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VigilAnses

The second quarter of each year is traditionally when data are available to take stock of the previous year's activity. This second issue of Vigil'Anses presents the results of two regulatory vigilance schemes for which ANSES is responsible, nutrivigilance and veterinary pharmacovigilance. Both rely on spontaneous reports of adverse effects: from the use of food supplements, novel foods, fortified foods or foods intended for specific populations for the first, and from the use of veterinary medicinal products for the second. Although veterinary pharmacovigilance obviously concerns adverse effects associated with the use of a veterinary medicinal product in the animal for which it is intended, this article shows that the scheme also covers adverse effects in humans.

This issue also includes two articles on the National Network for the Monitoring and Prevention of Occupational Diseases (RNV3P), coordinated by ANSES. The first presents the 2015 review of the data recorded in the national database by specialists from occupational disease consultation centres and occupational health services. This network of experts also works to detect emerging occupational risks through their identification by the network's clinicians, data mining of the RNV3P database, and literature monitoring. The idea here is to take action in primary prevention (risk reduction) and secondary prevention (screening), without waiting for the corresponding diseases to be identified in France. This is the case for the risk of silicosis among workers manufacturing artificial stone countertops with a high quartz content, as described in one of the articles. This article shows that the use of other popular materials for the same applications (kitchen and bathroom surfaces, or in commercial premises) also requires precautions, since diseases are now beginning to be attributed to these uses.

The 2016 review of surveillance of mushroom poisoning by the Poison Control Centres and ANSES will perhaps encourage caution among those who like picking wild mushrooms in the woods... Toxicologists at Poison Control Centres advise taking photos of foraged wild mushrooms before cooking and/or eating them. If symptoms appear in the hours or even days following consumption, these photos will help specialists identify the mushroom thought to be responsible and suggest the most appropriate medical treatment.

Lastly, in March 2017, the Ministry of Health's internet portal for reporting adverse health events was launched. You can find out what this contributes to ANSES's vigilance schemes and to public health in general.

Juliette Bloch, Editor-in-Chief of Vigil'Anses

The contribution of the portal for reporting adverse health events

On 13 March 2017, the Ministry of Health launched a single portal on its website for reporting adverse health events:

https://signalement.social-sante.gouv.fr

Its purpose is to promote reporting by enabling any healthcare professional or user to declare in just a few clicks "any adverse event or unusual effect with a negative impact on health" about which they become aware.

Its tree structure helps the healthcare professional choose the relevant vigilance scheme for the event (pharmacovigilance, haemovigilance, cosmetics vigilance, nutrivigilance, toxicovigilance, etc.), while users are guided by the choice of "agent" (medicinal product, blood derivatives, cosmetics, food supplements, everyday products, etc.).

Depending on the vigilance scheme, information on the adverse event is entered on the portal and the report is then transmitted to either the Agency or the organisation in charge of the vigilance scheme concerned. The person submitting the report is informed of the organisation to which the alert has been addressed. As the portal does not replace existing tools, the reporter may be redirected to an online form on the vigilance system's website, if an electronic reporting system is already in place.

Thus, with regard to the vigilance schemes for which ANSES is responsible, reports are submitted:

- for **nutrivigilance**: on ANSES's website for healthcare professionals and via the portal for users (whose reports are then transferred to a Poison Control Centre for investigation);
- for **veterinary pharmacovigilance**: if it is an event observed in a person (and not an animal), the report is submitted through the portal for healthcare professionals and users. Reports are then transferred to a Poison Control Centre for investigation. Effects observed in animals are not covered by this portal and should be reported to the French Agency for Veterinary Medicinal Products (ANMV) or the Veterinary Pharmacovigilance Centre in Lyon (CPVL);
- for **phytopharmacovigilance**: holders of marketing authorisations or parallel trade permits for plant protection products, manufacturers, importers, distributors or professional users of these products, as well as advisers and trainers of these users subject to mandatory reporting under the Act on the future of agriculture, food and forestry (LAAAF) of 13 October 2014, do so through the portal, which will then notify ANSES. The same applies to healthcare professionals, users and other professionals. All reports are then analysed by a Poison Control Centre;
- for **toxicovigilance**, all reports, whether from healthcare professionals or users, are submitted via the portal and then transferred to the Poison Control Centres for analysis.

The ANSES website pages for each of these vigilance schemes have been updated to direct reporters to the correct reporting site.

Reporters must leave their contact details so that they can be called back if necessary, in particular to document more precisely the product(s) or agent(s) involved, the effects observed and the timeline of events.

The "usability" of the reports, the percentage of misdirected reports (e.g. a food poisoning report sent to toxicovigilance instead of the Regional Health Agency), the proportion of people who need to be called back and consequently the additional workload this will entail, are for the moment unknown. All cases reported to the Poison Control Centres will be recorded in their information system (SICAP) and an initial review may be conducted 6 to 12 months after the launch of the site, in order to specify the volume of reports, how they were dealt with (followed up or not) and, lastly, the percentage of reports providing useful information for toxicovigilance.

Juliette BLOCH (Anses)

Wild mushroom enthusiasts, check what you have picked: mushroom poisoning report for 2016

Although wild mushrooms are popular delicacies, some species are nevertheless toxic or even fatal to humans. Recommendations on picking and consumption are regularly issued by the health authorities [1]; these include getting a specialist (pharmacists, mycology associations) to check the specimens you have picked in the event of any doubt, to avoid confusion between edible and toxic species; avoiding picking near polluted sites (roadsides, industrial areas, landfills); transporting the picked mushrooms in a basket and not a plastic bag; storing them in the refrigerator to avoid the growth of micro-organisms; and the importance of always cooking species containing thermolabile toxins.

Mushrooms mainly grow in summer and autumn, although some species appear in spring (morels), while others are found until winter (milk caps, chanterelles, etc.). However, their growth can vary greatly from one year to the next depending on weather conditions (rainfall, relative humidity, temperature, light). Some mushrooms may start growing in July, or not until September-October. In general, mushrooms start growing two weeks after an increase in rainfall and a drop in temperature.

