anses

NUTRIVIGILANCE

2020-2021 Activity Report

Since 2009, the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) has been responsible for implementing the French nutrivigilance scheme. The purpose of this scheme 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 Social Affairs and Health (https://solidarites-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 declarant 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 (causality). ANSES relies on the Nutrivigilance Working Group to carry out this task.

[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, the Agency establishes its priorities for risk assessment work to be undertaken based on the effects observed, the number of cases received and the causality of the products in question.

The nutrivigilance experts may also be asked to participate in the work of other working groups (WGs), 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 intended for healthcare professionals, consumers and manufacturers. These opinions are submitted to the ministries concerned to enable them to implement appropriate management measures.

Between the launch of ANSES's nutrivigilance scheme on 13 November 2009 and 31 December 2021, the Agency received 7235 reports.

KEY FIGURES

1869 REPORTS RECEIVED (907 IN 2020; 962 IN 2021)

- 58% of cases were analysable (compared with 43% in 2019);
- 5% of the analysable cases were severe[5] (severity levels 3 and 4).

35 ALERTS (18 IN 2020; 17 IN 2021)

- Cases with strong causality and high severity (life-threatening);
- Reports sent to the Ministries of Health and Consumer Protection in order to determine suitable management measures;
- Four alerts published in the form of opinions.

6 OPINIONS ON SEVERE CASES WITH STRONG CAUSALITY

- ANSES Opinion on a case of fatal fulminant hepatitis associated with consumption of the food supplement Slim Metabol®;
- ANSES Opinion on cases of severe acute life-threatening hepatitis associated with consumption of the food supplement Chewable Hair Vitamins®;
- ANSES Opinion on a case of severe acute hepatitis associated with consumption of the food supplement SriSri Kanchanara®;
- ANSES Opinion on a case of oesophageal perforation associated with consumption of the food supplement PreserVision 3® capsules.
- ANSES Opinion on a case of seizures associated with consumption of the food supplement Novanuit® Triple Action;
- ANSES Opinion on cases of vitamin D poisoning in infants due to misuse of food supplements.

2 OPINIONS ON "PLANT" HEALTH RISK ASSESSMENTS

These expert appraisals used the analysis of nutrivigilance cases.

- ANSES Opinion on the use of Melaleuca essential oils in food supplements;
- ANSES Opinion on the assessment of the risk of hepatotoxicity associated with the coumarin content of certain plants that can be consumed in food supplements or in other foodstuffs.

[5] The scale of severity in nutrivigilance goes from Level 1 (low severity) to Level 4 (death).

FATAL FULMINANT HEPATITIS ASSOCIATED WITH CONSUMPTION OF THE FOOD SUPPLEMENT SLIM METABOL®

On 1 April 2020, ANSES issued an opinion on a case of fatal fulminant hepatitis (Level 4 severity) involving consumption of the food supplement Slim Metabol®. The causality of this food supplement in the occurrence of this death was considered likely.

This food supplement contained numerous ingredients including *Garcinia cambogia* and red yeast rice. The link between these two ingredients and liver effects is well documented in the scientific literature.

Moreover, ANSES noted that *Garcinia cambogia* was the subject of a decision by the French Health Products Safety Agency (ANSM) prohibiting the importation, preparation, prescription and dispensing of magistral, officinal and hospital preparations containing it, as well as the prescription, dispensing or administration to humans of this same plant. On the other hand, it appears under the name *Garcinia gummi-gutta* (L.) Roxb in the list of plants that can be used in food supplements, published by the Directorate General for Competition, Consumer Affairs and Fraud Control (DGCCRF), without any health recommendation or restriction.

ANSES therefore strongly advised against consumption of the food supplement Slim Metabol® and issued an internal request to determine whether safe conditions for the use of food supplements containing *Garcinia cambogia* could be identified.

MELALEUCA ESSENTIAL OIL IN FOOD SUPPLEMENTS: THEIR CONSUMPTION MAY NOT BE SAFE

Although Melaleuca leaves have not traditionally been used for food purposes in France, they have given rise to tea tree, niaouli and cajeput essential oils found in multiple food supplements. Some consumers misuse them as auxiliary therapies to treat certain infections. This is despite the fact that these essential oils are discouraged or even banned in some European countries due to their potential neurotoxic effects. ANSES therefore received a formal request from the DGCCRF to study the risks associated with their ingestion, and confirmed that according to current knowledge, the oral absorption of certain compounds in Melaleuca essential oils poses neurological (niaouli and cajeput), carcinogenic, genotoxic and potentially reprotoxic risks. To prevent these risks, the Agency issued recommendations on the storage and dosing of these essential oils. Depending on the target population, it recommended that they be avoided or even prohibited. In particular, ANSES advised against their consumption by children and pregnant or breastfeeding women, and recommended banning the consumption of niaouli and cajeput essential oils by children under the age of 30 months and children with a history of epilepsy or febrile convulsions.

