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Not all squash are edible

In France, squash, pumpkins, melons and colocynths are often seen on market stalls and in family vegetable gardens. The species usually grown and marketed in Europe are the following: *Cucumis melo* (melon), *Cucumis sativus* (cucumber, gherkin), *Cucurbita pepo* (squash, courgette), *Cucurbita moschata* (butternut squash, etc.), *Cucurbita maxima* (pumpkin), *Citrullus lanatus* (watermelon). Many other vegetable varieties are also available under the name "squash". The species name *Cucurbita pepo* L. includes not only squash, courgettes and pumpkins (edible forms), but also ornamental colocynths (inedible forms).

Inedible *Citrullus Colocynthis* – Source: Pr A. Badoc

Not all "squash" are edible, and the shape and colour of some inedible squash can be misleading to the uninformed consumer. Individuals may have inadvertently planted inedible species in their vegetable gardens, but there may also be hybridisation of edible squash with inedible squash where several species are grown in close proximity.

The toxicity of inedible species is mainly digestive, due to the presence of bitter cytotoxic compounds called cucurbitacins. These are responsible for the unpleasant taste of the squash and above all for a drastic intestinal purgative action. However, there is still uncertainty about the link between cucurbitacin, bitterness and toxicity, and there is a lack of studies on the subject.

Against this background, Poison Control Centres (PCCs) are regularly consulted about the occurrence of digestive disorders associated with the consumption of supposedly edible "squash".

For example, in the five years between 1 January 2012 and 31 December 2016, 176 dossiers[1] concerning 353 people having eaten an inedible gourd were registered in the PCC information system. As expected, cases occurred most often (82% of cases) at harvest time in the second half of the year, and on average, two people were exposed to the same vegetable.

The origin of the inedible gourd was determined in 86 dossiers (48.8%) corresponding to 197 people:

- Purchased at the market, supermarket or market gardener ("market") for 32 dossiers (18.2%) involving 90 people;
- Grown in the family vegetable garden ("garden") for 52 dossiers (29.5%) involving 105 people;
- Collection of "wild" specimens for two dossiers involving two people.

More than two thirds (n=204) of the individuals experienced digestive symptoms, mainly diarrhoea (54.4%) and vomiting (47.5%), which most often appeared very rapidly after ingestion (a few hours) and lasted for up to several days.

There were no fatalities or serious cases. The worst affected individuals (n=14, 4%), mainly elderly people or very young children, who are therefore more vulnerable, suffered major digestive disorders that were poorly tolerated (hypotension, dehydration) and some required hospitalisation.

Poisoning from commercially purchased inedible gourds is not uncommon.

Inedible "ornamental" squash should be sold only in the "decoration" section of a shop or in a dedicated section during specific periods (Halloween, etc.), and not near edible squash. If, however, these squash are used to decorate a display in the vegetable section, the "inedible" label should be clearly visible, to avoid confusion in the event of purchase, with a clear separation from edible squash.

Cucurbita maxima or edible pumpkin – Source Pr A. Badoc

1. A dossier consists of one or more related cases: here, several people who have eaten the same product.

This would limit the risk of shoppers mistaking ornamental squash for vegetables.

In the case of home-grown "squash", it also seems important that garden centres or seed companies clearly indicate the species, variety and edibility on young plants or seed packets. They should also clearly mention the possibilities of hybridisation when two species of cucurbits – one of which is inedible – are planted in close proximity.

Magali LABADIE (Bordeaux Poison Control Centre)

TO FIND OUT MORE, VISIT:

http://www.centres-antipoison.net/cctv/CCTV_Courges_2017.pdf

The Toxicovigilance scheme in the French Caribbean

The French Caribbean toxicovigilance scheme (DTV Antilles) was set up in November 2014, as part of the measures taken following contamination of the soil by chlordecone and its health consequences. This is a toxicovigilance scheme and not a Poison Control Centre (PCC) because unlike the PCCs, the DTV Antilles does not have an emergency telephone hotline (RTU). However, if necessary, the Paris PCC can respond to telephone requests from the French Caribbean thanks to its round-the-clock service, seven days a week.