Surveillance of mushroom poisonings, for each second half of the calendar year, was set up in 2010 by the French Institute for Public Health Surveillance (InVS[1]) in conjunction with the network of French Poison Control Centres (PCCs). Its implementation was continued by ANSES after responsibility for coordinating toxicovigilance was transferred from the InVS to ANSES on 1 January 2016. This surveillance focuses on the weekly number of poisoning cases from weeks 27 to 52 (beginning of July to end of December) and the identification of severe cases, for alert and prevention purposes.

Since 2014, thanks to the national "Mycolist" network linking PCCs and mycology experts, fungi suspected of being responsible for poisonings have been identified when sufficient information is available (photographs, description, etc.); this rapid identification enables the PCCs' toxicologists to recommend the most appropriate treatment. And for the first time this year, information on how the mushrooms were obtained (foraged by individuals, purchased at a market or in a shop) was specifically studied, in order to better target possible measures to be taken: primary prevention among the population for foraged mushrooms, and management measures by the health authorities for mushrooms available for sale.

During the surveillance period, from July to December 2016, 864 cases of mushroom consumption (with or without symptoms) were reported to the PCC network. Of these, 616 were symptomatic, and in 603 of these cases the symptoms were found to be related, in varying degrees, to the mushrooms consumed.

Men and women were equally represented and ranged in age from 18 months to 90 years (median age 45.5 years).

Most of the mushrooms were picked by the consumers themselves (73%), while 6.1% (37 cases) were purchased at a market or in a shop (supermarket, grocery shop, etc.), either fresh or packaged. However, in 21% of cases, no information was provided on how the mushroom was obtained. This is because when a healthcare professional contacts a PCC about a poisoned patient, they do not always know the origin of the mushrooms at the time of the call.

In 79.4% of cases, the poisoning victims reported having consumed only one type of mushroom, while in 20.6% of cases a mixture had been eaten.

While almost all the people (97.7%) had been poisoned during a meal, 14 cases (2.3%) concerned accidental ingestion, almost exclusively by children (12 cases aged between 18 months and 7 years) or adults with mental disorders (2 cases): they had found a mushroom in a garden and had ingested it without the knowledge of their parents or carers.

On the other hand, 11 children under the age of 5 were poisoned by mushrooms served to them during a meal, even though the recommendations state that you should "never offer the wild mushrooms you have picked to young children if doubts persist about their edible nature and if they have not been identified by a specialist" [1].

Most poisonings occurred in October, with a peak of 84 cases in week 41, then in November (see Figure 1). Lastly, the proportion of poisonings associated with mushrooms purchased in shops was highest in early December (31.6% of cases in week 48, Figure 1), which can be explained by the limited growth of mushrooms at this time of year.

1. The French public health agency, *Santé Publique France*.

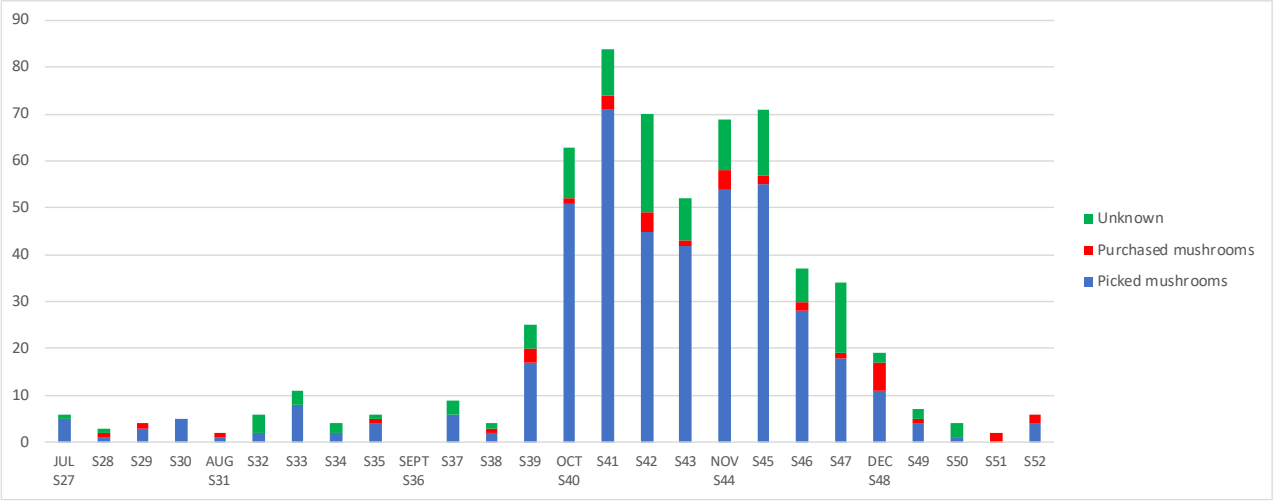

Figure 1: Weekly distribution of mushroom poisoning cases, by mode of procurement, reported to PCCs from July to December 2016 (Source: PCCs' information system)