Major projects

Overhaul of the reporting website and the nutrivigilance database

The project to overhaul the reporting website and the nutrivigilance database, initiated in November 2019, culminated in the launch of both tools in January 2021. The more user-friendly remote reporting site makes the process easier by enabling people submitting reports to provide the maximum detail on cases in a shorter time. The new database for in-house processing reduces the time needed to deal with these reports and optimises the use of information by making it easier to identify ingredients, products or situations posing a risk.

International network on nutrivigilance

Despite the existence of European Directive 2002/46/EC defining food supplements, regulation of these products varies considerably from one country to another. For example, with regard to their placing on the market, some countries do not impose any pre-marketing obligations, in accordance with the European Directive, while others have set up notification or authorisation systems. The composition of food supplements can also differ widely depending on the country. An ingredient authorised in one European country may be prohibited in another. Despite this, these products may be available throughout Europe due to the free movement of goods. The same disparity exists in the monitoring of adverse effects, since few European countries have developed a dedicated vigilance system. Nevertheless, several countries are considering or have already started establishing a system comparable to the French nutrivigilance scheme; they include Croatia, Italy, Ireland, the Czech Republic, Slovenia and Sweden.

To unify these schemes and raise awareness among other Member States, on 12 June 2014, ANSES had hosted a kick-off meeting in Maisons-Alfort for a nutrivigilance information exchange network, which was attended by 13 Member States.

Since then, the initial network has grown to include 28 countries: Austria, Germany, Belgium, Brazil, Cyprus, Croatia, Denmark, Spain, Estonia, Finland, France, Greece, Hungary, Ireland, Italy, Latvia, Luxembourg, Malta, Norway, the Netherlands, Portugal, Serbia, Slovakia, Slovenia, Sweden, Switzerland, the Czech Republic and the United Kingdom.

This network enables the sharing of information on cases, literature and the concerns of Member States. This pooling of knowledge on product composition and the cases reported in other European countries is essential in the context of the free movement of goods.

ANSES coordinated the drafting of an article involving the seven European countries with a vigilance scheme for food supplements. This article was published in May 2021.

Key events

Reporting by the general public now possible

Until August 2020, according to the French Public Health Code (Art 1323-2 and R1323-4), only healthcare professionals, other vigilance schemes and producers or distributors could report adverse effects under the nutrivigilance scheme. At the request of ANSES, the general public has now been added to the list of authorised reporting parties in the Public Health Code (Decree No. 2020-1094 of 27 August 2020). Any individual who has experienced an adverse effect can now report it directly to the nutrivigilance scheme. However, they are still advised to ask a healthcare professional to objectively assess the adverse effect and submit the report on their behalf.

Between 1 August 2020 and 31 December 2021, 89 cases were reported by the general public, accounting for 8% of the 1127 cases reported.

VITAMIN D POISONING IN INFANTS DUE TO MISUSE OF FOOD SUPPLEMENTS

The Agency was informed of three cases of severe hypercalcaemia (Level 3 severity), one of which was life-threatening, in infants following the use of adult food supplements containing 10,000 IU per drop of vitamin D. These adverse effects were likely or very likely due to vitamin D poisoning associated with the misuse of these products. In order to prevent further vitamin D poisoning, ANSES, together with the ANSM, paediatric scientific societies, the National College of Midwives and poison control centres, published a press release[6] in January 2021 aimed at healthcare professionals and parents, recommending that they opt for medicines rather than food supplements, check the doses administered (verify the amount of vitamin D per drop) and avoid combining the consumption of different products containing vitamin D. ANSES pointed out that the different ways of expressing vitamin D dosages (per mL or per drop) and the different intake regimens (daily or spaced) lead to confusion and increase the risk of misuse and therefore of severe adverse effects. This lack of uniformity should be limited in order to reduce the risk. The cases analysed clearly showed a huge discrepancy between the supplementation dose usually prescribed for infants and that applied after changing the source of vitamin D supplementation.

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

Outlook and future projects

The following expert appraisals were initiated in 2020 or 2021, in connection with the nutrivigilance scheme:

- Expert appraisal on the risks associated with consumption of food supplements containing turmeric;
- Expert appraisal on the risks associated with consumption of food supplements containing *Garcinia cambogia*;
- Request for an opinion on the risks associated with the use of *Withania* somnifera (L.) Dunal preparations in food supplements.

COMMUNICATION MEASURES TO PUBLICISE THE SCHEME

In 2020 and 2021, ANSES continued its training activities in order to raise awareness about the nutrivigilance scheme. More than 20 courses were given to students in pharmacy (third and fourth years, masters and DUs [university diplomas]), sports science (masters and DUs) and nutrition (masters and DUs) from different universities in France.
In addition to articles published in the scientific and mainstream press, nutrivigilance experts published six articles in the bulletin for all ANSES's vigilance schemes (Vigil'Anses)[7].

