.

6. Equipment purchase:

In the medium term

- 6.1. Improve dipping systems (access for ewes to the tank, system developed in the United Kingdom with cage and lift for several ewes and direct dipping, screens to protect operators from splashes),

- 6.2. Work with departmental or interdepartmental chambers of agriculture, departmental and regional GDSs, agricultural cooperatives and producer groups, to provide livestock farmers with effective, safe and suitable shared equipment (while keeping in mind biosecurity rules when equipment is shared),
- 6.3. Use more effective and safer equipment.

7. Misuse:

In the short term

- 7.1. Rigorously monitor and combat the inappropriate use of hygiene products (such as PT18) that are misused and applied to animals as EAPs, with all the consequences that this entails in terms of hazards for the "treated" animals, users, the environment and ecosystems, as well as for consumers of the foodstuffs produced,
- 7.2. For DDPPs or DDETSPPs, ensure that cases concerning the misuse of biocides/hygiene products are followed up.

In addition, specific recommendations for lumpy skin disease, hypodermosis and psoroptic mange are given in the report, along with research and development needs.

2) Prevention for exposed professionals

To put in place a preventive approach in occupational health, it is necessary to draw on the nine major general principles (Article L.4121-2 of the French Labour Code) governing the organisation of prevention.

1. Avoiding risks means eliminating the hazard or exposure to the hazard.

While responding to this internal request and following on from the findings of the ANSES WG on "Occupational exposure to pesticides in agriculture", whose finalised report was published in July 2016 (ANSES 2016), it was noted that the state of knowledge on EAP uses, circumstances of exposure and exposure levels among users and farmers during contact with treated animals was extremely fragmentary. However, the few data collected for a case study conducted by the aforementioned ANSES WG, as well as the hearings held while responding to this internal request, have shown that the levels of exposure are not negligible and that the conditions of use of these EAPs could be greatly improved. It is therefore necessary to determine the uses, exposures during treatment and when in contact with treated animals, their levels and their determinants, in order to more effectively prevent exposure in the context of compiling MA application dossiers, and also when prescribers are advising on the best possible conditions of use. A number of recommendations can be made.

In the short term

- 1.1. Prescribe medicines while providing users with all the relevant information on their correct use, as well as recommendations for prudent use as specified in Regulation (EU) 2019/6. The prescription must reiterate the rules for protecting users;

In the medium term

- 1.2. Organise collection, on a representative sample of livestock farms, of the information contained in the herd registers, in order to better document the uses, frequencies, conditions of application (fixed or mobile dipping tanks, showers, sprays, etc.), people concerned by the treatments, etc.;
- 1.3. Study the possibility of setting up a study of livestock rearing practices based on the studies of cropping practices carried out in the various crop systems over many years. These studies mainly document uses of inputs. Another option would be to adapt the study of livestock rearing practices carried out in 2016 on four farming types (cattle, goats, pigs and poultry) to sheep farming. However, this study did not examine the uses of inputs, or the frequencies, product types or conditions of use;
- 1.4. Produce measurements of exposure for livestock farmers and agricultural technicians while applying EAP treatments and of indirect exposure from contact with treated animals, following the OECD recommendations (OECD 1997, 2002; EFSA 2010) for pesticide exposure measurements and drawing on studies conducted by the UK's Health and Safety Executive (HSE)²³.

2. Assessing risks means assessing exposure to the hazard and the extent of the risk in order to prioritise the preventive measures to be taken.

No risk assessment could be proposed based on the above findings. If the above recommendations were followed, it would be possible to propose the development of predictive exposure models similar to those developed for plant protection products and certain biocides, in order to conduct a post-approval risk assessment of the EAP.

There are still too few data collected on the short-term adverse effects associated with the use of EAPs, as they are not surveyed in an organised way.

In the short term

- 2.1: Coordinate the pharmacovigilance missions for veterinary medicines (particularly EAPs and any other classes of medicinal products) with ANSES's phytopharmacovigilance missions for plant protection products. The aim of this is to centralise data for a single compound;

In the medium term

- 2.2. Encourage the production of health data on the adverse effects of exposure to EAPs;
- 2.3. Update the risk assessment conducted as part of MA applications for EAP DSSs, in order to refine the risk levels and identify the data to be collected more precisely.