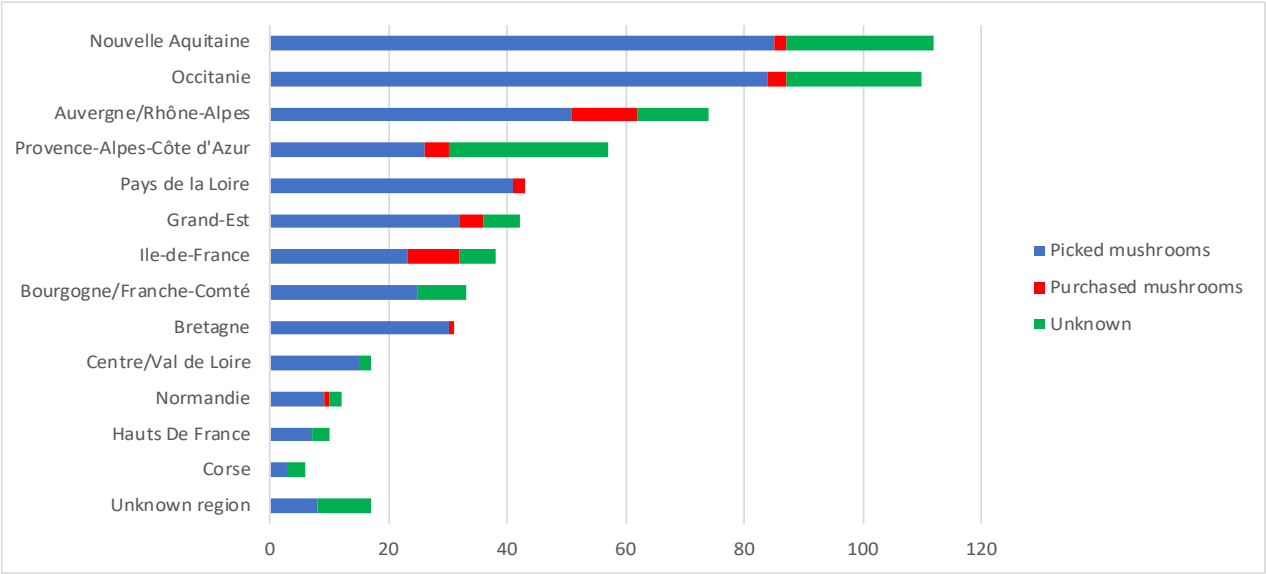

Figure 2: Regional distribution of mushroom poisoning cases, by mode of procurement, reported to PCCs from July to December 2016 (Source: PCCs' information system)

The regions most concerned by these poisonings were, in terms of gross number of cases, Nouvelle Aquitaine (18.6%), followed by Occitanie (18.2%) and Auvergne Rhône-Alpes (12.3%) (see Figure 2). The Ile-de-France region had the highest proportion of poisoning by mushrooms purchased in shops (23.7%) (see Figure 2).

The clinical signs or symptoms reported by the poisoning victims were mainly digestive, since 511 cases (84.7%) presented with at least one digestive sign (vomiting, nausea, diarrhoea or abdominal pain). General signs were also observed in 15.7% of cases (asthenia, tremors/shivers, discomfort, excessive perspiration, etc.), as well as neurological signs in 11.1% of cases (headaches, dizziness, etc.). Lastly, some people showed dermal signs (4.6%), mainly skin rash.

Nine cases were of high severity[2], with life-threatening symptoms. Amanita poisoning[3], responsible for the most serious cases of poisoning in France, was observed in six of them. However, no deaths were reported during the 2016 surveillance period.

Despite the investigation of poisoned individuals by the PCCs, in a quarter of cases the type of fungus involved (species or genus) could not be identified.

The mushroom species considered to be edible that gave rise to symptoms were cep, edible boletus, parasol, sweet tooth, clouded agaric, chanterelle, horn of plenty, fairy ring mushroom, field mushroom, etc. The poisoning may have been due to consumption of a specimen in poor condition, one that was undercooked or eaten raw, or to an "unverifiable" confusion with a toxic fungus species, despite the poisoned individual's reassuring description of the mushroom.

In addition, it is important to mention that some cases of poisoning were reported after the consumption of toxic, even potentially fatal species, identified subsequently by mycology experts (Jack o'lantern, *Entoloma sinuatum*, Satan's bolete, yellow stainer, death cap, European destroying angel).

This nationwide seasonal surveillance of mushroom poisoning helps with the dissemination of prevention messages each year during the mushroom season [2], which are relayed in the field by the press and regional mycology associations or societies. This surveillance, which since 2010 has relied on a network of experts with complementary skills (epidemiologists, toxicologists and mycologists), is increasingly precise and since 2016 includes information on how the mushrooms were obtained.

Sandra SINNO-TELLIER (Anses)

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[2]http://invs.santepubliquefrance.fr/Actualites/Actualites/Intoxications-liees-a-la-consommation-de-champignons-au cours-de-la-saison-2015.-Point-de-situation-au-05-10-2015.-Donnees-consolidees-au-05-10-2015

TO FIND OUT MORE, VISIT:

On 04/04/2017, ANSES published an "opinion on a draft order on edible varieties of cultivated and wild mushrooms". This opinion identified a list of 146 cultivated and wild edible mushrooms, along with their edibility conditions and the risks of confusion with toxic species. This list is updated according to new scientific knowledge and the observations reported to the vigilance networks.
https://www.anses.fr/fr/system/files/ERCA2015SA0180.pdf

2. Severity assessed based on the Poisoning Severity Score (Persson HE, Sjöberg GK, Haines JA, Pronczuk de Garbino, J. J Clin Toxicol. 1998;36 (3):205-13).
3. A syndrome manifested by digestive, liver and kidney disorders, which can be fatal if left untreated. It is caused by certain *Amanita*, *Lepiota* and *Galerina*.

National Network for the Monitoring and Prevention of Occupational Diseases: key figures for 2015

The National Network for the Monitoring and Prevention of Occupational Diseases (RNV3P) was set up progressively from 2001. By 2015, it included all 31 occupational disease consultation centres (CCPPs) across the country, along with eight occupational health services (SSTs).

Its general objectives are to identify and characterise risk situations in the workplace, with a view to prevention.

To do this, all occupational health problems (OHPs) identified during consultations in the CCPPs, as well as new OHPs diagnosed as occupational diseases by the SSTs, are recorded in a standardised manner in a national database. These data are then analysed in order to document exposures or activities associated with diseases of interest, and identify exposure/disease pairs or exposure/activity/emerging disease trios.

The network is also a forum for exchanges between clinicians and partners, particularly during meetings of the various thematic working groups (on emergence, methodology and data exploitation strategy) held at the French Agency for Food, Environmental and Occupational Health & Safety (ANSES), which is responsible for overseeing the network.

An additional strength of the RNV3P is its historical close ties and complementarity with prevention stakeholders, especially the occupational health and pension insurance funds (CARSATs).

