anses

NUTRIVIGILANCE

2023 Annual report

Since 2009, the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) has been responsible for implementing the French nutrivigilance system. Its purpose is to improve consumer safety by rapidly identifying any possible adverse effects related to the consumption of:

- food supplements[1];
- foods or beverages fortified with substances for nutritional or physiological purposes[2] (vitamins, minerals, amino acids, plant extracts, etc.) such as so-called energy drinks;
- novel foods and novel ingredients[3] (phytosterols, guar gum, noni juice, etc.);
- products intended as food for specific categories of the population[4] (infants, patients suffering from metabolic disorders, malnutrition, dysphagia, etc.).

Healthcare professionals (doctors, pharmacists, dieticians, etc.), private individuals and companies marketing the products are invited to report any adverse effects relating to these products of which they become aware.
Adverse effects can be reported on the adverse health event reporting portal of the Ministry of Labour, Health and Solidarity (https://sante.gouv.fr/soins-et-maladies/signalement-sante-gouv-fr/) or directly by completing the online reporting form (https://www.nutrivigilance-anses.fr).

These reports are recorded by ANSES, while preserving the consumer's anonymity. ANSES may contact the reporting party again to obtain any missing information. Sufficiently documented (analysable) cases are then examined by experts to define the severity of the effect and the likelihood of a link between consumption of a product and occurrence of an adverse effect (i.e. the causality).

To carry out this task, ANSES relies on the Nutrivigilance Working Group (WG) it set up.

[1] Governed by Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements.
[2] Governed by Regulation (EC) No 1925/2006 of the European Parliament and of the Council of 20 December 2006 on the addition of vitamins and minerals and certain other substances to foods.
[3] Governed by Regulation (EU) No 2015/2283 of the European Parliament and of the Council of 25 November 2015 on novel foods.
[4] Governed by Regulation (EU) No 609/2013 of the European Parliament and of the Council of 12 June 2013 on food intended for infants and young children, food for special medical purposes and total diet replacement for weight control.

The Agency informs the authorities of the cases it receives and may, if there is strong causality and high severity, be required to issue an alert. With the help of its experts and according to the effects observed, number of cases reported and causality of the products in question, the Agency then establishes its priorities for risk assessment work to be undertaken.

The nutrivigilance experts may also be asked to participate in the work of other working groups, in particular the WG on Plants, which was created by ANSES in May 2016 on the entry into force of the Ministerial Order of 24 June 2014 establishing the list of plants authorised in France in food supplements and the conditions of their use. This work leads to the publication of scientific opinions, along with recommendations for healthcare professionals, consumers and manufacturers. The opinions are submitted to the ministries concerned to enable them to take appropriate management measures.

Between the launch of the nutrivigilance system on 13 November 2009 and 31 December 2023, the Agency received 8695 reports.

KEY FIGURES

749 REPORTS RECEIVED IN 2023 (COMPARED WITH 711 IN 2022)

- 70% of cases were analysable, compared with 64% in 2022
- 6% of the analysable cases were severe[5] (severity levels 3 and 4), compared with 7% in 2022

18 ALERTS IN 2023

- Cases with strong causality[6] and high severity (life-threatening)
- Reports were sent to the Ministries of Health and Agriculture in order to determine suitable management measures
- Two alerts led to opinions being written

2 OPINIONS PUBLISHED ON SEVERE CASES WITH STRONG CAUSALITY

- ANSES Opinion on new cases of vitamin D poisoning in infants due to the misuse of food supplements
- ANSES Opinion on cases of bezoar associated with the consumption of enteral nutrition products

1 OPINION ON A PLANT-RELATED HEALTH RISK ASSESSMENT

This expert appraisal was based on an analysis of nutrivigilance cases.

- ANSES Opinion on the assessment of the relevance of applying warnings and recommendations expressed in the EMA's herbal monographs on medicinal products to herbal food supplements containing the same medicinal plants

[5] The scale of severity in nutrivigilance ranges from Level 1 (low severity) to Level 4 (death).
[6] The intrinsic causality score ranges from I0 (excluded) to I4 (very likely).