The DTV's operational objectives are to set up and coordinate networks on different themes specific to local characteristics or areas of interest, such as poisonings associated with pesticides, local fauna and flora, or certain traditional medicines [1]. The DTV works in close partnership with the competent authorities – regional health agencies (ARS), regional intervention units (CIRE), national health and safety agencies – and has joined the national toxicovigilance network coordinated by ANSES. For non-emergency cases and working closely with the Paris PCC, it responds to requests from healthcare professionals in the region and the public, for information on exposure to toxic mixtures or substances, on assessing the resulting risks and/or on their prevention. The DTV is exclusively funded by ANSES.

Below are the most important lessons learned from the first three years of operation.

1. Epidemiological surveillance of acute poisoning occurring in Guadeloupe's hospital emergency departments between 2013 and 2015 identified 2,822 poisoning cases (excluding alcohol) [2]. The study highlighted strong local specificities, in particular (suspected) cases of poisoning by ciguatera, a biotoxin found in certain fish and responsible for a neurological syndrome (n=59), Scolopendra centipede bites (n=214), lionfish stings (n=47), and poisoning by ammonia (n=94), aldicarb (an insecticide that has been banned since 2004) (n=8) and alpha-chloralose (n=9). The latter was also the subject of a national study by PCCs, which revealed a use specific to Guadeloupe: alpha-chloralose was prepared in pharmacies in a mixture with lard for use as a rodenticide. In view of the frequency and severity of the cases observed, a reminder was sent to the National Council of the Order of Pharmacists, specifying that since alpha-chloralose is no longer listed in the Pharmacopoeia, pharmacists are no longer authorised to prepare or sell alpha-chloralose products unless they comply with the biocide regulations in terms of concentration and packaging [3]. Lastly, a specific study on jellyfish stings showed that these poisoning cases, whose periodicity was correlated with the seasons and the moon cycle, were frequently associated with Irukandji syndrome (more severe envenomation with dermal signs, but also generalised delayed-onset symptoms, including extreme pain and other signs such as sweating, severe anxiety, nausea, vomiting, etc.). It included a description of the first case of cardiac decompensation outside the Pacific [4].

2. Reports from healthcare professionals helped identify the liver toxicity of a plant widely used by diabetics in the French Caribbean, Tinospora crispa [2], as well as the cardiac toxicity of manchineel fruit.

3. Toxicological expert appraisals carried out at the request of the health authorities led to detection of the presence of aristolochic acids, which are nephrotoxic and carcinogenic substances, in a traditional preparation containing caterpillars macerated in alcohol [5], and provided scientific support for local problems such as masses of Sargassum seaweed washing up on the coasts and water contaminated by hydrocarbons in a Guadeloupe municipality.

These selected examples show the value of DTV Antilles in improving knowledge and prevention of poisoning in the French Caribbean.

Juliette BLOCH (Anses)

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Cellulose wadding: how toxicovigilance data led to a regulatory restriction

Cellulose wadding is used as sound or thermal insulation in housing. It is applied by blowing, spraying or flocking into the walls and attics of homes.

Until 2011, boron salts were added to cellulose wadding insulation materials for their antifungal and flame-retardant properties. However, under the former Biocides Directive (repealed in 2012 in favour of Regulation (EU No 528/2012)), boric acid and its salts were banned as antifungal agents because of their toxicity to reproduction (harmonised classification "Reprotoxic Category 1B" – substances presumed to be toxic to human reproduction). As a result, boric acid and its salts could no longer be used in concentrations higher than 5.5%.

In France, because the Commission responsible for formulating technical opinions (CCFAT) decided not to renew opinions extending the authorisation of boron salts, cellulose wadding manufacturers replaced these salts with ammonium salts, as of November 2011. These additives made up between 6 and 12% of the total mass of the insulation.

In 2012, the French Poison Control Centre (PCC) in Angers received a complaint from a family exposed to an irritating ammonia odour following the installation of cellulose wadding insulation. A health technician visiting the home in question confirmed indoor air pollution with ammonia.

At the same time, the Directorate for Housing, Urban Planning and Landscapes (DHUP) was informed by the European Cellulose Insulation Manufacturers Association (ECIMA) and the French Scientific and Technical Centre for Building (CSTB) of a growing number of complaints of ammonia odours in homes following the installation of cellulose wadding insulation. ECIMA had registered 115 complaints with indoor air measurements of the buildings indicating the presence of ammonia.