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

Main publications

ANSES. 2021a. ANSES Opinion on a case of seizures associated with consumption of the food supplement Novanuit® Triple Action (Request No. 2020-SA-0123). Maisons-Alfort: ANSES. https://www.anses.fr/fr/system/files/NUT2020SA0123.pdf

ANSES. 2021b. ANSES Opinion on a case of oesophageal perforation associated with consumption of the food supplement PreserVision 3® capsules (Request No. 2020-SA-0071). Maisons-Alfort: ANSES. https://www.anses.fr/fr/system/files/NUT2020SA0071.pdf

ANSES. 2021c. ANSES Opinion on vitamin D poisoning in infants due to misuse of food supplements (Request No. 2020-VIG-0186). Maisons-Alfort: ANSES. https://www.anses.fr/fr/system/files/NUT2020VIG0186.pdf

ANSES. 2021d. ANSES Opinion on the assessment of the risk of hepatotoxicity associated with the coumarin content of certain plants that can be consumed in food supplements or in other foodstuffs (Request No. 2018-SA-0180). Maisons-Alfort: ANSES. https://www.anses.fr/en/system/files/NUT2018SA0180EN.pdf

ANSES. 2020a. ANSES Opinion on a case of severe acute hepatitis associated with consumption of the food supplement SriSri Kanchanara® (Request No. 2019-SA-0128). Maisons-Alfort: ANSES. https://www.anses.fr/fr/system/files/NUT2019SA0218.pdf

ANSES. 2020b. ANSES Opinion on a case of fatal fulminant hepatitis associated with consumption of the food supplement Slim Metabol® (Request No. 2019-SA-0136). Maisons-Alfort: ANSES. https://www.anses.fr/en/system/files/NUT2019SA0136EN.pdf

ANSES. 2020c. ANSES Opinion on two cases of severe acute life-threatening hepatitis associated with consumption of the food supplement Chewable Hair Vitamins® (Request No. 2019-SA-0212). Maisons-Alfort: ANSES. https://www.anses.fr/en/system/files/NUT2019SA0212EN.pdf

ANSES. 2020d. ANSES Opinion on the use of Melaleuca essential oils in food supplements (Request No. 2018-SA-0096). Maisons-Alfort: ANSES. https://www.anses.fr/fr/system/files/NUT2018SA0096.pdf

DOPTER, A. and MARGARITIS, I. 2021a. "Compléments alimentaires : vrais aliments ou faux médicaments : Déclarer aussi les effets indésirables observés des compléments alimentaires." ["Food supplements: real foods or fake medicines: Also report adverse effects observed from food supplements."] La Revue du Praticien Médecine Générale 71 (2): 160-163.

DOPTER, A. and MARGARITIS, I. 2021b. "Des compléments pour sportifs pas toujours fair play." ["Supplements for athletes are not always fair play"] La Revue du Praticien Médecine Générale 71 (2): 164.

EL OUADRHIRI, Y. and VO VAN REGNAULT, G. 2021. "Beware of the risk of liver toxicity from overconsumption of foodstuffs or food supplements containing cinnamon." Vigil'Anses (15): 15-16.

HURET, F. 2020a. "Fatal fulminant hepatitis associated with consumption of a food supplement." Vigil'Anses (10): 12-15.

HURET, F. 2020b. "Potassium chloride-based salt substitutes are not without health risks." Vigil'Anses (10): 16-18.

HURET, F. 2021. "What are the adverse effects of *Melaleuca* essential oils (tea-tree, niaouli and cajeput) taken orally?" Vigil'Anses (14): 16-18.

HURET, F, and VO VAN REGNAULT, G. 2021. "Severe acute hepatitis associated with consumption of a food supplement claimed as being Ayurvedic." Vigil'Anses (13): 19-21.

VO VAN REGNAULT, G., M. COSTA, A. ADANIĆ PAJIĆ, A. BICO, S. BISCHOFOVA, U. BLAZNIK, F. MENNITI-IPPOLITO, K. PILEGAARD, C. RODRIGUES, and I. MARGARITIS. 2021. "The need for European harmonization of Nutrivigilance in a public health perspective: a comprehensive review." Critical Reviews in Food Science and Nutrition: 1-17.

VO VAN REGNAULT, G. 2020. "Severe acute hepatitis associated with consumption of a food supplement." Vigil'Anses (12): 14-16

FRENCH AGENCY FOR FOOD, ENVIRONMENTAL
and Occupational Health & Safety

14, rue Pierre et Marie Curie
F94701 Maisons-Alfort cedex

www.anses.fr @Anses_fr

Investigate, evaluate, protect