NEW ALERT ON VITAMIN D POISONING IN INFANTS DUE TO MISUSE OF FOOD SUPPLEMENTS

In 2021, ANSES published its first opinion on three reports of severe adverse effects in infants following misuse of food supplements containing vitamin D[7], along with a joint press release[8] with the ANSM, paediatric scientific organisations, the national college of midwives and poison control centres, in order to prevent further vitamin D poisoning. The recommendations for healthcare professionals and parents were primarily to:

- opt for medicines rather than food supplements;

- check the doses administered (verify the amount of vitamin D per drop);

- avoid combining consumption of several products containing vitamin D.

After these publications appeared, ANSES received three additional reports of severe hypercalcaemia, of level 3 severity or level 3 with life-threatening prognosis, occurring in infants after the use of food supplements not intended for children under 7 years of age containing 5000 IU or 10,000 IU of vitamin D per drop. The occurrence of these three new cases showed that these strong recommendations were not enough to protect consumers, and led ANSES to publish a new alert on its website.

These six cases recorded by nutrivigilance followed the substitution of vitamin D in medicinal form by a food supplement. This substitution resulted from a decision of the parents or inaccurate advice from a healthcare professional. The dosing error was due to confusion between the different ways in which the vitamin D doses are expressed. The vitamin D concentration in a medicinal product is given per mL, whereas in the food supplements consumed it is given per drop. This disparity in the definition of a concentration was clearly responsible for the overdose cases. ANSES therefore strongly recommends standardising the way in which the dosage is expressed.

Furthermore, ANSES notes that these products were purchased on the Internet, which increases the risk of dosage errors due to a lack of guidance. Lastly, the ease in accessing food supplements containing very high doses of vitamin D is another risk factor for overdose. ANSES believes that adequate oversight of formulation practices would help limit the risks of poisoning.

[7] Opinion on vitamin D poisoning in infants due to misuse of food supplements available at the following address: https://www.anses.fr/fr/system/files/NUT2020VIG0186.pdf (in French)

[8] Press release available at: https://www.anses.fr/en/content/vitamin-d-children-use-medicines-and-not-food-supplements-prevent-risk-overdose

CASES OF BEZOAR ASSOCIATED WITH THE CONSUMPTION OF ENTERAL NUTRITION PRODUCTS

ANSES published an opinion after being notified of nine cases of bezoars[9] with severity level 3 to 4 (death) involving consumption of the enteral nutrition products Fresubin 2kcal HP Fibre® or Fresubin 2kcal HP®. The causality of the two enteral nutrition products in the occurrence of the bezoars was deemed very likely in eight cases and likely in one case. All the cases recorded in this opinion, like most of those reported in the literature, occurred in an intensive-care setting with the following contributing factors: digestive or neurological comorbidities, associated use of medication that slows digestive transit, the particular composition and administration methods of the enteral nutrition and a failure to comply with good practice recommendations. This opinion led ANSES to:

- alert hospital practitioners to the risk of bezoar formation in patients fed with enteral nutrition products, especially patients with slowed digestive transit;
- recommend that manufacturers of enteral nutrition products conduct studies to identify the conditions under which bezoars form with their products, particularly the interactions with medicines commonly used by enterally-fed patients;
- encourage healthcare professionals to report to ANSES any adverse effects associated with the use of enteral nutrition products that they encounter as part of their professional practice, in order to improve patient safety.

Since the opinion was validated by the CES on Human Nutrition, two new cases of bezoars whose causality was very likely, respectively with severity level 3 and level 3 with life-threatening prognosis and involving the products Fresubin 2kcal HP Fibre® and Fresubin 2kcal HP®, have been reported to the nutrivigilance system. This brings the total number of cases to 11.

[9]A bezoar is a compact aggregate of partially digested or undigested material that usually forms in the stomach and can lead to total obstruction of the digestive tract.

NUTRIVIGILANCE CASES INVOLVING PLANTS WITH AN EMA MONOGRAPH

ANSES's WG on Plants assessed the relevance of applying warnings and recommendations expressed by the European Medicines Agency (EMA) in its herbal monographs on medicinal products to herbal food supplements containing the same medicinal plants. This expert appraisal work was used to supplement the existing health recommendations on the use of plants in food supplements, building on the work carried out on their uses in medicinal products. A table summarising the recommendations on each plant for specific populations (children, pregnant or breastfeeding women), drug interactions and allergy risks was also published.