In 2015, the partners of the RNV3P, brought together through a framework agreement, were:

- the National Health Insurance Fund for Salaried Workers (CNAM-TS);
- the French Central Fund for the Agricultural Mutual Insurance Scheme (CC-MSA);
- the National Research and Safety Institute (INRS);
- the French Society for Occupational Medicine (SFMT);
- the French Institute for Public Health Surveillance (InVS), which became *Santé Publique France* in 2016;

The social security scheme for self-employed workers (RSI) joined the network in 2017.

In 2015, **31,707 new consultations** (30,353 in CCPPs and 1,354 in SSTs) were added to the database, representing 18,611 new patients (17,305 in CCPPs and 1,306 in SSTs). These patients were predominantly male (59.8% in CCPPs and 52.1% in SSTs) and presented with **19,787 new OHPs** (17,843 diagnosed by CCPPs and 1,024 by SSTs), bearing in mind that one patient can have two different OHPs.

The average age of the patients registered in the CCPPs was 50 years (52.3 years for men and 46.7 years for women). Patients were mainly referred by their occupational physicians (40.6%), but also by specialists (23.4%) and general practitioners (15.7%).

The main reason for the consultation was a request for help in diagnosing work-related diseases (57.6% of cases) (see Figure 1).

The patients registered in the network's SSTs were younger, with an average age of 44.2 years (45.8 years for men and 42.5 years for women).

At the end of the examination carried out by the CCPP physician, 54% (n = 9,705) of the occupational health problems behind the consultation were considered to be an occupational disease (see Figure 2), with the probability of a causal relationship between the patient's exposure to a hazard during their work and their disease estimated as non-null (defining a work-related problem).

More than half of these work-related problems were due to a single exposure (55.4%).

The diseases observed during consultations in the CCPPs were mainly psychological disorders (22% mental and behavioural disorders, overwork and stress), musculoskeletal disorders (19% diseases involving bones, joints and connective tissue, particularly carpal tunnel syndrome), malignant tumours (14%) and diseases of the respiratory system (12%). In the SSTs, musculoskeletal disorders (50%) and psychological disorders (33%) were the most common.

Juliette BLOCH (Anses)

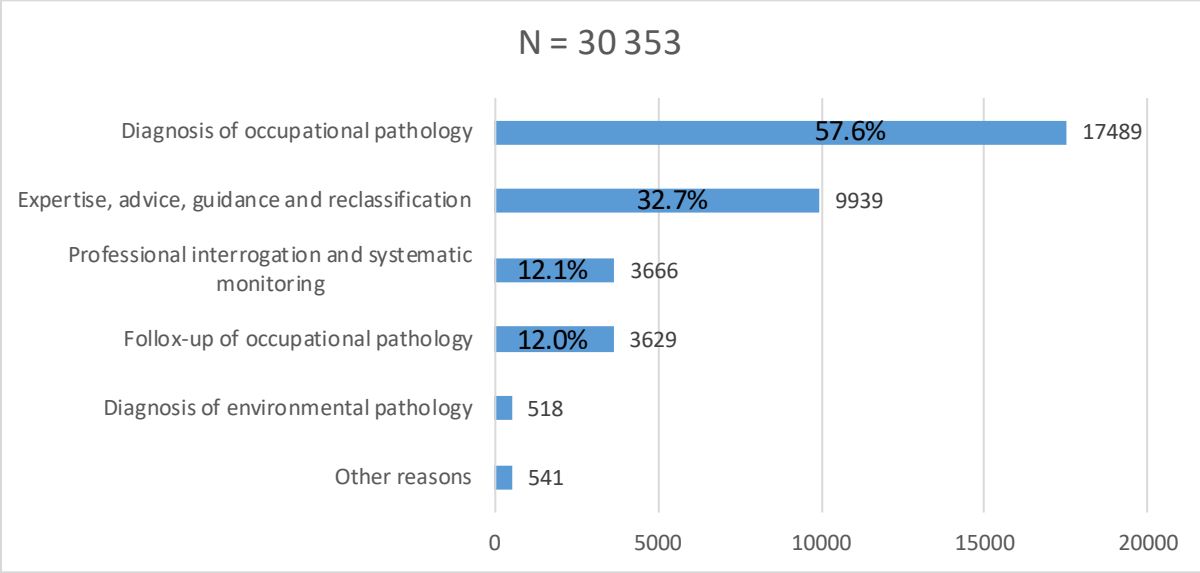

Figure 1: Breakdown of consultations recorded by the CCPPs in 2015 according to the reason for the patients' visit

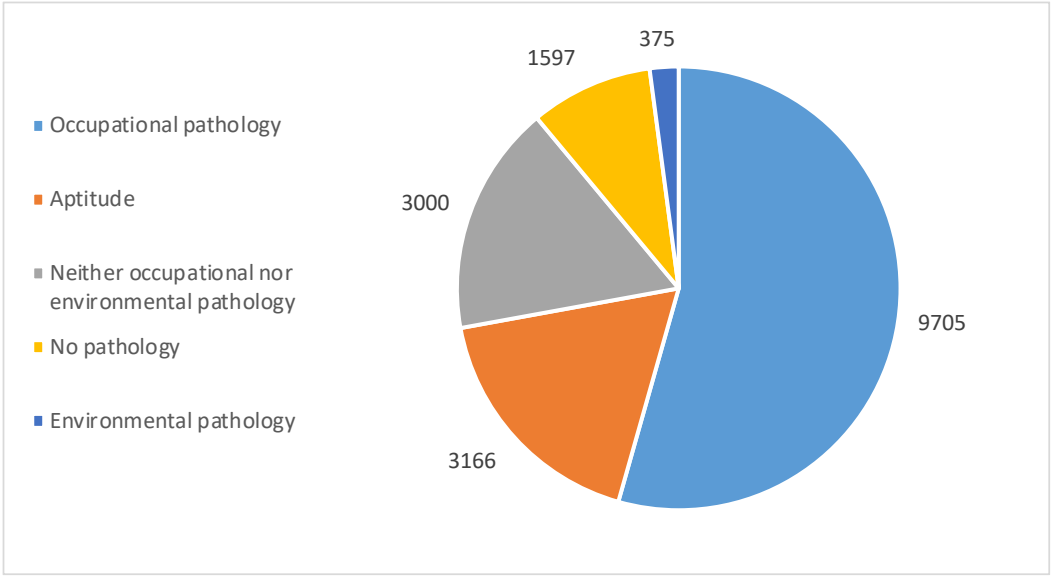

Figure 2: Type of conclusion about the OHPs following consultations in CCPPs in 2015