Testimonies collected on internet DIY forums also confirmed the high number of customer complaints due to the release of ammonia from this wadding.

In December 2012, the Directorate General for Health (DGS) requested a one-year retrospective analysis of cases registered by PCCs.

The retrospective study identified 10 dossiers involving 19 people exposed between February and November 2012: 14 adults and five children, almost all complaining of an odour in the home that had alerted them. In two cases, the exposed individuals had installed the cellulose wadding themselves. One case involved occupational exposure.

Fifteen exposure cases showed symptoms of irritation to the eyes, nose, throat (ENT) and airways, of mild to moderate severity. These symptoms were all accompanied by a characteristic smell. Indoor air measurements had been taken in only three homes and had indicated the presence of ammonia.

While in 2012, ECIMA estimated that 20,000 French homes were fitted with cellulose wadding insulation, the low number of cases identified by the PCCs and the few cases for which indoor air measurements had been taken, supported the need for a prospective survey. This was conducted with the support of the regional health agencies (ARSs), so that metrological analyses of indoor air could be carried out.

The ARSs were therefore asked to participate, together with the PCCs, in the collection of information on the environmental circumstances of the building concerned and the clinical manifestations of the cases identified. This led to 14 dossiers involving 43 patients being registered between January and July 2013, corresponding to 19 children and 24 adults. Symptoms included upper airway irritation, coughing and bronchospasm. Only four indoor air measurements were performed in the suspect dwellings, which indicated low levels of ammonia contamination. In five cases, the cellulose wadding was removed completely. In three cases, it was partially removed, which is possibly not enough to avoid potential recurrences of ammonia releases.

Alongside this prospective study, the National Network for the Monitoring and Prevention of Occupational Diseases (RNV3P) identified five cases of occupational exposure, for which signs of minimal ENT irritation were observed, including one case of *de novo* asthma.

An analysis of the exposure circumstances of the cases identified by the PCCs and the RNV3P concluded that humidity (e.g. wet weather) or contact of the cellulose wadding with

On the basis of these clinical observations, France prohibited the marketing, import, sale or distribution and manufacture of cellulose wadding insulation containing ammonium salts (Ministerial Order of 21 June 2013). These materials have therefore been recalled and withdrawn from the French market.

Following this regulatory action, France informed the European Commission, the European Chemicals Agency (ECHA) and the Member States that urgent action was needed at the European level to protect against ammonia emissions from ammonium salts incorporated in cellulose wadding.

Then, following Commission Implementing Decision of 14 October 2013 authorising the provisional measure taken by the France in accordance with Article 129(3) of Regulation (EC) No 1907/2006 (REACH), a restriction dossier was prepared within three months of the date of the Commission Decision. ANSES was mandated to prepare this dossier.

As part of this process, many industry stakeholders, all the Member States and the European PCCs were consulted, which revealed an absence of complaints and cases outside France, weakening the restriction proposal.

A third investigation was then conducted by the French PCCs between July and December 2013, which identified new cases of exposure (12 dossiers). This also supplemented the information from the previously identified cases, showing that in the vast majority of cases, no indoor air measurements for ammonia had been carried out. In clinical terms, the exposure aggravated symptoms in two children, one of whom – a known asthmatic – had a new asthma attack at the time of exposure. This third investigation also showed that the corrective measures taken in seven of the 12 dossiers (removal of the cellulose wadding) had led to the rapid disappearance of the odour and recovery from the symptoms.

Considering this new clinical evidence, considering the assays carried out by the CSTB to test the stability of ammonium salts in cellulose wadding under experimental conditions (emission test chamber, high relative humidity), and considering the modelling of exposure to ammonia in housing, ANSES concluded in June 2014 that there was a risk to the population's health related to the ammonia released by cellulose wadding containing ammonium salts. The restriction proposed by ANSES involved prohibiting the marketing in Europe of cellulose wadding containing ammonium salts unless the ammonia emissions of such materials were less than 3 ppm according to the CEN/TS 16516 technical specification with some adaptations (test duration of 14 days with a moisture content of 90%).

