



2022 THEMATIC ACTIVITY REPORT

TOXICOVIGILANCE



Contents

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Pa	ge	3	Р	rea	m	h	le

- Page 4 Key figures
- Page 6 Major projects
- Page 7 Highlights
- Page 8 Outlook and future projects
- Page 9 Focus
- Page 11 Key dates
- Page 12 Main publications

Since 2016, the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) has coordinated the toxicovigilance scheme and the vigilance activities of French poison control centres (PCCs). The purpose of toxicovigilance is to monitor and assess the acute or chronic toxic effects of exposure to natural or synthetic products available on the market or found in the environment, and which do not fall within the scope of other regulated national vigilance schemes (in particular, it excludes human medicine). It relies on data from the network of eight French PCCs, saved in SICAP (the information system shared by all the PCCs) following calls to their emergency telephone hotlines, as well as on toxicovigilance schemes in the French overseas territories.

ANSES is supported in this work by the Toxicovigilance Coordination Committee and its operational unit, as well as by the Strategic Committee for PCC Vigilance Activities¹.

Groups of experts (vigilance working groups) led by ANSES use PCC data to document risk situations for people and recommend preventive measures.

ANSES also receives and processes toxicovigilance signals and alerts.

¹ The members of this committee were defined in the Ministerial Order of 14 June 2017 on the composition of the strategic committee for vigilance of the organisations responsible for toxicovigilance

KEY FIGURES

11 ALERTS ISSUED BY ANSES AND RELAYED ON SOCIAL MEDIA

- Only use chemicals as a last resort to eradicate bed bugs
- Four tips for a festive season without risk
- Beware of decorative "cake design" dust
- CheniPRO: a study to assess occupational exposure to caterpillars with stinging hairs
- Watch out for carbon monoxide poisoning from your heating systems
- Fuel siphoning: watch out for the risk of poisoning
- This year again, beware of inedible gourds!
- How to avoid domestic accidents
- How to avoid confusing horse chestnuts with sweet chestnuts
- Wild mushroom season has begun: be vigilant!
- Which plants should you watch out for to avoid poisoning this summer?

5 STUDY REPORTS PRODUCED BY THE VIGILANCE WORKING GROUPS

- ANSES report on the seasonal monitoring of accidental mushroom poisoning cases Review of cases recorded by poison control centres between 1 July and 31 December 2021;
- ANSES report on the study of serious cases associated with biocidal products Retrospective study of observations recorded by French poison control and toxicovigilance centres from 1 January 2015 to 31 December 2019;
- ANSES report on the recreational inhalation of volatile substances Study of cases reported to poison control centres between 1 July 2013 and 31 December 2019;
- ANSES report on the adverse effects induced by liquorice consumed in the diet Study of cases recorded by poison control centres from January 2012 to December 2021;
- ANSES reports on poisonings caused by bed-bug control products Analysis of cases recorded by poison control centres from 1 January 1999 to 31 December 2021;
- ECHA's consultation of EU Poison Centres regarding anticoagulant rodenticides: primary and secondary poisoning data and reports on accidental poisoning (April 2022).

CONTRIBUTIONS BY POISON CONTROL CENTRES TO ANSES OPINIONS OR

REPORTS

- ANSES opinion on the ban on self-service sales of certain categories of biocidal products;
- ANSES opinion on the assessment of risks associated with the consumption of food supplements containing turmeric;
- ANSES opinion summarising two stages of the biomedical study on the safety of footwear and textile clothing;
- ANSES opinion on the representativeness of sampling for histamine screening in fish;
- Phytopharmacovigilance fact sheet Summary of monitoring data on Cyazofamid;
- Phytopharmacovigilance fact sheet Summary of monitoring data on Clopyralid;
- Phytopharmacovigilance fact sheet Summary of monitoring data on Metalaxyl-M;
- Phytopharmacovigilance fact sheet Summary of monitoring data on Isoxaflutole.