3. Combating risks at the source means integrating prevention as far in advance as possible, mainly at the design stage of treatment sites, equipment and operating procedures.

The available recommendations on plant protection products in general, as well as some recommendations made by the HSE in Great Britain for carrying out EAP dips, should be adapted for all phases of EAP treatments. A number of recommendations are therefore made.

In the medium term

- 3.1. Plan to apply the EAP treatment in the area where plant protection products are prepared if such an area exists. If not, plan for the organisation of such an area based on the specifications for areas where plant protection products are prepared;

²³ www.hse.gov.uk/pubns/ais41.htm

- 3.2. Conduct a survey of mobile or fixed equipment used to apply treatments in order to identify improvements to be made, such as those proposed by the HSE concerning mobile dips with integrated draining pens;
- 3.3. Organise a consultation with the manufacturers of this equipment to improve user safety in terms of workplace risks (chemicals, falls from a height, posture, etc.);
- 3.4. Introduce a technical inspection for mobile dips and shower cabins based on the inspections for sprayers, but while also prioritising user exposure;
- 3.5. Modify the packaging for veterinary medicines, which must prioritise user practicality and safety, and environmental protection. Adding a device (extended spout, translucent gauge, anti-opening device, etc.) to bottles for decanting products without pre-dilution would reduce exposure²⁴.

4. Adapting work to the person, while taking account of inter-individual differences, with the aim of reducing the health effects.

The populations affected by the use of EAPs are ill-defined. Various service providers are involved in applying the treatments. They may belong to the MSA scheme, but may also be employed or self-employed and covered by other health insurance schemes. They are often assisted by self-employed farmers, employees or even family members. Furthermore, even less is known about indirect exposure to EAP residues, even though these products are persistent on animals and may affect the same people during subsequent contact with treated animals, particularly during shearing. In the HSE's sheet on "Sheep dipping", it states that "In the weeks that follow dipping, dip residues remain on the sheep" and it is therefore recommended that waterproof clothing and disposable gloves be worn when handling the animals. This recommendation is imprecise (a few weeks) but illustrates the need to better document exposure through indirect contact, as recommended in point 1.4. It is therefore necessary to better identify the populations concerned by this direct or indirect exposure to EAPs in terms of their status (employed or self-employed on a farm or by a service provider), age groups and gender, in order to estimate the specific risks of health effects.

5. Taking account of technical developments means adapting prevention to technical and organisational changes.

Little is known about the technical and organisational aspects of dipping and spraying operations. Following the review proposed in recommendations 1.2 and 1.4, it will be necessary to organise annual monitoring of technical and organisational changes by carrying out these surveys on a regular basis.

6. Replacing what is dangerous with what is safer means avoiding the use of hazardous processes or products when the same result can be obtained with a method that is less hazardous.

There are few different active substances on the market today, making it difficult if not impossible to choose between different products.

In the short term

- 6.1. Avoid using carcinogenic, mutagenic or reprotoxic (CMR) products;

²⁴ Example proposed in the SPC via this link:
<http://www.ircp.anmv.anses.fr/rcp.aspx?NomMedicament=DELTANIL+10+MG/ML+SOLUTION+POUR+POUR-ON+POUR+BOVINS+AND+OVINS>

In the medium term

- 6.2. Put hazard symbols and risk phrases on the containers of these products as is done for plant protection products.

7. Planning prevention while including technology, working conditions and organisation, social relations and the environment.

In the short term

- 7.1. Ensure the safest possible conditions when preparing the treatment site by identifying the situations involving the most exposure: transporting and handling concentrated products, preparing treatment solutions and filling equipment,
- 7.2. Use PPE gloves, goggles and masks;
- 7.3. Treatment phase:
 - Comply with the prescribed doses;
 - Avoid using products that are out of date or that have been open too long, because of the risk of ineffectiveness;
 - Ensure correct and appropriate use of equipment;
 - Clean used tools and equipment;
 - Wash gloves and then hands;
 - Do not eat, drink or smoke during product preparation and treatment phases;
- 7.4. Exposure factors:
 - Take climatic conditions into account: avoid very high temperatures to ensure that PPE does not become too uncomfortable;
 - Anticipate technical incidents and unexpected events due to animal handling;