TO FIND OUT MORE :

RNV3P 2015 Annual Report:
https://www.anses.fr/en/content/rnv3p-national-network-monitoring-and-prevention-occupational-diseases

Risk of silicosis from the manufacture of artificial stone countertops with a high quartz content

In 2016, notified by the Emergence Working Group of the National Network for the Monitoring and Prevention of Occupational Diseases (RNV3P), ANSES alerted the Ministry of Labour of a risk of serious silicosis incurred by people working with **"artificial stone" containing between 70 and 90% quartz** embedded in epoxy or polyester resins (products described as "artificial stone", "high-silica-content artificial stone products", or "quartz conglomerates") [1].

These are high-end materials with excellent technical and aesthetic qualities, which can be through-coloured, and are mainly used for the manufacture of kitchen countertops, bathroom surfaces, sinks and washbasins, etc. While they are produced abroad (including by several suppliers in Europe), these materials are available for sale in France under various trade names (see Figure 1). Besides production, the exposed workers are mainly **stonemasons**. The high risk of silicosis was first identified in Israel in the production sector (25 cases requiring lung transplants [2]). Other cases were then observed that mainly concerned the shaping, sanding and installation of these products: in Spain (46 cases identified following the epidemiological investigation launched after the first three Spanish cases were reported) [3], Italy (7 cases), and Brazil.

In the United States, the occupational health and safety agencies (OASH[1] and NIOSH[2]) issued an alert in 2015 [4], following the documentation of a very serious case of silicosis (requiring a lung transplant) in a 37-year-old man with no previous medical history, after only ten years of exposure. NIOSH also noted that imports of these products have increased by 50% in recent years and that they are one of the most popular materials for kitchen and bathroom countertops. NIOSH's work found that three quarters of the 47 companies in the sector identified carried out at least one of the production steps in dry conditions (when the work should have been conducted under water to avoid dust inhalation) and that only 9% used appropriate methods for all steps [5]. Lastly, this exposure to artificial stone aerosols was associated with the occurrence of autoimmune diseases (a known risk associated with silica exposure) [6].

In France, the alert was issued to the DIRECCTEs[3], CRAMs[4] and CARSATs[5] and to occupational physicians in the field. A first case of silicosis, identified in the RNV3P network following the ANSES alert, is currently under investigation.

In order to be able to identify future cases in the RNV3P, a new code for silica exposure from the machining of this type of material has been created.

Lastly, following this alert, ANSES issued an internal request to investigate the matter, setting up a "Crystalline Silica" Working Group tasked with updating knowledge on the hazards, exposures (occupational sector study) and risks associated with crystalline silica, and proposing risk reduction and prevention measures. The results of this work are expected in 2018.

Photo 1: Display unit showing different shades and finishes of artificial stone with a high silica content. (Source: photo by Vincent Bonneterre

1. OASH: Office of the Assistant Secretary for Health
2. NIOSH: National Institute for Occupational Safety and Health
3. DIRECCTE: Regional Directorate for Business, Competition, Consumer Affairs, Labour and Employment
4. CRAM: Regional Health Insurance Fund
5. CARSAT: Occupational Health and Pension Insurance Fund

These materials have greater flexibility and can usually be machined on the same equipment used to cut wood. As a result, they are used more by **carpenters, fitters or processors approved by suppliers**.

One example is a material experiencing booming sales, which consists of two-thirds alumina trihydrate embedded in an acrylic resin (polymethyl methacrylate). It has several trade names (Corian®, Krion®, Avonite®). These composite materials containing smaller quantities of minerals are in principle less toxic than materials with a high crystalline silica content. Nevertheless, the machining and sanding of this material releases fine particles containing 85% aluminium trihydrate, 30% of which can penetrate the airways and deep into the lungs due to their particle size (peaks at 1 µm and 12 nm) [8]. Machining also causes the release of resin thermodegradation products with irritating properties (the thermodegradation of the resins explains their lower proportion in the particulate phase). Lastly, working with these materials requires the use of large quantities of methacrylic glues to bond the sheets together, fill the joints, etc. The very first sufficiently documented cases of respiratory diseases associated with this exposure were recently described. A first case of pulmonary fibrosis attributed to unprotected exposure to machining dust from this material was published in 2014 in the *New England Journal of Medicine* [7], and a first case of chronic obstructive pulmonary disease (COPD) in a patient working in France, with no other risk factors, has been diagnosed (both cases were based on mineralogical analysis).

In conclusion, with a view to increasing vigilance and secondary prevention (screening) in France, this information needs to be brought to the attention of occupational physicians, preventionists and pulmonologists. If there is any doubt about a related occupational disease, the worker must be referred for investigation to one of the occupational disease consultation centres located in almost every university hospital centre in metropolitan France, and more recently in Reunion Island.

With regard to **primary prevention**, the machining of these types of materials, which offer both technical and aesthetic benefits, should undergo a risk assessment and be carried out under conditions that minimise inhalation. This means prioritising wet methods *for machining artificial stone* (a technique that is far less suited to workshops machining solid-surface materials, which often use the same machines for wood and plywood), as well as HEPA-filtered local exhaust ventilation and the wearing of an effective and suitable respiratory protection mask, particularly for tasks involving the most exposure (e.g. sanding with a hand-held tool on surfaces that are not horizontal).

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(Grenoble Occupational Pathology Consultation Centres)

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[2] Kramer MR et al. Artificial stone silicosis: disease resurgence among artificial stone workers. *Chest*. 2012; 142(2):419-24.