5 MEASURES TAKEN BY THE COMPETENT AUTHORITIES FOLLOWING ALERTS

- Adulterated aphrodisiac honeys incriminated in poisoning: inspection of the physical point of sale by the Directorate General for Competition Policy, Consumer Affairs and Fraud Control (DGCCRF), seizure of the products for analysis;
- Household product sold in packaging resembling a soft drink bottle: investigation by the Departmental Directorate for the Protection of Populations (DDPP) in the supermarket where the product was purchased, implementation of a product withdrawal/recall measure and investigation of the product's distribution channel in France;
- Slimming food supplement adulterated with sibutramine: investigation by the customs services and the DGCCRF, health enforcement decision taken by the French Health Products Safety Agency (ANSM);
- GP-5 gas mask with filter cartridges containing asbestos: investigation of the online sales
 platform and withdrawal by the platform of the addresses of third-party sellers of these masks
 and cartridges;
 - buyers informed by the online platform of the risks associated with these masks;
- **poisoning by a descaler with a high concentration of nitric acid and poor labelling**: retail outlet inspected, products withdrawn, suppliers contacted.

MAJOR PROJECTS

Revision of the method for determining causality

Causality assesses the strength of the causal link between exposure to a xenobiotic (chemicals, plants, fungi, medicines, food supplements, etc.) and the occurrence of an effect on the body in the form of a symptom, syndrome or disease, or a measurable paraclinical effect.

Although used routinely by toxicologists at poison control centres and in studies drawing on their data, this method has not been fully validated or published in any scientific paper.

Following a recommendation from the ANSES Scientific Board, a group of experts, coordinated by ANSES and bringing together methodologists and toxicologists from poison control centres, began supervising work to validate this method and ensure its reproducibility.

Skin burns caused by the use of biocidal disinfectant products in schools

On 28 May 2021, the French Directorate General for Health sent ANSES a report of a case of skin burns in a young girl following the use of a biocidal disinfectant product in a nursery school. The event occurred after the girl had sat on a chair on which a few drops of undiluted product had been spilled. This was due to the product having been diluted on the spot and not in the storage room as stipulated in the protocol for use. In June 2021, there were two other accidents of the same type following the use of biocidal disinfectants in schools.

In view of the increase in these reports, especially since the COVID-19 health crisis, ANSES issued an internal request to analyse the skin disorders related to the use of disinfectant products that occurred among children in community facilities, with the aim of identifying the circumstances in which these accidents took place and the products involved and, where necessary, proposing preventive measures.

A programme to monitor cases of ciguatera

Ciguatera is a type of food poisoning caused by eating fish contaminated with marine toxins called ciguatoxins, which are produced by microscopic algae found in coral reefs. The toxins are ingested by small herbivorous fish, which in turn are consumed by larger carnivorous fish that humans may eat. Knowledge of the risk of contamination of fishery products by ciguatoxins is essential for developing prevention and control measures, in order to limit population exposure. If the ciguatera diagnosis is based on the occurrence of symptoms consistent with poisoning following the consumption of fish from species known to pose a risk, this can be confirmed by ciguatoxin analyses in the leftovers of the incriminated fish, if available. In the event of suspected poisoning, tests are carried out on imported or locally caught fish, depending on the circumstances, by ANSES's National Reference Laboratory for marine biotoxins (NRL-MB). In this context, after publishing a retrospective review of ciguatera cases recorded by poison control centres over the period 2012-2019, and then a review for 2020, ANSES set up continuous ciguatera monitoring in order to better document the symptoms observed at the time of poisoning and their progression, along with the characteristics of the fish consumed (fish name, place where it was fished and purchased, etc.) and the exposure circumstances (method of preparation, quantity consumed, etc.).

Improving monitoring of mushroom poisoning

ANSES has been monitoring cases of mushroom poisoning since 2016. However, some information that could shed light on these poisonings was not being systematically recorded. To address this, a specific data collection questionnaire was developed in the PCCs' information system, to be completed for anyone calling with symptoms after eating mushrooms. It records information about the person(s) exposed during the meal, the observed symptoms and their progression, the poisoning circumstances (such as how the mushrooms were obtained – whether they were foraged, purchased at a market or eaten in a restaurant), the mushroom species sought when foraging, whether a photo of the mushroom was taken to identify it, and how the mushrooms were transported, stored and consumed.

