Therapeutic gaps in the Bee sector

Hearing of 15/12/25

Participants: Claude JOLY (ReProgen, SNGTV Beekeeping Commission), Lionel Grisot (Veterinary practitioner in Franche Comté, beekeeping appointed veterinarian for DDPP, member of the CSMV), Florentine Giraud (Beekeeping veterinarian in Haute Savoie, FNOSAD-LSA project manager, GDSA consulting veterinarian), Stéphanie Franco (ANSES – Sophia Antipolis laboratory, Head of the LNR bee health, veterinarian).
for the ANMV: L. Baduel, B. Leroux, F. Pillet, J. Bietrix, L. Fabry**.**

Reminder of the responsibility of the remarks made during the hearing and reported in this report:
- The identification of therapeutic gaps (and the details of the situations expressed and the alternatives envisaged) is the responsibility of the representatives of the veterinary profession
- The ANMV provides supplements or answers to the technical and regulatory questions addressed. These supplements are systematically preceded by "Info ANMV: ... to distinguish the origin of the words expressed.

Prioritization and Evolution of gaps since the last meeting in December 2023: see pages 7 and 8

Table summarizing the comments of the representatives of the veterinary profession (*new elements since the last hearing – in blue):*

0 VMP (Absence of appropriate veterinary medicinal products) **is highlighted in yellow when requesting a medicinal product with a veterinary marketing authorization for the species and indication concerned**

Disease	**Problem encountered:** **PhV: Pharmacovigilance (efficacy or safety perceived as unsatisfactory)** **Disp : Availability, shortage** **Reg: Regulatory ("cascade" use, withdrawal period, restricted access)** **0 VMP: Lack of appropriate veterinary medicinal products (VMPs)** **0 TS: Lack of a therapeutic solution**	**Problem Type : PhV, Disp, Reg 0 VMP 0 TS**	**Alternatives identified**	**PRIORITIES Major: M minor: m**
Varroosis	• **Decrease in effectiveness and questioning of certain treatments** Lack of effectiveness of authorized VMPs, resistance of varroa mites? Decreases in amitraz efficacy recorded by the FNOSAD-LSA for several years and even more significant during the efficacy tests carried out in 2022 => Resistance research via LDA 39 or the company APINOV has been conducted but is difficult because it requires a lot of live varroa mites. Problem because of the wide use (except in organic beekeeping) of strips which are the easiest to use. Their use alone, as an end-of-summer treatment, often seems not to be enough.	PhV	The list of available medicines has stabilised with 16 marketing authorizations, including 1 recent and one withdrawal: - CALISTRIP BIOX 6.44g tape: marketing authorisation (MA) in France (*via* Mutual Recognition / MR) on 22/11/24 and - POLYVAR YELLOW 275 MG beehive strip: discontinued on 28/09/2020. After resistance, possible return to sensitivity: after 3 to 4 years for tau-fluvalinate.	**M n° 1**