[3} Pérez-Alonso A, et al. Outbreak of silicosis in Spanish quartz conglomerate workers. *Int J Occup Environ Health*. 2014; 20(1):26-32.

[4] Friedman GK, et al. Notes from the field: silicosis in a countertop fabricator - Texas, 2014. *MMWR Morb Mortal Wkly Rep*. 2015; 64 (5):129-30.

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[7] Gannon P, Rickard RW. Pulmonary fibrosis associated with aluminum trihydrate (Corian) dust. *N Engl J Med*. 2014;370(22):2156-7.

[8] Qi C, et al. Dust from Cutting Corian®, a Solid-Surface Composite Material, in a Laboratory Testing System. *Ann Occup Hyg* 2016; 60(5): 638-642.

TO FIND OUT MORE :

ANSES's Crystalline Silica WG
https://www.anses.fr/fr/system/files/2016_01_GT_Silice_cristalline_role_et_missions.pdf
List of occupational disease consultation centres
https://www.anses.fr/fr/system/files/RNV3P-CPP.pdf

Veterinary pharmacovigilance also covers the adverse effects of veterinary medicinal products on humans

Veterinary medicinal products are authorised after an assessment of data on their quality, safety and efficacy has confirmed that the benefits associated with their use outweigh the risks.

The purpose of veterinary pharmacovigilance is to collect and analyse adverse reactions to veterinary medicinal products, in order to ensure that the benefits continue to outweigh the risks. The French Agency for Veterinary Medicinal Products (ANSES-ANMV) is responsible for running this scheme.

The scope of veterinary pharmacovigilance is very broad since it encompasses the reporting of:

- adverse effects in animals after administration of a veterinary medicinal product;
- adverse effects in animals after administration of a medicinal product for human use in the framework of the "cascade" approach[1];
- information about suspicions of lack of efficacy;
- residue problems when the withdrawal period defined in the MA has been complied with;
- environmental problems;

as well as the *reporting of adverse effects in humans after exposure to a veterinary medicinal product*.

These adverse effects in humans can occur through contact with treated animals, through direct contact with a veterinary medicinal product during administration to animals, or following an error of handling or use, such as accidental ingestion by a child, for example.

The risk to the user is assessed as part of the marketing authorisation (MA) procedure for veterinary medicinal products. Any precautions to be taken by the user are mentioned in each medicinal product's summary of product characteristics (SPC) (http://www.ircp.anmv.anses.fr/).

Thanks to feedback via the veterinary pharmacovigilance scheme starting from when the medicinal products are placed on the market, appropriate risk management measures – ranging from the addition of a precaution for use to the withdrawal of the MA – can be taken if necessary.

In France, there are multiple channels for reporting adverse effects in humans (see Figure 1). Most cases requiring a medical response are recorded by the French Poison Control Centres (PCCs) via the toxicology emergency telephone hotline (RTU) after the exposed individual or their doctor has called the PCC for medical advice on the action to be taken.

If there is no emergency, any adverse effects occurring in humans following the use of a veterinary medicinal product can, since March 2017, be notified through the Ministry of Health's **portal for reporting adverse health effects**. These reports are then forwarded to the poison control centre with territorial jurisdiction for analysis.

Since April 2017, all cases recorded by the PCCs have been transmitted to ANSES.

Some reports are sent directly to the o MA holder for the veterinary medicinal product involved. In accordance with the regulation, these cases must be notified to ANSES within 15 days.

As veterinary pharmacovigilance is governed by a European framework, all the cases recorded by ANSES are fed into the European veterinary pharmacovigilance database, which therefore capitalises on all the information from all the countries in the European Union.

2016 review of reports of adverse effects of veterinary medicinal products in humans

Through their emergency telephone hotline activity, the PCCs receive an average of 190,000 calls every year, 40% of which concern cases of symptomatic exposure.

Cases of human exposure to veterinary medicinal products recorded by PCCs are unusual. In 2016, 1,127 calls were related to a veterinary medicinal product, of which 364 cases (32%) were symptomatic. Sixty additional reports concerning humans were also registered directly by ANSES-ANMV.

The main therapeutic categories concerned by these 424 reports (involving 455 veterinary medicinal products) were antiparasitics (40%) followed by vaccines (22%). The remaining reports were divided among the other therapeutic categories.

1. Non-MA use regulated by the French Public Health Code (L.5143-4), which defines under what conditions a veterinary practitioner can in exceptional circumstances use a human medicinal product if no veterinary medicinal products are available on the market to treat a diagnosed disease in a given species.