HIGHLIGHTS

Publication of the order concerning the operation of SICAP, the information system shared by all the PCCs

The order concerning the operation of SICAP was published on 21 February 2022. It describes the different categories of data processed, and designates the legal entity responsible for processing the data stored in the SICAP as part of the PCCs' emergency telephone hotline service, and the data covered by business secrecy (composition of dangerous mixtures declared by manufacturers). This order includes a list of persons who have access to SICAP, as well as provisions relating to data security and the rights of persons whose data have been saved. Lastly, it specifies the data retention period, which varies according to the module concerned: the national database on products and compositions (BNPC) or the national database of poisoning cases (BNCI).

Publication of the order creating the French Caribbean toxicovigilance scheme (DTV Antilles)

The order authorising the creation of two toxicovigilance schemes in the French Caribbean – one in Martinique and the other in Guadeloupe – was published on 7 July 2022. They will be funded by the relevant ARS and by ANSES.

Seminar for the DGCCRF/Customs/Oclaesp/PCCs/ANSES

On 21 April 2022, ANSES organised a virtual seminar bringing together the DGCCRF, customs services, the Central Office for Combating Damage to the Environment and Public Health (Oclaesp) and the poison control centres on the subject of alerts involving everyday products. The various organisations presented their respective areas of activity, then all the participants discussed possible actions in the event of an alert concerning adulterated food supplements or food products, defective or dangerous toys, cosmetics that look like food, misleading claims, the possibility of purchasing banned products on the internet, or products with an unclear regulatory status.

These exchanges helped the various stakeholders to get to know each other better, which will facilitate future cooperation.

OUTLOOK AND FUTURE PROJECTS

Study on essential oil poisonings

Essential oils are complex mixtures of natural origin. They are increasingly offered to the general public, on their own or in products, for a variety of everyday uses such as to "purify the air", relieve various ailments or even combat certain diseases. Essential oils can be used to flavour foods and add fragrance to cleaning products, and are also found in cosmetics and certain products claiming biocidal activity ("cleaning" sprays). Several different regulations may apply to essential oils, depending on their use: chemicals, biocides, plant protection products, cosmetics, medical devices, medicines, flavourings or food supplements.

Because of this, ANSES's supervisory ministries wished to find out more about their adverse effects, for all their uses. They therefore asked ANSES to analyse the cases of poisoning by essential oils reported to poison control centres, in terms of the number of cases and trends in recent years. ANSES will identify a list of priority essential oils responsible for the greatest number of cases and/or the most serious cases. For the oils on this list, it will then provide the detailed composition of all the compounds classified according to their hazard properties (acute toxic, specific toxic to certain target organs, carcinogenic, mutagenic, toxic for reproduction, endocrine disruptor, neurotoxic, sensitising, irritant).

ANSES's work will also include an analysis of diseases related to the use of essential oils diagnosed in patients who have visited an occupational and environmental disease consultation centre.

The results of this work are expected in summer 2023.

Detection of signals on exposure circumstances

ANSES has set up a new programme for the automated detection of signals on the exposure circumstances of people who made calls to the poison control centres. This programme uses the same method as the one implemented for the automated detection of medical entities or "syndromes" in the PCCs' database ('syndromic surveillance').²

The aim is to be able to detect an unusual increase in exposure occurring in the same circumstances, regardless of the type of agent or associated product.

The statistical algorithm was tested on petroleum fuel siphoning accidents recorded since 2008. As expected, it identified an unusual peak in accidents described during each fuel shortage period (October 2010, May 2016, and more recently October 2022). It can also be used to monitor other circumstances – such as malicious acts, drug-facilitated crime, etc. – in "real time".