This restriction was adopted by the European Commission in June 2016, prohibiting the placing on the market and use of cellulose wadding containing ammonium salts after 14 July 2018, unless it complies with the emission limits proposed by ANSES.

Research and development work has been then undertaken, in particular by ECIMA, to identify new additive formulations for cellulose wadding.

In France, in late 2012, the CCFAT issued new technical opinions authorising the use of boron salts as cellulose wadding additives at concentrations of less than 5.5%. The CCFAT extended the validity of these opinions until less hazardous alternatives to ammonium salts were identified.

This example illustrates the role and importance of toxicovigilance data in a European public health context, allowing the implementation of binding, harmonised regulatory measures at EU level. This situation also illustrates the possible pitfalls of attempts at substitution, which require constant vigilance.

Cécilia SOLAL (Anses)

TO FIND OUT MORE, VISIT:

European restriction dossier
https://echa.europa.eu/documents/10162/ceea529c-8aed 471a-9010-b465ac833b38

ANSES Opinion:
https://www.anses.fr/fr/system/files/REACH2014re0001.pdf

CCTV reports:
http://www.centres-antipoison.net/cctv/Rapport_CCTV_Ouate_de_cellulose_VF_Fevrier_2013.pdf
http://www.centres-antipoison.net/cctv/Rapport_CCTV_Ouate_de_cellulose_VF_Septembre_2013.PDF

Phytopharmacovigilance: the only vigilance scheme of its kind in Europe

Plant protection products designed to protect plants and crop products against pests can pose risks to human health, ecosystems and living organisms, which need to be identified and monitored in order to better prevent them. With this in mind, the legislator created a scheme, known as phytopharmacovigilance, for detecting and monitoring adverse effects associated with the use of plant protection products available on the market. Implementation of this vigilance scheme, enshrined in the Act on the future of agriculture, food and forestry of 13 October 2014, was entrusted to the French Agency for Food, Environmental and Occupational Health & Safety (ANSES). Phytopharmacovigilance is the latest addition to ANSES's missions on prior assessment of risks associated with plant protection products, as part of the process to issue marketing authorisations.

In this context, ANSES is tasked with collecting all reports of adverse effects related, or potentially related, to the use of plant protection products. This vigilance scheme, set up in 2015 and the only one of its kind in Europe, covers all adverse effects concerning the environment, food, and plant, animal and human health.

It operates on the basis of information produced by existing surveillance or vigilance networks, reports of adverse effects, and the possibility of conducting studies to answer specific questions.

The surveillance and vigilance networks taking part in phytopharmacovigilance were appointed by the Ministerial Order of 16 February 2017. About 15 organisations operating in the many fields covered by phytopharmacovigilance (adverse effects of plant protection products on humans, farmed and wild animals or ecosystems, as well as the appearance of resistance phenomena) provide ANSES with regular reports and data collected under the scheme, and alert the Agency in the event of any serious, immediate or unexpected risk.

Specifically with regard to human health, these organisations are:

- Poison control centres (PCCs), whose toxicovigilance activities are coordinated by ANSES;
- The Phyt'attitude scheme of the Agricultural Mutual Insurance Scheme (MSA);
- The National Network for the Monitoring and Prevention of Occupational Diseases (RNV3P), coordinated by ANSES; *Santé Publique France*;
- The AGRICAN cohort[1] led by the François Baclesse Centre.

Whether it concerns humans, farmed and wild animals, ecosystems, or the appearance of resistance phenomena, reporting the adverse effects of plant protection products is mandatory for certain professional stakeholders such as holders of marketing authorisations and parallel trade permits[2] for plant protection products, manufacturers, importers, distributors or professional users of plant protection products, as well as advisers and trainers of these users. In these cases, reports are transmitted to the body competent to deal with them, which informs ANSES via a notification. Cases can also be sent directly to ANSES via the web page devoted to reporting. However, anyone can report an incident, accident or adverse effect, associated or potentially associated with a plant protection product or an adjuvant.

How should an adverse effect in humans be reported?

Anyone experiencing an adverse effect requiring medical advice or treatment should contact a doctor or a poison control centre.

