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Annual Report 2023

Editorial

Valérie Delahaye-Guillocheau, Chair of the ANSM Management Board
Christelle Ratignier-Carbonneil, Director General of ANSM (until June 2024)

In 2023, ANSM was once again fully mobilised by a series of challenges and significant actions carried out for the benefit of patients.

The Agency continued to roll out its initiatives to protect the public and ensure the safety of health products. It reinforced the public health policy to combat the misuse of medicines, launched in 2022 and co-constructed with all stakeholders, healthcare professionals and patients. This took the form of a new communication campaign targeting the general public, which raised everyone's awareness of the need to use medicines properly.[1]

As part of this information campaign, the Agency used various media outlets to reach out to users more effectively via this type of message. This was key to ensuring their receptiveness. In a context marked by the growing importance of social media and an increase in disinformation, it is essential for a public health authority such as ANSM to be able to restore confidence and address citizens, patients and healthcare professionals via channels they are familiar with.

As well as raising awareness of the misuse of medicines, ANSM is also committed to safety. In recent years, this has led us to take an increasingly strong stance whenever we have considered that the risk-benefit balance is, or has become, negative. 2023, for example, saw particularly strong action on oral vasoconstrictors, with a powerful media impact on households nationwide.[2]

Even though ANSM's efforts to persuade the European Medicines Agency's Pharmacovigilance Committee did not bear fruit, use of these medicines did drop sharply last winter, which is further evidence of the success of this public health initiative, based on clear and hard-hitting communication carried out in conjunction with all the players involved.

Our commitment to ensuring fair access to medicines and healthcare products was a major priority once again for ANSM, particularly through our involvement in the design and roll-out of the 2023-2024 Winter Plan.[3]

At the Ministers' request, the signing of the Commitment Charter by all players in the medicines chain illustrated the total responsibility of each link in the chain for ensuring and securing access to essential resources for all.[4]

In this way, the Agency confirmed its pivotal role, at both national and European level, in taking up the challenge posed by pressures and disruptions to supplies of medicines and healthcare products. The signing of this Charter in November 2023 was the fruit of these dialogue- and partnership-based activities with all stakeholders, which are central to ANSM's values. In addition, the work carried out by the Agency and its European counterparts enabled the drafting of recent decisions at EU level aiming

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[1] Read “Medicines are not ordinary products, and their use should not be taken lightly: ANSM rolls out an information and awareness campaign to encourage the proper use of medicines”, page 18.
[2] Read “Oral vasoconstrictor medicines: ANSM recommends their avoidance by anyone with a cold”, page 20.
[3] Read “Combating shortages of medicines: ANSM activates the first edition of its Winter Plan for 2023-2024”, page 36.
[4] Read “Commitment charter for stakeholders in the medicines chain to ensure fair access to medicines for patients”, page 37.

to secure access to medicines of major therapeutic interest. With the new national and European regulatory instruments at its disposal, the Agency will continue to build its capacity for action in this field.

In 2023, ANSM's teams once again demonstrated their responsiveness and ability to anticipate. With their relentless commitment, they make an invaluable contribution to the fulfilment of our missions, for the benefit of patients. Quite simply, these are the people who run ANSM on a day-to-day basis and we extend our sincerest thanks to them.

We hope you enjoy reading our Annual Report, and please remember: “Medicines are not ordinary products, and their use should not be taken lightly.”

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WHO ARE WE?

The French National Agency for Medicines and Health Products Safety (ANSM) is a public establishment under the authority of the French Ministry of Health. On behalf of the French State, it is responsible for the safety of health products and promotes access to therapeutic innovation. It acts on behalf of patients, alongside health professionals and in consultation with their respective representatives in all the Agency's bodies. Through its evaluation, expertise and monitoring policy, ANSM ensures that the health products available in France are safe, effective, accessible and properly used.

It carries out the following main missions:

- enabling early and rapid access to innovative products;
- authorising clinical trials;
- authorising the marketing of medicines and biological products;
- monitoring all health products throughout their life cycle;
- collecting and analysing adverse effect reports;
- studying the impacts of their use;
- ensuring the availability of “essential” health products;
- controlling product quality in its laboratories;
- inspecting manufacturing and distribution sites.