Launch of a vigilance scheme for carbon monoxide (CO) poisoning

ANSES has set up a vigilance scheme for carbon monoxide poisoning, based on cases reported to poison control centres, in order to identify high-risk heating practices that could be new phenomena.

² https://vigilanses.anses.fr/sites/default/files/VigilAnsesN7_February2019_syndromicsurv.pdf

A survey form was created by the poison control centres and placed online in their information system. It will be completed for every case of carbon monoxide poisoning. The toxicologist will be able to indicate whether the circumstances are unusual: for example the misuse of a domestic appliance (brazier, power generator or other device) for indoor heating purposes, which could represent a new risk.

More than a thousand such poisoning cases were reported to poison control centres between September and December 2022, and ANSES warned the general public of the risks associated with heating indoor spaces using braziers, as this type of misuse was particularly common during this period. By automating the processing of data entered on this new form, it will now be possible to quickly identify new situations where there is a risk of carbon monoxide poisoning.

Changes in access to SICAP

Amendments are planned to the order concerning the operation of SICAP, which was published on 21 February 2022. They concern:

- access to SICAP data for the research community;
- storage of data contained in the decisional information service (SID) after 30 years;
- access by the occupational health and pension insurance funds (CARSATs) via the French National Research and Safety Institute (INRS), or direct access;
- access to the medical cases service for inputting dossiers from the overseas territories (excluding the emergency telephone hotline service) by the DTVs.

FOCUS

Exposure to bed-bug control products

In 2016, the death of a child following the use of a product to combat a bed-bug infestation in the home – a product that was banned in France for use by private individuals and had been imported illegally – led ANSES to analyse poisoning cases caused by bed-bug control products recorded in the PCCs' database.

This database had recorded a total of 1056 people exposed to such products. According to data for the period between 2007 and 2021, the number of these poisonings has increased each year since 2010, and even more so since 2016, before falling in 2020 and 2021, possibly as a result of the reduction in tourist movements linked to the COVID-19 epidemic. The worst affected regions were Ile-de-France and the south-eastern quarter of France, with cases being more numerous in summer. The most common symptoms were mild signs of irritation. Nearly 1% (n=12) of cases were of moderate to high severity. Serious cases were more common with the use of substances that have been banned for this purpose, mainly phosphides. Thus, there were around 9% of serious cases or deaths involving prohibited substances, compared with around 1% with non-prohibited substances.

Iterative uses or use in excessive quantities demonstrated the difficulty of eradicating bed bugs.

The health consequences of bed-bug infestations cannot be summed up simply in dermatological, infectious or toxicological terms, as this overlooks the major psychological and social repercussions.

Glycyrrhizin poisoning

Liquorice is widely used, especially in the tobacco, cosmetics, food and pharmaceutical industries. However, its consumption carries health risks, mainly a drop in blood potassium levels and arterial hypertension (pseudo-hyperaldosteronism), even in people who have never suffered from high blood pressure. In France, several serious poisoning cases recently reported to poison control centres or the nutrivigilance system led ANSES to analyse poisonings due to liquorice consumption.

This study covered 64 cases occurring between 2012 and 2021. The products consumed were mainly soft drinks, alcoholic beverages such as pastis, confectionery, herbal infusions and food supplements. Consumption was usually chronic and in excessive amounts. The severity of the pseudo-hyperaldosteronism appeared to be correlated with the amount of glycyrrhizin ingested. Rare cases of allergic-type reactions occurred with acute poisoning. Severity was high in 42% of poisoning cases, and one death occurred in a person already suffering from severe liver damage. All types of products were involved, except for liquorice syrup and food supplements, but cases most commonly concerned beverages (pastis with or without alcohol and AntésiteTM). The outcome was favourable in almost all cases, often after hospital care, although one patient suffered sequelae following a stroke complicating a hypertensive crisis.

ANSES is conducting an assessment of the risks associated with dietary consumption of liquorice, mainly to establish a toxicity reference value (TRV) for glycyrrhizin. Following this work, the labelling of products containing liquorice or its derivatives may be modified.