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	For the record: Different approaches to detecting resistance to acaricides exist: phenotypic or genomic. Work is underway on methods for detecting these resistances. **LNR:** A method, based on a biological test for exposure to tau-fluvalinate and amitraz, was developed by the company Apinov as part of a university thesis (see publication: Almecija, 2020). A molecular method for identifying **the genetic resistance of Varroa mites to tau-fluvalinate** has been developed by a Spanish research team (J. Gonzalez). The LNR began work on this method in 2020. Work is underway on a method to detect genetic resistance(s) **of Varroa to amitraz**. The LNR is in contact with the Apinov company and Spanish researchers on this subject. The results of the analyses carried out on French samples show that there is a good correlation for tau-fluvalinate between genotypic and phenotypic resistance (Almecija, 2022). In the case of amitraz, two mutations related to the observation of a loss of efficacy were described by the Spanish team (Hernandez-Rodriguez, 2022). More recently, Rinkevich et al. (2023) have shown a good relationship between the mutation observed in the United States and resistance to this substance. Research is underway on varroa mite populations in France to link certain mutations present in receptors to octopamine and tyramine. Genetic tests are currently based on the analysis of individual varroa mites, which takes time and involves a fairly high cost for the analyses. In order to overcome these constraints, the LNR is also working on the possibilities of mixing varroa mites from the same colony/apiary. The advantage of genetic methods for detecting resistance is that they can use dead varroa mites. ITSAP and ADA AURA are also involved in a project to study Varroa resistance to acaricides (SEMIVAR project). APINOV conducts research (thesis in progress) on behavioral resistance. **The FNOSAD-LSA** mentions **practical difficulties for the implementation of phenotypic resistance tests:** 1) there must be enough **live** varroa mites, which is not always easy to obtain, and often possible only towards the end of July – August, 2) dates when the laboratory's working capacities are limited or exceeded, and when it is often no longer possible to order suitable medicines (notably via the PSE), 3) the cost of these analyses is high (€200 to €300) and must be covered by the FNOSAD-LSA's own funds. => A test on dead varroa mites for amitraz as well as for tau-fluvalinate would be easier to implement. **Lionel Grisot** points out that the **tests are not always easy to use:** the strips have to be cut, the tests only cover phoretic varroa mites and expiry dates,		There are currently insufficient data on this return to sensitivity in the case of amitraz resistance, but work carried out by APINOV should be published soon. A study on resistance to oxalic acid has also been initiated. ⇨ **Wish for rapid diagnostic tests** to find out if tau-fluvalinate and amitraz are effective and therefore usable. **Info ANMV:** Tests APINOV, Pettis, Apiarium ➢ Communication to **stimulate research on new drugs?** A new molecule and/or pharmaceutical form of oxalic acid would be required for use in the presence of brood. Could the RFSA stimulate at national level the development of research and testing in case of resistance issues? ➢ **Research on galenic forms better adapted** to the kinetics of diffusion of molecules (repeated rather than prolonged exposure to reach the varroa mites present in the brood). Release of active ingredients not always "repeatable" in the strips. **ANSES info:** in the US there is NORROA™ (Norroa), a treatment (approved in September 2025) containing RNAi, which specifically targets Varroa mites and acts by stopping the production of their offspring. It is applied in the hive via the feeding of the workers, who will themselves feed the young developing bee larvae. **ANMV info:** In the EU, RNAi is classified as a " non immunological biological substance". In addition, recent guidelines impose an efficacy threshold of 90 to 95% for a varroocidal effect. ➢ Methods of distribution of active ingredients in the hive are not well known. **ANMV info:** no new information on this point, to our knowledge.	

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	and orders for treatments placed well in advance by the OSADs do not allow treatments to be adapted in the event of a problem of effectiveness. **The FNOSAD-LSA** renews its tests every year. The results are published in La Santé de l'Abeille. Overall, the results are worse each year, with a proportion of hives reaching the expected efficiency, of 28% for APIVAR and 55% for APITRAZ in 2024. However, the median efficacy remains at 92.24% and 96.5%: 327_LSA_TESTS_EFFICACITE_2024_FNOSAD_LSA.pdf. Decreases in efficiency and in particular in speed of action have been noted since 2017. Publications of interest: *Comparing the efficacy of synthetic Varroacides and Varroa destructor phenotypic resistance using Apiarium and Mason jar bioassay techniques - Bahreini - 2024 - Pest Management Science - Wiley Online Library* Results in Canada : *Arising amitraz and pyrethroids resistance mutations in the ectoparasitic Varroa destructor mite in Canada - PubMed.* ***For the record*** **ANMV info:** the number of PhV declarations is relatively limited and ± stable (about 30/year) since 2017 with an increase to 50 cases in 2019 in connection with the establishment of the network of the Observatory of Honey Bee Mortalities and Weakenings - OMAA). In the absence of data on the level of colony infestation, other causes of treatment failure such as excessive parasite pressure at the time of treatment are not excluded. The ANMV reminds that no "flash" effect of the strips is claimed and that it is necessary to wait 6 to 10 weeks before obtaining a sufficient reduction in the parasitic population. (cf. SPC APIVAR or APITRAZ § Route of administration and dosage: "In the presence of brood, the strips should only be removed after 10 weeks of treatment.") Since 2021, writing a guide document on the ANSES website, an article in Bee Health to promote pharmacovigilance and an article in GTV Bulletin on Good Practice for the use of VMPs against Varroa. The document with the important elements to be declared has been online on the ANMV website since 2022. However, there are still concerns about the rigour of detection and a lack of counting before treatment. Warnings concerning the risk of resistance are mentioned in the SPCs of VMPs with tau-fluvalinate or amitraz. It is important to know that the problems encountered in France are not necessarily reported in other European countries. **ANMV info:** The more exhaustive data concerning the apiaries concerned for the cases reported by the FNOSAD-LSA since 2022 have been received and integrated.			