In the medium term

- 7.5. Ensure that there are dedicated premises and improve storage conditions. Create a product preparation area, and a waste recovery and treatment area for soiled PPE and effluent recovery;
- 7.6. Provide personal protection kits with gloves, goggles and masks;
- 7.7. For sheep:
 - Recommend hydraulic dipping cage systems (e.g. models used in the United Kingdom);
 - Set boundaries around the treatment area;
 - Channel the animals to facilitate their entry and exit;
 - Operators must be able to move around unhindered;
 - The area around the treatment site must be kept clear of all obstructions;
 - The use of restraint corridors, part of which are fitted with solid walls 85 to 90 cm high and 45 cm wide, or less for lambs, makes it easier to restrain the animals and prevents them from turning around.
- 7.8. For cattle:
 - Here too, the restraint corridors, part of which are fitted with 1.60 m solid walls, or lower for calves, force the animals to raise their heads as they attempt to look at their surroundings. These corridors optimise restraint and prevent the animals from retreating, making treatment easier;
 - A platform running the length of the corridor ensures that the operator is in a raised position, making work on the animals easier;

- In all cases, operators are freer to move around and more at ease in their activities.

8. Giving priority to collective protective measures.

In the short term

- 8.1. Some systems can be carried on the operator's back. In this case, there is a risk of product leakage. Spraying EAPs from these tanks requires the use of a trigger, which is also a potential leakage factor. Dermal penetration requires essential protection of the operator's skin, mainly the hands. Nitrile or neoprene gloves are recommended, ideally with long cuffs covering the forearm and upper arm, as they are resistant to many chemicals, acids and petroleum products often used as excipients;
- 8.2. Users must protect themselves from splashes with PPE (hat, goggles, gloves, cape, overalls and boots), all of which must be able to shield them from the products used. This protective equipment must fit the users and comply with the standards in force. Thought should be given to establishing a procedure for dressing and undressing, while carefully avoiding mixing work clothing with everyday clothing;
- 8.3. It is important not to wash soiled clothes, accessories and overalls in the family washing machine;
- 8.4. Operators or managers must replace any worn, damaged or ageing protective equipment;
- 8.5. Operators or managers must observe hygiene measures for the storage and maintenance of this equipment;

In the medium term

- 8.6. The use of secure collective systems to treat animals is recommended, along with the other recommendations made above (restraint corridors (7.7 and 7.8), dip bath maintenance (3.4), design of product packaging (3.5), etc.);

In the long term

- 8.7. Research and development into the quality, effectiveness and design of collective protective measures and PPE should be promoted.

9. Giving appropriate instructions to users and prescribers, and training and informing employees so that they are aware of the risks and preventive measures.

In the medium term

- 9.1. Include information on the short- and long-term health risks of EAPs to users, in the initial training of operators (farmers, technicians, etc.). This information should be included in the reference standards for the BTSA diplomas currently being updated. It could be used as an opportunity to raise awareness of the risks and provide training in good practice, using the usual channels (GDSs, cooperatives, veterinarians). Provide brochures, leaflets and written recommendations on good practice.
- 9.2. In continuing education for livestock farmers, develop the Certiphyto and Certibiocide specifications to formally include EAPs and veterinary medicinal products more broadly (at least those with a pesticidal action similar to that of PPPs), as well as certain biocides;
- 9.3. Make the "Farmer as farm nurse" training courses mandatory (these already exist but are optional). These courses, run through partnerships between the attending veterinarian, departmental or regional GDS and regional or national GTV,

provide farmers with basic knowledge of veterinary medicines and explain the guidelines for good practice in the use and storage of veterinary medicines;