For other situations, or if some time has passed since their occurrence, if the adverse effects resulting from the use of plant protection products specifically affect the health of farmers and/or people affiliated to the MSA, they must be reported to the MSA's specific Phyt'attitude scheme via the French freephone number: 0 800 887 887.

1. The AGRICAN (AGRIculture and CANcer) cohort study is an epidemiological study launched in 2005 to address the lack of information on occupational risks in the French agricultural population (exposure to plant protection products, fertilisers, UVs, mechanical risks, animal viruses, mould, etc.). Scheduled to continue until 2020, it is based on the follow-up of 180,000 agricultural insurance holders and is now one of the largest studies in the world on health in agriculture.

2. A plant protection product that is authorised in one Member State (Member State of origin) may, subject to the granting of a parallel trade permit, be introduced, placed on the market or used in another Member State (Member State of introduction) if the latter establishes that the plant protection product is identical in composition to a plant protection product already authorised in its country (reference product). The application is submitted to the competent authority of the Member State of introduction.

All other reports (by non-farmers and/or anyone not affiliated to the MSA, healthcare professionals), can be formalised via the Ministry of Health's portal for reporting adverse health events (https://signalement.social-sante.gouv.fr/psig_ihm_utilisateurs/index.html#/accueil). Professionals subject to the reporting obligation have a dedicated area for submitting their reports on this same portal.

The reports registered on the portal are processed and assessed by MSA doctors for reports to Phyt'attitude, or by the regionally competent PCC for other cases. Anonymised data on adverse effects are regularly communicated to ANSES, which will immediately be notified of any reports submitted by a professional subject to the reporting obligation.

The reporting channel for adverse effects occurring in humans following the use of plant protection products is shown in Figure 1.

Depending on the severity of the effect mentioned and the results of the investigations carried out, ANSES and/or the competent authorities can then immediately take all measures necessary to limit the impact (e.g. by amending the product's conditions of use).

How should an adverse effect not related to human health be reported?

Adverse effects of plant protection products on animals, plants, food, environments or ecosystems must be reported using a dedicated form[3] depending on the status of the reporter, and sent to ANSES by post[4] or by email (ppv@anses.fr).

Ad hoc studies are financed under the phytopharmacovigilance scheme when information on adverse effects provided by surveillance and vigilance organisations is deemed to warrant further clarification, or in order to improve the quality and accessibility of information from partner networks for phytopharmacovigilance purposes.

The phytopharmacovigilance scheme pools the information derived from the surveillance or vigilance schemes, conducts *ad hoc* studies and collects spontaneous reports to meet its three objectives:

- enable the marketing authorisation conditions of products currently on the market to be adapted, if necessary (for example, by reducing doses, adapting the conditions of application or withdrawing a marketing authorisation);
- define cross-cutting management measures, for example for protecting people in the vicinity of treated areas;
- contribute to enforcing compliance with bans on the use of products, especially those whose active substances are no longer approved at European level.

Anita VIGOUROUX-VILLARD

TO FIND OUT MORE, VISIT:

ANSES page:
https://www.anses.fr/fr/content/signalement-deffets-ind%C3%A9sirables-li%C3%A9s-%C3%A0-lutilisation-de-produits-phytopharmaceutiques

Act No. 2014-1170 of 13 October 2014 on the future of agriculture, food and forestry: https://www.legifrance.gouv.fr/affichTexte.do?cidTexte=JORFTEXT000029573022&categorieLien=id

Decree 2016-1595 of 24 November 2016 on phytopharmacovigilance: https://www.legifrance.gouv.fr/jo_pdf.do?id=JORFTEXT000033478559

3. The reporting forms are available on the ANSES website from the following page: https://www.anses.fr/fr/content/signaler-un-effet-indésirable-ne-portant-pas-sur-la-santé-humaine-lié-à-lutilisation-de

4. ANSES, Direction de l'évaluation des risques, Unité phytopharmacovigilance et observatoire des résidus de pesticides, 14 rue Pierre et Marie Curie, 94 701 Maisons-Alfort Cedex, France