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	In 2024: 55 cases of reported lack of efficacy, including 44 from the FNOSAD-LSA (incl. 28 cases from the 2022 tests not reported the previous year, and 16 cases from the 2023 tests) 2025: 38 cases of reported lack of efficacy, incl. 26 cases from the 2024 FNOSAD-LSA tests. The cases reported in 2025 were less complete than in 2024 regarding the description of apiaries and the methods of application of drugs (dose, repositioning, etc.), which generally did not allow us to conclude on the role of the VMP. Regular reporting of cases is very important to monitor efficacy. **FNOSAD-LSA:** Additional information may be provided. As a reminder, the number of declarations does not necessarily strictly reflect the situation on the field, but progress is being made thanks to better beekeepers' management and queens' caging. **L. Grisot & C. Joly** noted that vigilance on the precocity of treatments was improved in the regions sensitized by the GDS or the OMAA.			
	• **"Illegal" use of pure oxalic acid** (much cheaper). Handcrafted manufacture of glycerin-based strips. The fact that some beekeepers use this type of treatment all year round could lead to a risk of developing resistance in the long term. This use persists due to advertising on internet and in beekeeping equipment magazines and also to the price difference (e.g. €3 for crude oxalic acid *vs*. €350/kg for VARROXAL).		3 MAs for the use of oxalic acid in dripping (incl. VARROXAL MA of 08/09/23 - Very limited sales). It can also be used in sublimation for APIBIOXAL and VARROXAL and in spraying for VARROXAL. **MA in 2024 for CALISTRIP BIOX 6.44g strips**, but very expensive and its efficacy as summer treatment (when needed), is still to be demonstrated.	
Tropilaelaps	**Anses:** The expansion of these mites, mainly located in brood and originating from Southeast Asia, is an increasingly important threat to the EU. They can multiply very quickly. The diagnosis is not so easy. The early detection and identification of these mites and the crucial role of reference laboratories are therefore very important. France's current policy is eradication.	0 VMP	Existing miticides should be active, but the presence of mites mainly in the brood requires specific galenic forms, different for example from strips (liquid forms of formic acid in diffusers? FORMICPRO would be potentially interesting). Other formulations of formic acide are available abroad (FORMIVAR) It is essential to **look for solutions now** because registration by PSE requires a MA (as the use "*via* the cascade" of a VMP authorized against Varroa is not allowed in this context). **ANMV post-meeting info:** Two FORMIVAR products (NL/V/0265/001-002/MR) are authorized in 5 EU member states (AT, HU, NL, PT, SI): - FORMIVAR 60, 60 g formic acid /100 g bee-hive solution for honey bees - FORMIVAR 85, 85 g formic acid /100 g bee-hive solution for honey bees France was not involved in the mutual recognition (MR) procedure that led to these MAs in the 5 countries mentioned. No application for authorization to import FORMIVAR has been submitted to date.	**M n°2 or m+**