Recreational misuse of volatile substances

In June 2012, following the death by asphyxiation of an adolescent who had inhaled deodorant for recreational purposes, the health authorities asked the centres for evaluation and information on drug dependence and addiction monitoring (CEIP-As) and the PCCs to conduct an investigation into such cases of self-induced intoxication with volatile substances.

Between 1 July 2013 and 31 December 2019, 408 cases of exposure of this type (of which 306 were symptomatic) were reported to poison control centres. The number of cases has fallen over the years. Consumers were young, with 70% being minors.

Inhalation mainly took place in the user's home, and chronic use was reported in a third of cases. The symptoms reported were headache, loss of consciousness and drowsiness in more than half of cases, and signs of inebriation or agitation in a third of cases. The cases involved products in everyday use, which may explain the high proportion of children among consumers, as they can easily find them at home without having to buy them. The vast majority of these products were deodorants, followed by dust removers and air fresheners. Of the 13 very serious cases, five of the victims suffered cardiorespiratory arrest, with a favourable outcome following defibrillation. Four people suffered neurological problems (coma or loss of consciousness).

The risks associated with this practice are well documented in the literature, and yet seem to be little known, particularly among children and adolescents. Information campaigns therefore appear to be necessary. These could include specific labelling, explicitly warning of the fatal risk of deliberately inhaling large volumes, and awareness campaigns targeting children and adolescents and their families, as well as healthcare professionals, paediatricians, general practitioners and medical teams in schools, to ensure early detection.

Histamine poisoning

Histamine poisoning is one of the main causes of foodborne illness related to fish consumption. Histamine is naturally synthesised in humans and animals, and is found in all fish, normally at low levels. It is not degraded by cooking or freezing.

In response to a formal request, ANSES studied cases of histamine poisoning treated by poison control centres between 2012 and 2021. It selected a total of 173 meals causing poisoning, accounting for 543 patients. The main symptoms, flushing and urticaria, were characteristic of histamine poisoning. The symptoms lasted an average of three and a half hours, and were minor overall with a favourable outcome. The standard treatment is based on antihistamines. Most of these cases were due to the consumption of fresh fish eaten in restaurants or purchased in shops and prepared at home. Tuna was incriminated in the majority of meals that caused poisoning. Most of the fish had been stored in the refrigerator. Some consumers had not maintained the cold chain to store the fish, thereby promoting bacterial growth and the formation of histamine. Whether it has been caught or purchased in a shop, fish must be refrigerated or frozen promptly, and not left at room temperature or exposed to sunlight.

KEY DATES

21 February: Publication of the order concerning the operation of SICAP

11 April: Publication of the order on the composition of the Strategic Committee for PCC Vigilance Activities

July: Integration in SICAP of the ranking of biocidal products

12 July: Publication of the order amending the order of 8 March 2017 establishing the list of regional hospital centres with a poison control centre or toxicovigilance organisation

Main publications

ANSES. 2022. Seasonal monitoring of accidental mushroom poisoning cases: Review of cases recorded by poison control centres between 1 July and 31 December 2021. Toxicovigilance study report (Study report no. 2022-VIG-0107). ANSES. Maisons-Alfort. 25 p

ANSES. 2022. Study of serious cases associated with biocidal products. Retrospective study of observations recorded by the French poison control and toxicovigilance centres from 1 January 2015 to 31 December 2019. (Request No 2020-SA-0008). ANSES. Maisons-Alfort. 47 p

ANSES. 2022. Recreational inhalation of volatile substances. Study of cases reported to poison control centres between 1 July 2013 and 31 December 2019 (Request 2019-SA-0217). ANSES. Maisons-Alfort. 44 p

ANSES. 2022. Poisonings caused by bed-bug control products. Analysis of cases recorded by poison control centres from 1 January 1999 to 31 December 2021 (Request 2021-SA-0147). ANSES. Maisons-Alfort. 34 p

ANSES. 2022. Adverse effects induced by liquorice consumed in the diet. Study of cases recorded by poison control centres (from January 2012 to December 2021). Toxicovigilance study report (Internal request 2022-AUTO-0077). ANSES. Maisons-Alfort. 26 p