Its priorities for action are set out in the Objectives and Performance Contracts that it enters into with the French State.[5]
ANSM is actively involved in European and international projects. Its activities are very much in line with European procedures and its activities are carried out in coordination with the European Medicines Agency, the European Commission and the other national agencies of the European Union. It also collaborates with international health organisations.[6]
ANSM has a Management Board,[7] a Scientific Advisory Board[8] and Advisory Commissions.[9] It is also backed by an Ethics of Expertise Department and an Ethics Advisor who help guarantee the independence and impartiality of the Agency’s decisions.[10]
It is based on three sites: in Saint-Denis (headquarters and laboratories), Lyon and Vendargues (laboratories).

An ISO 9001-certified agency for the following activities:

- monitoring healthcare products;
- managing high-risk situations;
- controlling healthcare products;
- inspecting;
- combating shortages of medicines;
- organising the quality control of medical devices and in vitro diagnostic medical devices;
- examining user requests;
- authorising new MA applications and amendments;
- managing facilities.

For more information about ANSM:
https://ansm.sante.fr/qui-sommes-nous/

[5] Read “Our objectives”, page 101.
[6] Read “Increased involvement in European and international projects”, page 30.
[7] Read “Our governance bodies”, page 99.
[8] Read “Our governance bodies”, page 99.
[9] Read “Consultation and multi-disciplinarity: the work of our advisory bodies”, page 12.
[10] Read “Independence and impartiality: our ethical obligations”, page 15.

2023 in brief

HIGHLIGHTS IN 2023

- Risk of meningioma and progestins: ANSM convenes a new committee of experts composed of patients and healthcare professionals (January)
- Change in the pregnancy pictogram: creation of a temporary scientific committee (January)
- Ozempic (semaglutide): implementation of enhanced monitoring (March)
- *Medicines are not ordinary products, and their use should not be taken lightly*: the ANSM rolled out an information and awareness campaign to encourage the correct use of medicines (June)
- Renewal of standing scientific committees (September)
- Stock shortages: implementation of a winter plan (October)
- Oral vasoconstrictor medicinal products: ANSM recommends their avoidance by anyone with a cold (October)
- Renewal of the Scientific Advisory Board (October)
- Signing of the charter committing stakeholders in the medicines chain to fair access to medicines for patients (November)
- ANSM designated as pilot of the European "JAMS 2.0" project (November)
- ANSM committed to ecological planning of the healthcare system: signature of the Agreement on Ecological Planning of the Healthcare System (December)
- Reappointment of the Director General of ANSM and appointments to the post of Deputy Director General for Operations

KEY FIGURES

ACTING IN COMPLETE TRANSPARENCY THROUGH DIALOGUE AND OPENNESS

102 Standing Scientific Committee meetings
909 public conflict-of-interest statements (DPIs) checked
1,174 ethics contributions and analyses
111 news items published
4,209,711 unique visitors to the ANSM website
120,042 LinkedIn subscribers
8 information and discussion webinars with health professionals, patient associations, and operators and manufacturers
10,035 requests submitted to the User Reception Department

ENSURING THE SAFETY OF PATIENTS EXPOSED TO MEDICINES AND HEALTH PRODUCTS

34 new high-risk situations (HRS) with an average of 40 HRS in progress

- **Medicines**

58,996 cases of adverse effects were collected, analysed and registered by the Regional Pharmacovigilance Centres (Centres Régionaux de Pharmacovigilance – CRPVs), **52,831** of which were not related to COVID-19 vaccines, in the French national pharmacovigilance database

39,695 cases of adverse effects were reported by pharmaceutical companies, **39,124** of which were not related to COVID-19 vaccines

70 pharmacovigilance studies were in progress in 2023, and 9 new studies were begun

France acted as Rapporteur for **127** cases entered on PRAC[11] agendas

7,225 spontaneous notifications of abuse, drug dependence and misuse were collected, analysed and recorded by the Centres for Evaluation and Information on Pharmaceutical Drug Dependence - Addiction Vigilance (CEIP-A), in the French national pharmacovigilance database

21 addiction vigilance studies were underway in 2023

3,075 medication error or risk-of-medication-error reports were transmitted to ANSM

4,925 reports of stockouts or risks of stockouts were managed by ANSM, as were strategies for finding therapeutic alternatives to critical products

1,968 quality defect reports were submitted

- **Blood products**

7,993 adverse effects related to haemovigilance were reported among donors of labile blood products

9,650 adverse effects related to haemovigilance were reported among recipients of labile blood products

