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NUTRIVIGILANCE

2022 Activity 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 reporter 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. These 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 2022, the Agency received 7946 reports.

KEY FIGURES

711 REPORTS RECEIVED IN 2022

- 64% of cases were analysable (compared with 58% in 2020–2021);
- 7% of the analysable cases were severe[5] (severity levels 3 and 4), compared with 5% in 2020–2021.

19 ALERTS IN 2022

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

1 PUBLISHED OPINION ON A SEVERE CASE WITH STRONG CAUSALITY

- ANSES opinion on a case of grade 3 anaphylaxis associated with consumption of the food supplement Actirub®.

1 SCIENTIFIC AND TECHNICAL SUPPORT NOTE

- Scientific and technical support on the plants and essential oils most commonly implicated in the nutrivigilance reports submitted to ANSES.

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 risks associated with the consumption of food supplements containing turmeric.

[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).

PLANTS AND ESSENTIAL OILS MOST COMMONLY IMPLICATED IN NUTRIVIGILANCE REPORTS

The Directorate General for Competition, Consumer Affairs and Fraud Control (DGCCRF) asked ANSES to obtain quantitative and qualitative information on the 50 plants and essential oils most commonly implicated in nutrivigilance reports associated with the consumption of food supplements over the last five years.

Between 1 January 2016 and 15 October 2021, expert appraisals were conducted on 507 reports implicating at least one food supplement containing at least one plant, and on 66 reports implicating at least one food supplement containing at least one essential oil, for which the Nutrivigilance WG concluded that causality was at least possible. The ten most commonly implicated plants were:

1. *Curcuma* spp.
2. *Melissa officinalis*
3. *Passiflora incarnata*
4. *Camelia sinensis*
5. *Vitis vinifera*
6. *Paullinia cupana*
7. *Panax ginseng*
8. *Eschscholzia californica*
9. *Cynara scolymus*
10. *Piper nigrum*

The ten most commonly implicated essential oils were:

1. *Thymus vulgaris*
2. *Rosmarinus officinalis*
3. *Eucalyptus radiata*
4. *Cinnamomum* sp.
5. *Melaleuca alternifolia*
6. *Mentha piperita*
7. *Eugenia caryophyllus*
8. *Citrus limon*
9. *Cinnamomum camphora*
10. *Lavandula officinalis*

TURMERIC OR CURCUMIN IN FOOD SUPPLEMENTS: THEIR CONSUMPTION MAY NOT ALWAYS BE SAFE

Turmeric rhizomes have historically been used in powder form as a spice (curry, ras-el-hanout, etc.) in various traditional cuisines, but also in phytotherapy in Asia and Europe, mainly for their potential digestive, antioxidant and anti-inflammatory properties. Many food supplements on the French market also contain turmeric or its active substance curcumin. Turmeric is considered to have a protective effect on the liver, but studies suggest that high doses of turmeric or curcumin are hepatotoxic in animals. Signs of hepatotoxicity in humans have also been noted by various vigilance systems, in particular the Italian phytovigilance and French nutrivigilance systems. These identified more than 40 cases of hepatitis from consumption of food supplements containing turmeric or curcumin, occurring between 2002 and 2021.

In nine of these, causality was deemed to be likely or very likely. So far, these reports have not identified any risk factors specific to the consumers. In particular, the absence of any history of liver disease among the turmeric consumers in the reported cases means that there are currently no grounds for issuing any particular warning to people with a history of liver damage. However, this finding needs to be confirmed through increased vigilance, which involves raising awareness among food supplement consumers, healthcare professionals and the companies placing these products on the market, in order to prevent the occurrence of adverse effects or to manage and report them when they do occur.

ANAPHYLAXIS ASSOCIATED WITH CONSUMPTION OF THE FOOD SUPPLEMENT ACTIRUB®

A case of grade 3 anaphylaxis in a 49-year-old woman following consumption of the food supplement Actirub® was reported to the nutrivigilance system. This product contains extracts from several plants: purple coneflower (*Echinacea purpurea*), green chiretta (*Andrographis paniculata*), astragalus (*Astragalus propinquus* = *A. membranaceus*), common mullein (*Verbascum thapsus* L.), common thyme (*Thymus vulgaris*), white willow (*Salix alba*), feverfew (*Tanacetum parthenium* L.), black elder (*Sambucus nigra*) and essential oil of narrow-leaved peppermint (*Eucalyptus radiata*), as well as N-acetyl-L-cysteine, vitamin C and zinc. The observed anaphylaxis may have been due to several of the Actirub® ingredients, acting through a combination of mechanisms, some of which are IgE-dependent. The combination of *Echinacea purpurea* and *Andrographis paniculata* in the product may also have increased the allergic reaction. It is important to note that an allergic reaction to purple coneflower is possible from the very first oral exposure, if a person has already been sensitised to Asteraceae pollen through respiratory exposure. ANSES recommends informing atopic people about the risk of severe allergic reaction associated with the consumption of these two plants. Atopic individuals should carefully read the composition of the food supplements and seek advice from their pharmacist if they are in any doubt about one or more ingredients. In addition, heightened vigilance is needed with products containing multiple ingredients, because this increases the risk of cross-reaction with other allergens previously encountered (including by other routes of exposure, such as airborne pollen via the respiratory tract), and the risk of stronger allergic reactions occurring due to the simultaneous triggering of different mechanisms (allergic, mechanical or sensitisation).

Major projects

Upgrade of the remote reporting website and the nutrivigilance database

In January 2021, ANSES launched its new online reporting website for the nutrivigilance system and began using a new database for internal processing.

These two new tools were then further developed in 2022. Reporters can now upload attachments (medical reports, product photos, etc.) when submitting their online reports. This ensures that as much information as possible is available when the report is initially submitted, enabling a robust causality analysis to be carried out.

A new function has also been developed to enable multiple reports to be imported into the database simultaneously from an Excel file. Manufacturers can send their reports to the nutrivigilance system in Excel format, and they are then grouped together and quickly saved in the database.

Lastly, documents such as summaries of reports can now be generated automatically.

Key event

Renewal of the Nutrivigilance Working Group

In 2022, the members of the Nutrivigilance Working Group were renewed. Previously made up entirely of medical doctors, the new group now includes two pharmacists, bringing the expertise they have acquired in pharmacovigilance. This new area of competence was added to strengthen the analysis of possible interactions between products falling within the scope of nutrivigilance and medicines taken concomitantly. The 14 experts of this new group meet once a month. As a reminder, its main mission is to analyse the causality of products covered by nutrivigilance in the occurrence of adverse effects in consumers.

Outlook and future projects

The following expert appraisals in connection with the nutrivigilance system were initiated in 2022:

- Expert appraisal on the risks associated with the consumption of food supplements containing shiitake (*Lentinula edodes*), maitake (*Grifola frondosa*) and reishi (*Ganoderma lucidum*) mushrooms;
- Expert appraisal on the risks associated with dietary consumption of liquorice.

COMMUNICATION MEASURES TO PUBLICISE THE SYSTEM

In 2022, ANSES continued its training activities in order 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 (masters and DU) and nutrition (masters and DU) from different universities in France.
In addition to articles published in the scientific and mainstream press, nutrivigilance work provided input for four articles in the bulletin for all ANSES's vigilance systems (Vigil'Anses)[7].

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

Main publications

ANSES. 2022. Opinion of the French Agency for Food, Environmental and Occupational Health & Safety on the assessment of risks associated with the consumption of food supplements containing turmeric (Internal Request 2019-SA-0111). ANSES (Maisons-Alfort).

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