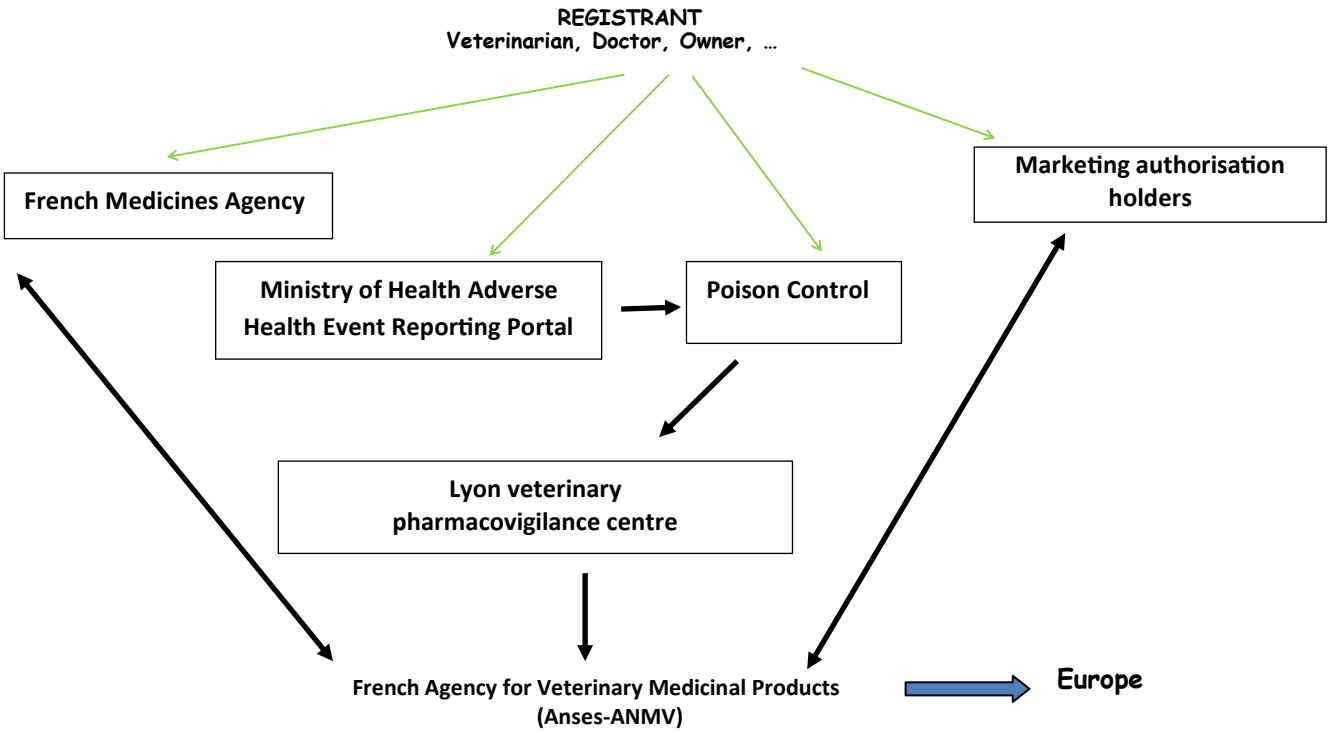

Figure 1: Reporting channel for adverse effects of veterinary medicinal products in humans

This breakdown reflects the sales of these products:

- Antiparasitics proved to be the most frequently implicated veterinary medicinal products. They are widely used in routine treatment for the animal population as a whole (not just sick animals) and are frequently administered by the owners themselves.
- Vaccines were in second place, essentially due to accidental injections. Although this is a category of products whose use potentially concerns all animals (due to it being preventive and not curative), 95% of the 86 reports that stated the name of the vaccine were due to the use of vaccines in production livestock (mainly swine and poultry). This finding is unsurprising insofar as mass vaccination in industrial sectors is more likely to lead to accidents than individual vaccination.

The symptoms described were mainly transient and relatively benign irritations: essentially dermal, eye and/or respiratory signs with ectoparasiticides, or inflammatory reactions in the case of accidental injections. In this framework, a national prospective study (2016-2018) on the risk of complications from accidental needle-sticks involving veterinary vaccines is being conducted by the Poison Control Centres and ANSES.

Sylviane LAURENTIE (Anses-ANMV)

TO FIND OUT MORE, VISIT:

https://www.anses.fr/fr/content/la-pharmacovigilance-vétérinaire

Nutrivigilance: 2016 review of ANSES's national scheme

Implementation of the national nutrivigilance scheme was entrusted to ANSES in July 2009 under the French Act on Regional Health Governance (HPST). The purpose of this scheme is to improve consumer safety by rapidly identifying any possible adverse effects related to the consumption of:

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

Healthcare professionals (doctors, pharmacists, dieticians, etc.) are invited to report these specific foods when they identify adverse effects in their patients that they suspect of being related to their consumption. Consumers who wish to submit an individual report should preferably contact a healthcare professional. The reports are recorded and then analysed initially by the Agency to determine the severity of the incident, the product's composition, any overlap with previous reports, etc. For each report, ANSES may contact the reporter again to obtain any missing information. Reports containing sufficient information and falling within the scope of nutrivigilance (valid cases) are then submitted to medical experts, who analyse the likelihood of a link between consumption of a product and occurrence of an adverse effect (causality).

Causality is determined according to the method defined in the ANSES opinion No. 2010-SA-0195 of 11 May 2011 [1]. Causality may be: excluded (I0), unlikely (I1), possible (I2), likely (I3) or very likely (I4). The Agency informs the authorities (in particular the Ministries of Health and the Economy) of the cases received and may be required to issue an alert (for example, for cases with strong causality and where symptoms are life-threatening). Cases are then examined by a group of specialised experts from ANSES. According to the effects observed, the number of cases received and the likelihood of them being associated with consumption of the product in question, the Agency may decide, with the help of these experts, to conduct a more thorough risk assessment of certain products. This work leads to the publication of scientific opinions and recommendations intended for healthcare professionals and consumers. These opinions are submitted to the ministries concerned to enable them to take appropriate management measures (regulations imposing a maximum limit in food supplements, withdrawal from the market, etc.).

Between the launch of ANSES's nutrivigilance scheme in 2009 and 31 December 2016, the Agency received 2,649 reports of adverse effects.

In terms of reports, 2016 saw a decrease in the number of cases compared to the previous year (340 cases in 2016; 432 cases in 2015) (see Figure 1) with, however, an increase (+26 cases) in the number of spontaneous reports i.e. cases transmitted to nutrivigilance without any request having been issued.