- **Medical devices (MDs) and in vitro diagnostic medical devices (IVDMDs)**

26,722 adverse effects related to medical device vigilance were reported, **658** of which were received from patients and patient associations

1,642 adverse effects were reported in reagent vigilance

- **Laboratory tests and inspections**

553 inspections were carried out, of which:

  - **9%** were random inspections,
  - **6%** were inspections conducted outside France

3,781 laboratory tests were carried out

FACILITATING PATIENT ACCESS TO INNOVATIVE TREATMENTS

377 scientific or regulatory support missions via the Innovation and Referral Service were managed

85 European scientific opinions were attributed to France

57,176 compassionate access authorisations granted and **24,346** patients treated

25 opinions favourable to the granting of early access authorisations issued

3,027 patients included in the medical cannabis trial since it began

687 authorised clinical trials for medicines

54 clinical investigation authorisations for MDs issued

496 marketing authorisations (MAs) and registrations issued by ANSM (national procedure and decentralised European and mutual recognition procedures)

15 MA applications under a centralised procedure assigned to France

France appointed rapporteur or co-rapporteur for **99** Paediatric Investigation Plans (PIPs)[12]

France is ranked the **leading** Member State in terms of the number of vaccine batches released on the European market

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[11] Also read: "https://ansm.sante.fr/qui-sommes-nous/nos-missions/informer-echanger-avec-notre-environnement/p/participer-aux-instances-internationales#title"

[12] Also read: "https://ansm.sante.fr/qui-sommes-nous/nos-missions/informer-echanger-avec-notre-environnement/p/participer-aux-instances-internationales#title"

MOVING FORWARD, DRAWING ON OUR RESOURCES

Budget: **€137.43 M** in funding from the French national health insurance system and **€10.79 M** in EMA revenue

943 FTEs under the ceiling authorised in the initial budget and **47.7 FTEs** beyond the ceiling

more than 155 applications used each day across **360** servers

Acting in complete transparency through dialogue and openness

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FOCUS ON… THE CORRECT USE OF MEDICINES

In 2023, ANSM maintained its commitment to combating the misuse of medicines by working with stakeholders to identify the risks of misuse and implement preventive measures as part of its public policy to tackle misuse. Claire Férard, Head of the Safety Unit in the Surveillance Division, and Anne-Claire Goyet, Head of the Institutional Communication and Public Information Unit in the Communication and Information Division, tell us more about the actions taken by ANSM.

How do we define the misuse of medicines and its impact on patients?

Claire Férard: Misuse refers to the unjustified use of a medicine in a way that does not comply with scientific evidence. The patient may be exposed to avoidable adverse reactions which may be serious. For example, 16% of hospital admissions associated with medicine-related adverse reactions occur in the context of non-compliant use of medicines. It is therefore important to prevent adverse reactions linked to misuse, particularly those affecting the most vulnerable populations. Furthermore, misuse leads to an increase in morbidity and mortality (mortality due to disease), in addition to its economic cost to society. This is why ANSM has introduced a public health policy to combat the misuse of medicines. Preventing misuse and promoting the correct use of medicines help to reduce the risks associated with misuse, and are priorities of the Agency.

What measures has the ANSM put in place to promote the correct use of medicines?

Anne-Claire Goyet: As part of a dedicated public health policy, ANSM has consulted the interface committees and stakeholders to discuss the misuse situations they have identified and the means of remedying them. The event held on 4 October 2023[13] gave us an opportunity to work together on this theme. We have also conducted opinion surveys to gain a better understanding of how the French perceive and use medicines. These surveys have revealed that a large proportion of the population is unaware of the dangers and risks associated with the misuse of medicines.

C.F: On a daily basis, ANSM strives to ensure the proper use of medicines through its decisions on risk monitoring and management. In addition, it has introduced a public health policy dedicated to this issue, focusing on three key areas to underline its commitment to promoting the correct use of medicines. The first objective is to anticipate the risks of misuse by identifying the classes of medicines and situations posing the greatest risk. Preventive measures have already been taken, notably for painkillers, benzodiazepines and GLP-1 analogues used for weight loss.
Secondly, ANSM implements educational initiatives to raise awareness of high-risk situations and provide notification or even warning of their consequences. We pay particular attention to raising young people's awareness of the dangers of misusing medicines. To this end, over the past two years, the Agency has been involving health students enrolled in the “Health Service” (Service Sanitaire) scheme and encouraging them to spread messages about preventing the misuse of medicines in schools.