An extraction of nutrivigilance cases involving food supplements containing at least one plant or plant essential oil examined as part of this work, was carried out. The results of this extraction are presented in the annex to the expert appraisal report.

Major projects

European project on emerging risks associated with food supplements

The safety of food supplements containing ingredients other than vitamins and minerals has often raised concerns at European level. The issue has been discussed on numerous occasions at the Advisory Forum[10] of the European Food Safety Authority (EFSA). Since 2006, EFSA's Scientific Committee has been working on guidelines for assessing the safety of plants and has created a directory of 2600 plants and the substances they contain (the *Compendium of Botanicals*). The Emerging Risk Exchange Network (EREN) asked EFSA to undertake a project to proactively identify emerging risks associated with food supplements.

Discussions with EFSA began in late 2022 and continued into 2023, with a view to determining the benefits to ANSES (and the other Member States) of participating in this project.

In autumn 2023, EFSA submitted a proposal for a project consistent with the focal points' tailor-made activities, concentrating on two areas:

- analysis of reports from nutrivigilance or other appropriate vigilance systems;
- identification of the presence on the market in Member States of food supplements containing plants identified in the aforementioned European compendium as potentially having toxic properties (identified by QSAR[11] methods).

This project will provide input for the discussions of a committee of the European Heads of Food Safety Agencies (HoA), which is drawing up a list of substances to be assessed by EFSA as part of a procedure under Article 8 of Regulation (EC) No 1925/2006 on food fortification. This procedure enables certain substances to be regulated where necessary (ranging from restricting the conditions of their addition through to prohibiting them) in food, particularly in food supplements.

A project group of thirteen countries (France, the Netherlands, Belgium, Italy, Portugal, Denmark, Ireland, Sweden, Croatia, Latvia, Slovenia, the Czech Republic and Hungary) has been set up and is being led by France (ANSES).

[10] The EFSA Advisory Forum forms the main link between EFSA and food safety institutions with a similar remit in the Member States.
[11] QSAR: Quantitative structure-activity relationship is a modelling method based on the quantitative and qualitative relationships between chemical structure and biological activity.

COMMUNICATION MEASURES TO PUBLICISE THE SYSTEM

In 2023, ANSES continued its training activities to raise awareness about the nutrivigilance system. More than 10 courses were given to students in pharmacy (third and fourth years, masters and DU university diplomas), sports science (degrees, masters and DU) and nutrition (masters and DU) from different universities in France.

In addition, an oral presentation was given at the congress of the Francophone Society of Nephrology, Dialysis and Transplantation (SFNDT) and a poster was presented at the congress of the European Society for Clinical Nutrition and Metabolism (ESPEN). The aim of these two presentations was to explain how the nutrivigilance system works and how the data obtained from adverse effect reporting are used.

Lastly, in addition to articles published in the scientific and mainstream press, nutrivigilance work provided input for an article in the bulletin for all ANSES's vigilance systems (Vigil'Anses)[12].

[12] https://vigilanses.anses.fr/

Main publications

ANSES. 2023. Opinion of the French Agency for Food, Environmental and Occupational Health & Safety on new cases of vitamin D poisoning in infants due to the misuse of food supplements (2022-VIG-0166). ANSES (Maisons-Alfort).

https://www.anses.fr/fr/system/files/NUT2022VIG0166.pdf

ANSES. 2023. Opinion of the French Agency for Food, Environmental and Occupational Health & Safety on cases of bezoar associated with the consumption of enteral nutrition products (2022-VIG-0182). ANSES (Maisons-Alfort).

https://www.anses.fr/fr/system/files/NUT2022VIG0182.pdf

ANSES. 2023. Opinion of the French Agency for Food, Environmental and Occupational Health & Safety on the assessment of the relevance of applying warnings and recommendations expressed in the EMA's herbal monographs on medicinal products to herbal food supplements containing the same medicinal plants (2019-SA-0155). ANSES (Maisons-Alfort).

https://www.anses.fr/fr/system/files/NUT2019SA0155.pdf

MONDIER CASINI, A and F. HURET. 2023. "Cases of chronic vitamin D poisoning in infants caused by the misuse of food supplements" Vigil'Anses 19: 16-19

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