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Depopulation of the colonies	Products for euthanasia are considered as VMPs according to EU Reg 2019/6, which makes mandatory their administration by a veterinarian. The dangerousness of SO_2 requires professional use. One should have an easy-to-use device, in the form of a cylinder, for example, which would be more appropriate than wicks. **It is urgent to think about this because otherwise, with the risks of Aethina and Tropilaelaps introduction, we might be caught off guard.**	0 VMP	Unregistered and hazardous use of SO_2 wicks. It would be necessary to have an approved product available to beekeepers (not reserved for a veterinary act) because the elimination (= euthanasia) of sick colonies as soon as possible is one of the good beekeeping practices to be encouraged.	**M n°3 or m+**
Acarapidosis due to *Acarapis woodi*	This disease, whose agent is located in the tracheae and is mostly observed at the end of winter, was very rarely diagnosed in France (disappeared due to Varroa treatments?). However, it remains to be monitored. Indeed, for about four years, the OMAA has been finding them in different regions (AURA, Pays de la Loire, Occitanie, PACA, etc.) and sometimes out of season (June, August): resurgence or under-diagnosed before? In some cases, the symptoms are marked and can increase in the apiaries concerned. In others, it is a question of fortuitous discoveries.	0 VMP	Treatment with off-label volatile anti-varroa VMPs *via* the cascade (e.g. thymol-based VMPs, FORMICPRO). Recurrences observed in Isère despite treatments with APILIFE Var. Note: OMAA allows us to finance the initial visit triggered by the disorder observed, but not epidemiological investigations, hence the importance of raising awareness among beekeepers.	**m+**
Virosis	- DWV (Deformed Wing Virus) plays an important role in Varroa-related morbidity. The therapeutic issues are related to the fight against Varroa. - Chronic bee paralysis due to the Chronic Bee Paralysis Virus (CBPV) is also a disease with a high prevalence. - Many viruses identified but not always with clinical consequences. - Lack of treatment for these viruses.	0 VMP	Research on RNA interference (honey MRL). The current limitations are the difficulties of application and the cost of this type of treatment. **Info Anses:** A vaccine is marketed in the US by DALAN against American foulbrood (Bee Vaccine | Protect Your Hives Today — Dalan Biosciences) and would also be effective on DWV.	**m**
European Foulbrood	Disease well present. In the OMAA follow-up, disease in the "top 4" in the PACA and AURA regions. More frequent, more recurrent or more virulent cases. (cf. ECLEA study conducted by the LNR: 2017-2019). No medication allowed.	0 VMP	Ditto American Foulbrood.	**m**
American foulbrood	No medication allowed. But there is a risk of illegal use of antibiotics, leading to the development of resistance and problems of contamination of honey (residues). No need for chemical drugs (Tetracyclines forbidden (no MRLs), and inactive on *Paenibacillus larvae spores*). *For the record* **Note FNOSAD-LSA post 2021 hearing:** What are the benefits of bacteriophages (see publications below)? T. S. Brady *et al.*, 2017. Bacteriophages as an alternative to conventional antibiotic use for the prevention or treatment of *Paenibacillus larvae* in honeybee hives. *Journal of Invertebrate Pathology*, Volume 150, Pages 94-100, ISSN 0022-2011.	0 VMP	Vaccine in research project based on the vaccination of queens. See article 2022 : Frontiers | The oral vaccination with *Paenibacillus larvae* bacterin can decrease susceptibility to American Foulbrood infection in honey bees—A safety and efficacy study (frontiersin.org), et article dans la Santé de l'Abeille n°314 (Colin, 2023). The requirements on vaccines are different in Europe and the US, especially on the levels of efficacy. The methods of managing foulbrood are also different in Europe and the US. **Info Anses:** there is a "vaccine" marketed since 2023 in the US and Canada by DALAN (conditional authorization in the US) against American foulbrood. The company DALAN had contacted the ITSAP to carry out tests in France. *For the record:*	**m**

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	SB Santos *et al.*, 2019. Identification of the first endolysin Cell Binding Domain (CBD) targeting *Paenibacillus larvae*. *Sci Rep.* 2019 Feb 22; 9(1):2568. doi: 10.1038/s41598-019-39097-2. It should be noted that bacteriophages are expressly named in Annex II of the New Regulation 2019/6 as Advanced Therapies. Faced with the uncertainties linked to the change in the management of this disease (implementation of the LSA, abandonment of public health measures), it may one day be useful to have a drug control method provided that it is easy to use (easier than transfer for example) and not too expensive (and with all the qualities of a VMP).		**LNR:** Presentation of DALAN's product at various meetings organised at ANSES-Sophia Antipolis (which is LNR, LRUE and OMSA laboratory), WOAH, DGAL and FNOSAD in 2023. The efficacy, evaluated under laboratory conditions (larval rearing), is a priori average (30-50%). Effectiveness field data are still needed. Research is underway to develop vaccines for other diseases (European foulbrood and brood mycosis) Satisfactory treatment by transfer, change of bee strains, rules of sanitary measures.	
Nosemosis	A potentially fatal disease rarer than European foulbrood and much rarer than Varroa or viruses. N. apis *nosema* (symptomatic) seems to have disappeared in favour of *N. ceranae* (less symptomatic, weakening factor in the context of co-exposures). Rarely diagnosed. **LNR:** A case of *N. Apis* nosemosis was identified in the North-East of France in 2023, with remission. No new cases have been detected since. No medication. No MRLs for fumagillin (but not really necessary).	0 VMP	Many biotechnical methods are used to manage the emergency (change of queen, movement and ventilation of the hive). There is no real need for medication because it would be difficult to prescribe a treatment to fight a disease that is very difficult to diagnose, as Nosema is considered by many to be opportunistic.	**m**