BLOCH, J. 2022. "Natural" products... that contain dangerous drugs. Vigil'Anses 16: 16-18

Boels D, Greillet C, Langrand J, Labadie M, Le Roux G, de Haro L, Bloch J, Sinno-Tellier S. Shiitake dermatitis: experience of the Poison Control Centre Network in France from 2014 to 2019. Clin Toxicol (Phila). 2022 Aug;60(8):954-959. doi: 10.1080/15563650.2022.2059496

CARE, W., SINNO-TELLIER, S. 2022. Consume drinks, sweets and other foods containing liquorice in moderation. Vigil'Anses 18: 2-4

CREUSAT, G., PAGES, R. 2022. Biocidal products should be used with caution. Vigil'Anses 18: 8-10

DUBOIS, C., SOLAL, C. 2022. New chemicals involved in skin allergies related to clothing and footwear. Vigil'Anses 16: 10-13

GREILLET, C., SOLAL, C. 2022. Inhalation of volatile substances: on the decline but still dangerous. Vigil'Anses 17: 6-8

Jarrige, X., Glaizal, M., Sinno-Tellier S. et al., Scombrotoxism: A case series from the French Poison Control Centre Network from 2012 to 2021, Toxicologie Analytique & Clinique, https://doi.org/10.1016/j.toxac.2022.11.005

LANGRAND, J., PAGES, R. 2022. Exercise caution with the products used to eradicate bed bugs. Vigil'Anses 18: 5-7

PELISSIER, F., FRANCHITTO, N., SOLAL, C. 2022. E-cigarettes: only a few serious poisoning cases but vigilance still needed. Vigil'Anses 17: 13-17

Sinno-Tellier S, Abadie E, de Haro L, Paret N, Langrand J, Le Roux G, Labadie M, Boels D; French PCC Research Group, Bloch J, Delcourt N. Human poisonings by neurotoxic phycotoxins related to the consumption of shellfish: study of cases registered by the French Poison Control Centres from 2012 to 2019. Clin Toxicol (Phila). 2022 Jun;60(6):759-767. doi: 10.1080/15563650.2022.2034840

SINNO-TELLIER, S., DE HARO, L. 2022. Monitoring ciguatera poisoning to identify contaminated fish species. Vigil'Anses 16: 3-6

SINNO-TELLIER, S., DE HARO, L. 2022. Histamine poisoning: keep your fish cold! Vigil'Anses 17: 2-5

SOLAL, C. 2022. Decorative "cake design" dust is not always edible. Vigil'Anses 18: 11-12

TOURNOUD, C., PAGES, R. 2022. Bitterness and taste disorders after eating pine nuts: what's new since 2017? Vigil'Anses 16: 7-9

Sinno-Tellier, S. Cet été, à quelles plantes faire attention pour éviter les intoxications ? The Conversation 31 July 2022, ANSES https://theconversation.com/cet-ete-a-quelles-plantes-faire-attention-pour-eviter-les-intoxications-187451

Posters

F. Pélissier, J. Bloch, B. Labarbe, C. Solal, N. Franchitto. E-cigarette and e-liquids: national reports received by French Poison Control Centers from July 2019 to December 2020. Call of abstracts "International conference on the E-Cigarette: patterns of use and health impacts" - Paris, on 5-6th December 2022. Poster & oral presentation

Sinno-Tellier, Sandra & Abadie, Eric & Boels, David & Langrand, Jerome & Roux, Gaël & Labadie, Magali & Bloch, J. & Paret, Nathalie & Delcourt, Nicolas. (2022). Human poisoning by neurotoxic phycotoxins related to the consumption of shellfish: cases registered by the French Poison Control Centres from 2012 to 2019. May 2022 DOI:10.1080/15563650.2022.2054576

Conference: 42nd International Congress of the European Association of Poison Centres and Clinical Toxicologists (EAPCCT) 24-27 May 2022, Tallinn, Estonia



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