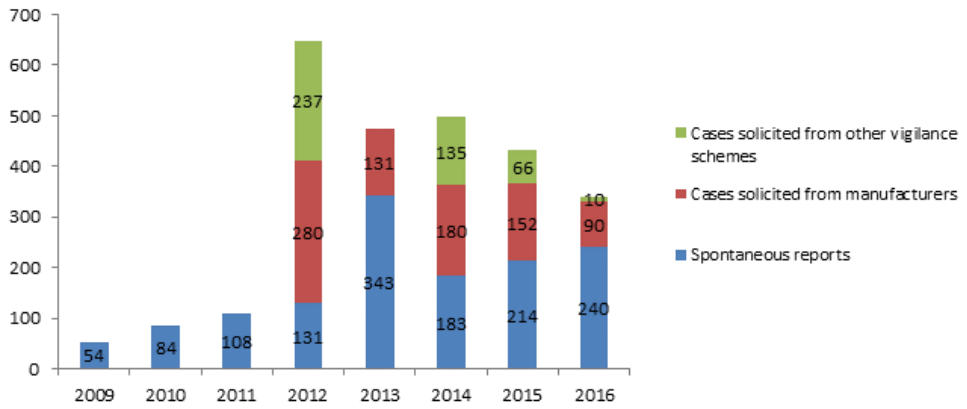

Figure 1: Change in the number of reports received since 2009

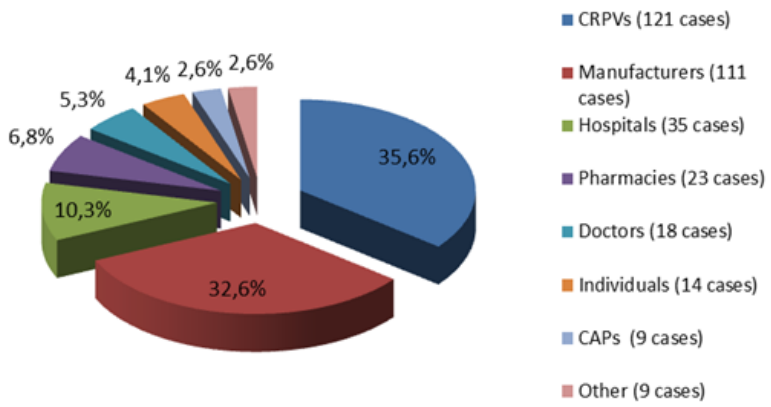

Figure 2: Identity of the reporters.

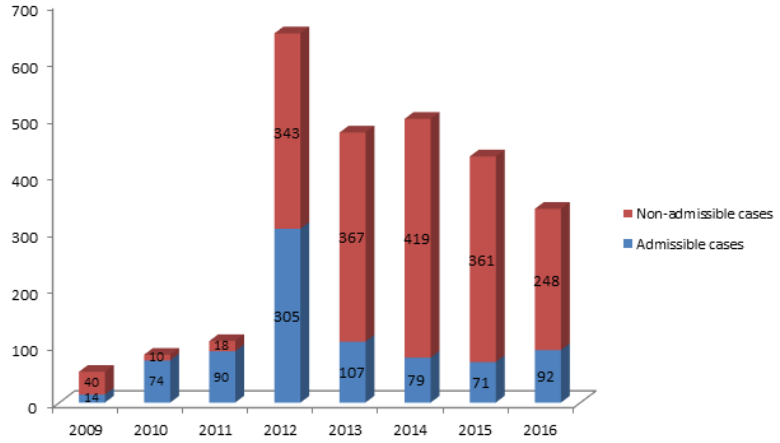

Figure 3: Change in the proportion of valid cases since 2009.

Accounting for more than 35% of the reports transmitted, the regional pharmacovigilance centres (CRPVs) were the main reporters, followed by manufacturers (32.6%). Healthcare professionals in hospitals accounted for around 10% of reporters, pharmacists 7% and non-hospital doctors 5%. Members of the public, who are not meant to notify ANSES's nutrivigilance scheme directly, reported 4% of cases. Lastly, the Poison Control Centres (PCCs) and other professionals (nurses, medical testing laboratory staff, the General Agency for Health Equipment and Products (AGEPS) etc.) each submitted less than 3% of reports (see Figure 2).

In 2016, the proportion of valid cases rose sharply (26% compared to 16% in 2015) with large variations depending on the reporter (50% for pharmacies; 18% for manufacturers) (see Figure 3). Unfortunately, the main reason preventing exploitation of cases was a lack of data on, for example, the dates the product was taken or the progression of the adverse effect.

As in previous years, the vast majority of the cases received involved food supplements (89.9% of the valid cases received in 2016). These are mainly intended for people seeking "joint comfort", or improved "vitality" or "vision".

Most of the reported adverse effects were of a general nature (impaired general state of health, fever, etc.) or concerned the digestive system (intestinal or hepatic). In 2016, causality of the products was found to be likely in 35% of cases and very likely in 3% of cases.

In terms of publications, ANSES issued an opinion on food supplements for athletes in 2016 [2] and an opinion on food supplements for pregnant women in June 2017 [3].

ANSES is also continuing its work to produce opinions on the risks associated with consumption of:

- food supplements containing spirulina;
- food supplements containing melatonin;
- food supplements for joint comfort containing glucosamine and/or chondroitin.

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The Agency reminds healthcare professionals of the importance of their participation as reporters to notify ANSES of cases of adverse effects that they suspect of being associated with the consumption of food supplements. ANSES asks them to continue questioning their patients during medical consultations about their use of food supplements and other special dietary foods such as fortified foods, and to notify the nutrivigilance scheme of any adverse effects they are made aware of.

References

[1] Method for determining causality in nutrivigilance https://www.anses.fr/fr/system/files/NUT2010sa0195.pdf

[2] Opinion on food supplements for athletes https://www.anses.fr/fr/system/files/NUT2014SA0008Ra.pdf

[3] Opinion on food supplements for pregnant women https://www.anses.fr/fr/system/files/NUT2013SA0240Ra.pdf

ANSES is in charge of several health vigilance systems: pharmacovigilance for veterinary medicinal products, nutrivigilance, phytopharmacovigilance, toxicovigilance and vigilance for occupational diseases. Our vigilance activities make little noise and are therefore poorly known to public health actors, health professionals, marketers and users in general. And so, in order to make our work more visible we have decided to create a dedicated newsletter entitled Vigil'Anses.

As news on each of our vigilance topics crops up, this quarterly newsletter presents the main results of the work carried out by ANSES within the framework of its vigilance missions, in conjunction with its partners, professional networks and expert groups, as well as the actions we have undertaken.
The articles are deliberately short, and are intended for all those involved in the occupational and environmental health and safety field: public authorities, health agencies, institutes and expert bodies that are partners of ANSES, prevention policy managers, the scientific community, professionals, associations and users. Vigil'Anses also invites the interested reader to delve deeper and discover publications, opinions and reports available online that will further their knowledge.

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