- 9.4. Include the adverse effects of EAPs on user health in continuing education for technicians (from cooperatives for the use of agricultural equipment and GDSs) and veterinarians;
- 9.5. Given the virtual absence of data on exposure levels and especially on their determinants, it will be difficult to make precise recommendations for reducing exposure levels until such data are generated. Generic recommendations can be made, but without ranking them:
 - For PPE: study the possibility of applying the AFNOR standards used for PPE intended for plant protection products, to EAPs. In addition, raise farmers' awareness of the importance of wearing and maintaining PPE;
 - For the management of used PPE, unused EAPs and rinsed or unrinsed packaging: set up a system similar to that for plant protection products via A.D.I.VALOR (Farmers, distributors and industrialists for the recovery of agricultural waste)²⁵;
 - Develop and make available educational videos or leaflets on good practice in EAP treatment.
- 9.6. Encourage healthcare professionals (general practitioners, pharmacists, etc.) to take account of chemical risk, in line with the actions of the PNSE²⁶. Communication campaigns could be carried out using posters in the premises of healthcare professionals. The data in the SPC constitute the main communication tool for veterinary medicines. An INRS toxicology sheet could be drawn up and made available to users and professionals.
- 9.7. Communicate with farmers/employees about risks and preventive measures via specialist journals, groups and the relevant professional organisations.

3) The environment

1. Prescription

In the short term

- 1.1. DSSs can only be used on veterinary prescription. The attending veterinarian must include in the prescription recommendations for disposing of waste water according to the farm's characteristics;

2. Animals

In the short term

- 2.1. Keep animals in a confined area (away from any water body or source) after treatment for at least 10 minutes to allow the solution to drip from their fleeces. This should ideally be a covered area to avoid waste water being washed away by rain;
- 2.2. If there are no buildings, leave the animals in a dedicated plot for 24/48 hours (check that there are no nearby water sources, streams, etc.) so that they can finish draining outside without the risk of contaminating surface water.

3. Fate of waste water

²⁵ www.adivalor.fr

²⁶ National Environmental Health Action Plan

In the short term

- 3.1. After dipping, recover all water used to rinse equipment along with the drinking water for the confined animals, and add it to the dip water or waste water from spraying;
- 3.2. Store the dip/spray water in closed containers, inaccessible to animals and humans, for 12 weeks to allow a significant reduction in the active substance content;
- 3.3. On the basis of current knowledge, discharging waste water into manure or slurry is not recommended (see Research needs);
- 3.4. Spread water on plots (meadows/pastures) after it has been diluted to a quarter. A maximum volume of 5000 L/ha can be spread in this way, avoiding plots rich in nectar-producing and attractive flora (points to watch in particular: spreading period, time of day, type of flora present). A plot should not receive any more than one application per year. When spreading in the wild, the applicator must ensure that the selected site and period comply with the appropriate environmental conditions (avoid frost or very dry weather, soil that is cracked or saturated with water, or karstic soil, and prioritise the use of permeable soil, on flat ground, located at least 50 m from any source or body of water, etc.);
- 3.5. The fate of the waste water should be recorded in the herd register, identifying the plot(s), if applicable, and the products and volumes applied.

If it is spread on land, disposal of the waste water must be traced. Plant protection product registers, or preferably herd registers, can be used to record the date, the medicine disposed of, the plot treated (and the crop if applicable), its surface area and the volume spread;

A collection voucher or invoice should be issued for treatment of residual product by a service provider, which can be recorded in the register.

In the medium term

- 3.6. Introduce a nationally organised and coordinated collection system (such as Cyclamed) for veterinary medicines and residual product. This collection system should first determine how it will be funded, as the current economic model is unable to cover the cost.

4. Training

In the medium term

- 4.1. Offer suitable training (based on the examples of Certibiocide or Certiphyto) for the farmers concerned, who will have an environmental "permit" for the disposal of DSS residues.

5. Veterinary medicinal products

In the medium term

- 5.1. Develop an "EcoScore" (based on the NutriScore® model) for EAPs that takes into account criteria such as persistence, bioaccumulation and toxicity. This "EcoScore", which should be directly accessible on the leaflets and packaging, would enable practitioners to determine the suitability of using one or other effective medicinal substance according to the prescribing context;
- 5.2. Ensure that MA holders specify the recommendations tailored to their products on the SPCs, and address the lack of information;

- 5.3. As recommended in the part on exposed professionals: conduct an independent risk assessment by estimating the frequency of exposure to active substances and determining a high level of uncertainty, in order to refine the risk levels and identify the data to be collected more precisely.

In the long term

- 5.4. Implement a risk assessment/management model taking into account the various possible scenarios for the disposal of EAP waste.