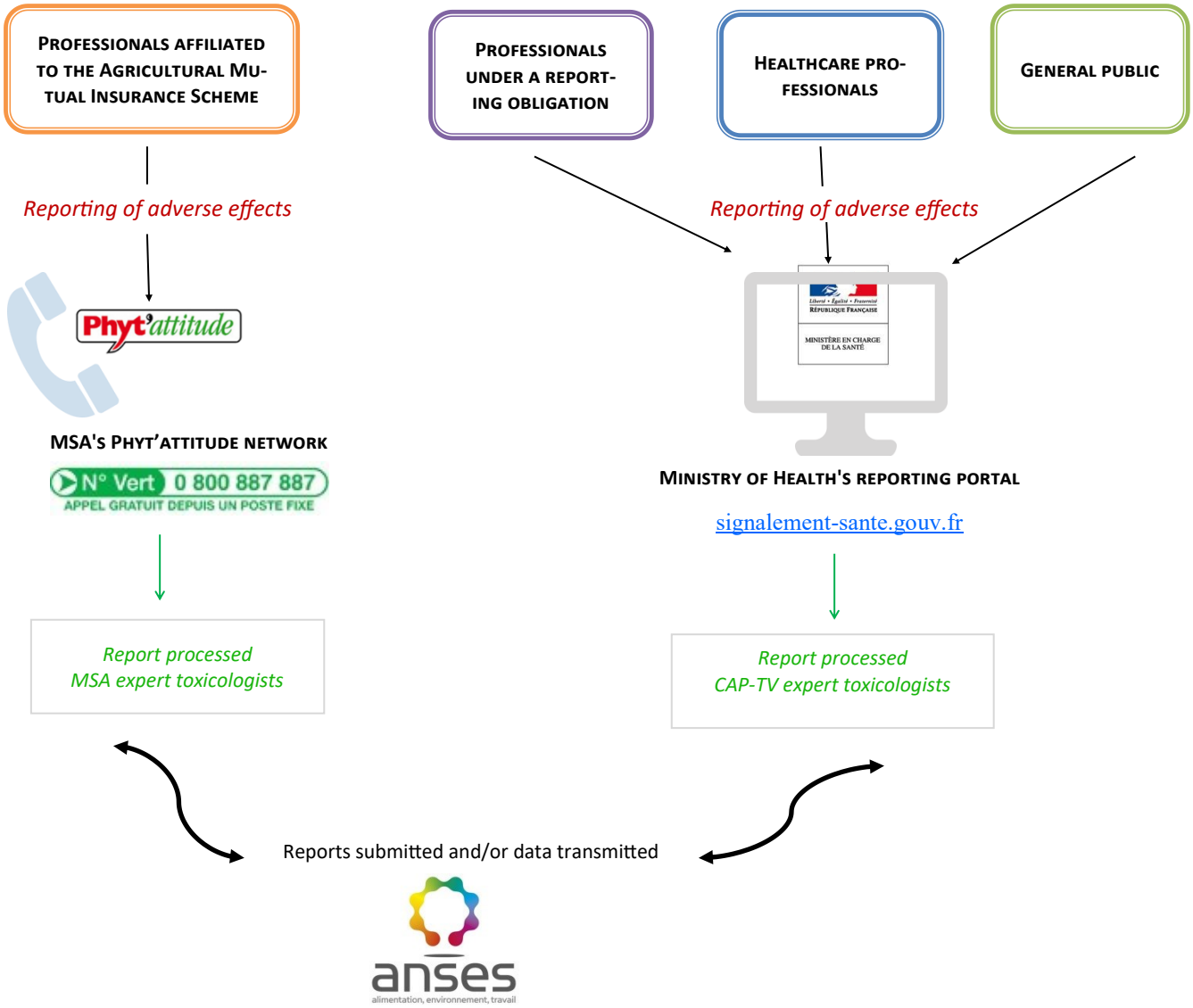

Figure 1: The phytopharmacovigilance scheme: channels for reporting adverse effects in humans

Sentinel systems in occupational health and detection of new occupational diseases

The history of the relationship between health and work is punctuated by the description of new diseases, which then raise questions about their prevalence and incidence, primary prevention (identification and consideration of their risk factors), secondary prevention (screening and diagnosis), and possible recognition under occupational disease regulations.