Pathology: in the process of being resolved **with existing solution** **± being resolved?**	**Initial problem of the sector**	**Problem Type**	**Solution / Alternatives** **Reason for:** **Resolution in progress / Disappearance of the therapeutic gap**	**GAP initially** **Major: M** **minor: m**
	Varoosis: • **"Illegal" use of pure oxalic acid** (much cheaper). Artisanal manufacture of glycerin-based strips => if used all year round, risk of developing resistance in the long term? • **Resistance detection**	€	**=> New marketing authorisation** (CALISTRIP BIOX 6.44g strips) with oxalic acid (without residues in the waxes) and in the form of strips. It is an interesting alternative to the illegal use of "long-lasting" strips without MA, but at a very high price. Several years of use are needed before judging because any new drug arouses curiosity, but it is in the medium term that we can see if it provides a real solution **=> Several tests available** but not always easy to use	**M n°1**

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Prioritization of gaps by representatives of the veterinary profession

Prioritization of participants (excluding ANMV) Gaps identified	Claude JOLY	Lionel GRISOT	Florentine GIRAUD	Stéphanie FRANCO	PRIORITIES for 2023 Major: M minor: m
Varroosis	**M n°1**	**M n°1**	**M n°1**	**M n°1**	**M n°1**
Tropilaelaps	**m+**	**M n°2**	**M n°2**	**M n°2**	
Depopulation of the colonies	**M n°2**	**M n°3** Thoughts to be made on a drug for depopulation of the colonies	**m+** (Desire for a status other than a VMP: intermediate between biocide and VMp)	**M n°3**	
Acarapidosis due to *Acarapis woodi*	m	**m+**	**m+**	**m+**	**m**
Virosis	m	m	m	m	**m +**
American foulbrood	m	m	m	m	**m**
European Foulbrood	m	m	m	m	**m**
Nosemosis	m	m	m	m	**m**

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Changes in gaps since the last hearing in December 2023:

Rather favourable trend for:

- **Varroosis :**
  - Vigilance **and regular monitoring**, awareness-raising efforts and the increased precocity of treatments are positive, but there is still a lot of room for improvement in the heterogeneous world of beekeepers. In the field, many beekeepers are still losing colonies because of varroosis and have great difficulty in control. Development of **research and availability of tests on resistances**, but not always easy to use.
  - **New marketing authorisation** (CALISTRIP BIOX 6.44g strips) with oxalic acid (without residues in the waxes) and in the form of strips. Interesting alternative to the illegal use of "long-lasting" strips without MA, but very high price and its effectiveness as summer treatment still to be demonstrated.
- **Virosis and Foulbrood:** potential new therapeutic approaches based on vaccination and the use of RNAi (drugs currently available in the North American market).

Less favourable trend for:

- **Tropilaelaps,** an increasing acariosis, at the gates of Europe, without suitable, available and approved solution to date.
- **The depopulation of colonies,** in the absence of an approved and secure solution, if necessary.
- **Acarapidosis,** which remains to be monitored (upsurge in diagnosed cases), absence of medication with marketing authorization currently available in France.

	Hearing of 18/12/23	Hearing of 15/12/25
MAJOR PRIORITIES	1. **Varroosis** **- Decrease in effectiveness and questioning of certain treatments** **- "Illegal" use of pure oxalic acid** (much cheaper)	1. **Varroosis** **- Decrease in effectiveness and questioning of certain treatments** **- "Illegal" use of pure oxalic acid** (much cheaper) 2. **+ Tropilaelaps** 3. **+ Depopulation of the colonies**
Minor Priorities	• Virosis • American foulbrood • European Foulbrood • Nosemosis **+ Acarapidosis** due to *A. woodi*	• Acarapidosis due to *A. woodi* • Virosis • European Foulbrood • American Foulbrood • Nosemosis
± being resolved?		**Varroosis :** **Several resistance tests are available,** but not easy to use **New MA for oxalic acid in strips,** but cost >> "artisanal strips"
Existing solution	**Varroosis :** ☑ Caramelization of APIBIOXAL in sublimation **thanks to MA (09/23) for a new VMP** ☑ Availability and presentation problems for VARROMED **thanks to no more shortages**	