A.G: Anticipation is central to our activities. Raising awareness – through education, as Claire mentioned, as much as through communication – is a key strategic focus for informing all audiences about the consequences of misuse. It is important to repeat messages to ensure that they are noticeable and understood. To this end, in 2023 we rolled out a major information and awareness campaign on the “proper use of medicines”[14] Using four different situations and a deliberately offbeat approach to lighten

[13] Also read: “A commitment from all players to combat the misuse of medicines” https://ansm.sante.fr/actualites/un-engagement-de-tous-les-acteurs-pour-lutter-contre-le-mesusage-des-medicaments
[14] Also read: *Medicines are not ordinary products, and their use should not be taken lightly*: the ANSM rolls out an information and awareness campaign to encourage the proper use of medicines, page 18.

the mood, this campaign emphasises the central message: communicating with a healthcare professional.

Is it possible to measure the effectiveness of this public health policy?

A.G: It is difficult to distinguish between what is due to public health policy and what is due to all the other actions, whether carried out by ANSM or other players. Year after year, decision after decision, announcement after announcement, campaign after campaign, it is the combined efforts of all actors – public institutions, healthcare professionals, manufacturers and, of course, each and every one of us – that are helping to raise awareness of the risks and the right reflexes to adopt in order to use healthcare products properly.

CONSULTATION AND MULTIDISCIPLINARITY: THE WORK OF OUR ADVISORY BODIES

Since 2019, ANSM's policy of reaching out to civil society has been reflected in the systematic involvement of healthcare system users in its expert advisory bodies. The Agency is indeed convinced of the need to act in consultation with patients and health professionals to ensure that its actions address the challenges they face on a daily basis.

For this reason, our decisions are based on the opinions of several advisory committees, in which the expertise of representatives of civil society, their perspective, and their vision of the health sector allow for objective and informed decision-making. For example, since 2019, the Standing Scientific Committees (SSCs) have been supporting the Agency's decisions based on the provision of multidisciplinary, collegial and transparent expertise. Together, through this major component of the policy of openness to stakeholders, healthcare professionals and patients are actively contributing to ANSM's increasingly effective and relevant activities at the service of healthcare system users.

In 2023, the ANSM renewed the membership of its 15 permanent scientific committees and created four Temporary Scientific Committees (TSC).

For more information about the advisory bodies:
https://ansm.sante.fr/qui-sommes-nous/notre-organisation/nos-instances/p

Renewal of Standing Scientific Committees

Following the call for candidates issued in March 2023, the Director of ANSM appointed the new members of the 15 Standing Scientific Committees (SSCs).
In addition to internal evaluation, the 15 SSCs are tasked with issuing advisory opinions based on strict ethical rules, multiple expert contributions, collegiality and transparency of debate. They each have between eight and 39 members, and include between one and four representatives of patients' and users' associations, experts in the Agency's fields of expertise, healthcare professionals and members of vigilance networks. Members are appointed for four-year terms.

The SSCs now have new internal rules setting out their operating procedures.

Creation of a Temporary Scientific Committee for the “Re-evaluation of the Pictogram on the Outer Packaging of Teratogenic or Foetotoxic Medicines”

ANSM has been tasked with re-evaluating the “Pregnant women” pictogram currently affixed to certain boxes of medicines or products whose summary of product characteristics mentions teratogenic or foetotoxic effects. To assist the Agency with the conduct of this project, a Temporary Scientific Committee (TSC) for the “Re-evaluation of the Pictogram on the Outer Packaging of Teratogenic or Foetotoxic Medicines” was established in 2023.

This committee is responsible for:

- updating and completing the review of the situation resulting from previous consultations carried out by the French Ministry for Health with the various stakeholders;
- re-evaluating the criteria for affixing a pictogram and, if necessary, proposing changes to the arrangements for affixing the pictogram.