The number of people affected by diseases that have only recently been linked to work (or whose link to work had not previously been demonstrated) is related to three different time factors: 1) the time needed to formulate the hypothesis that a given exposure constitutes a risk of inducing a disease, 2) the time needed to substantiate this hypothesis if necessary (experimental studies, epidemiology, risk assessment), 3) the time needed to take the risk into account and implement effective preventive measures. Actions that identify early relevant signals should therefore help reduce more effectively the number of diseases associated with emerging occupational risks.

Over the last decade, the issue of emerging occupational health risks has regularly been on the agenda of the European Union's occupational health strategy [1,2]. This has enabled the European Agency for Safety and Health at Work (EU-OSHA) to set up an observatory on emerging risks. For several years, this observatory has been advocating an a priori approach working on the drivers of emergence, such as globalisation and its consequences, new technologies (e.g. nanoparticles), emergence of the green economy ("green jobs"), or more recently additive manufacturing ("3D printing"), surveillance technologies in the workplace, etc. Relying on expert forecasts commissioned by EU-OSHA, this observatory considers emerging risks to be those that are both new and whose importance increases over time. The concept of "new" is quite broad and includes psychosocial risks and musculoskeletal disorders. This approach is ill-equipped to accurately predict the emergence of new diseases, and is certainly unable to identify them.

In addition to this first essential risk-based approach, therefore, another approach should be developed that focuses primarily on investigating the occupational origin of certain diseases that seem to be associated with new occupational settings. This approach, based on sentinel and alert systems, has been promoted by the European Modernet network, one of whose most active partners in this area is the National Network for the Monitoring and Prevention of Occupational Diseases (RNV3P), run by ANSES. The RNV3P has the most extensive experience in developing an approach to detecting, assessing and taking into account emerging risks, and has been leading the discussions on the subject within Modernet. The RNV3P's approach, detailed in its 2014 scientific report [3,4], consists of three stages: signal detection, expert appraisal and action. The detection of suspected emerging cases is based on: 1) either the reporting by clinicians of diseases that seem to reveal new risks, 2) or the identification, by statistical non-targeted data mining methods applied to the RNV3P database (containing more than 250,000 observations), of similar cases that are not known to be occupational diseases, 3) or lastly, by literature monitoring (as in the situation of silicosis related to the machining of new types of quartz surface materials, presented in the previous issue of Vigil'Anses) [5]. After undergoing expert appraisal, the situations are then analysed using a three-dimensional algorithm (severity1, causality and number of cases). This enables the type of action to be taken to be defined in a transparent and reproducible manner. Out of nearly 50 situations investigated to date, four have led to national alerts [6-9].

EU-OSHA commissioned and supervised a summary of the sentinel and alert networks working to identify new occupational diseases, the first volume of which has been available on the EU-OSHA website since late August 2017. This is a review of the systems for collecting occupational diseases, or suspected occupational diseases, identified at the international level.

A total of 75 systems from 26 countries were identified. Of these, 22 are linked to a reporting process with a view to redress/compensation, 16 of which are at least partially open to non-listed diseases in a restrictive manner and which could therefore, theoretically, be used to identify new diseases. On the other hand, 34 other systems are designed for the epidemiological monitoring of certain families of diseases (e.g. respiratory diseases), usually without any expert appraisal of occupational causality, which may limit their ability to identify new work-related diseases.

Only 12 "sentinel" systems were identified, whose objective is to highlight situations requiring intervention or even alerts. Four of these systems are capable of identifying new occupational diseases of any kind.

1. Estimated severity according to the Poison Severity Score (PSS)

These include the new SIGNAAL system to enable field occupational physicians in the Netherlands and Belgium to report suspected new occupational hazards, and the US SENSOR (Sentinel Event Notification System on Occupational Risks), which is only currently in operation for effects attributed to pesticides. The second volume of EU-OSHA's review, which should be available soon, is a qualitative study of 12 of these systems, three of which are French: the RNV3P run by ANSES, as well as the occupational health alert groups (GASTs) and the EpiNano cohort run by *Santé Publique France*. Other systems are detailed, including the Norwegian RAS sentinel system, which is unique in that it is led by the labour inspectorate and directly linked to a response in the field.

The way these systems assess occupational exposure and ensure feedback to assist with prevention are also compared.

Lastly, this work highlights the importance of international cooperation. In this regard, ANSES developed for the Modernet consortium the prototype of a tool enabling partner occupational disease experts to share anonymised cases of suspected new diseases online, in order to conduct joint expert appraisals (OccWatch platform). The report welcomed this as an opportunity. The platform, funded and supervised by ANSES, will be available on 1 January 2018.

In conclusion, several European initiatives are coming together to help identify new occupational diseases. These initiatives are not yet as well structured and permanent as the well-established pharmacovigilance and toxicovigilance schemes, but are likely to become so, and should improve responsiveness to emerging health issues likely to affect workers.

Vincent BONNETERRE

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TO FIND OUT MORE :

Methodologies to identify work-related diseases: Review on sentinel and alert approaches. EU-OSHA 2017

Endocrine and metabolic risks associated with vitamin D and iodine intake through food supplements during pregnancy

Five cases of neonatal hypercalcaemia and two cases of congenital hypothyroidism involving food supplements for pregnant women have been reported under the national nutrivigilance scheme overseen by ANSES. These reports led ANSES to assess the risks associated with the consumption of food supplements containing vitamin D or iodine intended for pregnant women.

Neonatal hypercalcaemia and vitamin D

The analysis of the reports received showed that the doses of vitamin D provided by "pregnancy" food supplements are not by themselves likely to lead to hypercalcaemia in a pregnant woman or a healthy foetus.

Nevertheless, if the child has a genetic hypersensitivity to vitamin D, intake of this vitamin during pregnancy may result in neonatal hypercalcaemia. Screening for this anomaly, which is not routinely carried out, would have been able to confirm the origin of the hypercalcaemia reported to the nutrivigilance scheme.

Congenital hypothyroidism and iodine

Iodine is needed for the neurological and behavioural development of the foetus. However, an excessive iodine intake (oral or transdermal) during pregnancy increases the risk of hypothyroidism, hyperthyroidism or goitre in the newborn.

For the two cases of congenital hypothyroidism received by the nutrivigilance scheme, the available data could not be used to formally incriminate the food supplement, which was not the only source of iodine to which the mother was exposed.

ANSES's recommendations

Besides the cases associated with the consumption of vitamin D and iodine that were reported to the nutrivigilance scheme, ANSES warns against combining multiple sources of vitamins and minerals in the absence of an identified need. In some cases this may lead to the upper intake levels being exceeded.

For pregnant women:

- ANSES reminds pregnant women that they should not consume food supplements without first seeking the advice of a healthcare professional, and recommends that they inform their doctor, pharmacist or midwife of any product (medicine or food supplement) they have taken, whether it was issued on prescription or purchased over the counter.

For healthcare professionals:

- The consequences of hypercalcaemia on newborn health, in the event of hypersensitivity to vitamin D, require appropriate preventive measures to be implemented. In the event of confirmed hypercalcaemia in a pregnant woman, it will be necessary to search for the cause with the appropriate examinations and reconsider the relevance of vitamin D supplementation.

- In newborns, in cases of unexplained hypercalcaemia, it is important to screen for a mutation in the gene predisposing the child to hypercalcaemia.

- The simultaneous exposure to multiple sources of iodine (from drugs or food supplements) increases the risk of thyroid disorders in newborns and must therefore be avoided during pregnancy.

- The Agency stresses the importance of not combining different sources of vitamins and minerals without regular biological monitoring.

Lastly, the Agency reminds healthcare professionals of the importance of notifying the nutrivigilance scheme of any adverse effects they are made aware of, which could be related to the consumption of food supplements.

Gwenn VO VAN REGNAULT (Anses)

TO FIND OUT MORE, VISIT:

ANSES OPINION and REPORT on the endocrine and metabolic risks related to the intake during pregnancy of vitamin D and iodine through food supplements involved in cases of nutrivigilance. May 2017
https://www.anses.fr/en/system/files/NUT2013SA0240EN.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.

anses

French agency for food, environmental
and occupationnal health and safety
14 rue Pierre et Marie Curie
94 701 Maisons-Alfort Cedex

www.anses.fr / @Anses_fr

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