It consists of 19 members appointed for 18 months, who are chosen for their expertise and representativeness in the fields of general medicine, pharmacy, gynaecology and obstetrics, pharmacovigilance, teratogenicity and foetotoxicity, epidemiology, midwifery, educational sciences, ethics and psychology, as well as representatives of patient associations and healthcare system users. The first meeting was held on 24 January 2023, and the committee's activities are ongoing.

https://ansm.sante.fr/actualites/evolution-du-pictogramme-grossesse-creation-dun-comite-scientifique-temporaire

Creation of a Temporary Scientific Committee on "Progestins and the Risk of Meningioma"

On 13 January 2023, ANSM convened a new Temporary Scientific Committee (TSC) on "Progestins and the risk of meningioma", composed of representatives of patient associations and healthcare professionals. The purpose of this committee is to issue an opinion on the conditions for use of progestins other than those based on cyproterone acetate, nomegestrol and chlormadinone, with regard to the risk of meningioma, so that people for whom these treatments are justified can continue to benefit from them under safe conditions.
The ANSM recommendations stemming from the work of this TSC are aimed at healthcare professionals, with a view to improving the protection of users of these medicines.

https://ansm.sante.fr/actualites/risque-de-meningiome-et-progestatifs-lansm-reunit-un-nouveau-comite-dexperts-patients-et-professionnels-de-sante

Creation of a Temporary Scientific Committee on "Virology and Emerging Viruses"

In order to anticipate and provide rapid preventive and therapeutic responses to viruses, particularly emerging viruses, ANSM established a Temporary Scientific Committee (TSC) for "Virology and Emerging Viruses" on 21 February 2023 for a period of twelve months.

The aim of this TSC is to advise the ANSM on any question relating to viral pathologies, including emerging viruses, and to take up a position, for certain cases submitted by the Agency, on applications concerning preventive or curative treatments for these pathologies:

- clinical trial authorisation applications;
- compassionate access and early access authorisation applications;
- marketing authorisation applications and requests to amend these authorisations.

It has seven members appointed for one-year terms, who are chosen for their competencies and representativeness in the fields of virology, infectiology and pharmacovigilance, and include a representative of patients and healthcare system users.

The committee met for the first time on 28 March 2023.

https://ansm.sante.fr/actualites/creation-dun-cst-virologie-et-virus-emergents-renforcer-lexpertise-de-lansm-et-accelerer-la-prise-de-decisions-face-aux-virus

Another highlight

- **Creation of a Temporary Scientific Committee on "Analysis of the Use of GLP-1 Analogues"[15]**

https://ansm.sante.fr/actualites/creation-dun-comite-scientifique-temporaire-pour-analyser-lusage-des-analogues-du-glp-1

[15] Read "Ozempic (semaglutide): therapeutic indications for the treatment of type 2 diabetes", page 45.

2023 DATA

- 102 Standing Scientific Committee meetings
- 33 Temporary Scientific Committee (TSC) meetings, organised by 7 different TSCs
- Creation of four new TSCs:
    - “Re-evaluation of the Pictogram on the Outer Packaging of Teratogenic or Foetotoxic Medicines”
    - “Analysis of the Use of GLP-1 Analogues”
    - “Progestins and the Risk of Meningioma”
    - “Virology and Emerging Viruses”

INDEPENDENCE AND IMPARTIALITY: OUR ETHICAL OBLIGATIONS

Given the public health issues linked to health product usage, the impartiality and independence of individuals participating in the work of ANSM bodies are crucial to ensuring the quality, legitimacy, and credibility of the Agency's scientific assessment system, as are the plurality and free expression of viewpoints, compliance with adversarial proceedings, and the collegial nature of discussions.

Read more about our ethical requirements:
https://ansm.sante.fr/qui-sommes-nous/deontologie-et-transparence/deontologie-et-transparence/p/nos-exigences-deontologiques#title

Ethical control: how is it organised?

Since July 2022, the Compliance, Ethics and Probity Department has been attached to the Regulation and Ethics Division, which in turn reports to the Director General of ANSM.

The department provides support, advice and legal expertise to the Director General and all departments for the prevention and management of potential conflicts of interest and breaches of confidentiality. This department also provides information and training on ethical issues, both to the Agency's staff and to the external experts the Agency uses in addition to internal assessment. It has also been entrusted with an internal control mission to ensure the effectiveness of the rules of professional conduct established within the agency.

Operating independently of this department, an Ethics Advisor – a post held by a person from outside the Agency – provides external support in matters of public service ethics.
The Ethics Advisor may issue advice on compliance with the ethical principles of the civil service at the request of any staff member who submits a request in this regard, and may also be asked by Senior Management to issue an opinion in the event of doubt concerning the compatibility of an ANSM employee's duties with a previous activity in the competitive sector or one that is being considered.

His or her role is to advise and assist Senior Management with any general ethical issues and the prevention of conflicts of interest, as well as in matters relating to the ethics-related control environment.

Following a decision dated 22 December 2023, with effect from 1st January 2024, the Director General appointed Christophe Pallez as Ethics Advisor at ANSM.

Renewal of all standing scientific committees and of the Scientific Council of ANSM, and continued reinforcement of training and information for ANSM staff on ethical rules and the prevention of breaches of probity

Any appointment to an ANSM collegial body (standing and temporary scientific committees) is subject to prior analysis by the Ethics Department. It examines the special-interest ties reported by each expert on the public conflict-of-interest statement (DPI), their CV and the information contained in the “Health Transparency” database, with the aim of identifying any activity that might be incompatible with the mandate of the body in question and any risks of conflicts of interest that should be avoided.

By 31 December 2023, the Ethics Department had carried out a preliminary analysis of the ethical risk for 411 expert applications, 288 of which specifically related to the renewal of all ANSM standing scientific committees in the summer of 2023.

Pursuit of efforts to raise ANSM staff and experts' awareness of the rules of professional ethics and the prevention of breaches of probity

Ramping up of training initiatives, both for Agency staff and for external experts involved in its activities:

- an in-house training course run by the Ethics Department to raise awareness of anti-corruption issues among the Agency's staff, whose programme is currently being drawn up. It should be followed by practical workshops to meet employees' needs and answer their questions on this subject.
- In collaboration with the Scientific Delegation and the Human Resources Division, training has been provided on the use of expertise and the associated rules of ethics.

In addition, as part of the renewal of the ANSM standing scientific committees during the summer of 2023, the new rules of procedure for these committees and the related ethical aspects were presented to their members at each of the first meetings of these 15 committees. Lastly, these rules were also set out in detail at an information day which provided an introduction to the agency and its operating procedures for members of the standing committees.

This introductory presentation raised members' awareness of these issues and reminded them not only of how the Agency's scientific committees operate, but also of their ethical obligations.

These issues were also presented at the renewal of the ANSM's Scientific Advisory Board.

At the same time, tools and information documents have also been developed and disseminated:

- a deferral procedure exists for all ANSM staff, which enables employees to be exempted from handling a case, issuing instructions or using their delegation of signature if, for a given case, they have any links that are likely to call into question their objectivity or impartiality.
- In 2021, the Ethics Department launched a study to examine the provision of a common tool for the traceability and management of reservations by divisions. This study, which continued in 2022 with an analysis of existing practices, led to the provision of an example of a traceability tool for divisions in 2023, together with the reservations applying to their staff.

2023 DATA

Second-level internal audit operations carried out by the Ethics and Probity Department concerned:

- the compliance of the public conflict-of-interest statements (DPIs) submitted by the staff listed in the organisation chart with their annuality and publication requirements,
- the monitoring of reservations applying to ANSM staff (issued at the time of recruitment, during and after employment);
- the assessment, by the relevant divisions, of risks of conflicts of interest when using the services of ad hoc experts.

As part of these operations, **355 public conflict-of-interest statements were audited**.

Cases that led to an ethics risk analysis by the Ethics Department

614 cases analysed for ethical risk, including:

- 75 applications from prospective candidates during the pre-recruitment phase
- 17 pharmacy interns' or trainees' applications;
- 20 cases of employees leaving ANSM
- 2 requests for authorisation to hold multiple simultaneous posts
- 40 requests to participate in external events
- 411 appointments of committee members and 21 appointments or requests to appoint ad hoc experts, i.e. 432 expert applications

As part of these analyses, **554 public conflict-of-interest statements were checked** in relation to recruitment and the use and appointment of experts.

Cumulative breakdown of analyses

1,174 ethics contributions and analyses, consisting of:

- 466 opinions issued on internal expertise (40%)
- 627 opinions issued on external expertise (53%)
- 72 contributions following requests from ANSM divisions (6%)
- 9 contributions following institutional requests (1%)

DIALOGUE AND INFORMATION SHARING WITH OUR STAKEHOLDERS

ANSM is vigorously pursuing its commitment to inform its audiences. It has stepped up its commitment to public health by including more information initiatives for each of its health policies.

The Agency has also continued to develop a more educational approach to its communications by implementing an increasingly proactive information strategy through its relations with the media and its stakeholders, and by increasing its presence on social networks. ANSM is also developing a staff communication strategy based on an integrated vision of internal and external communications, which contributes strongly to building its employees' commitment.

In 2023, ANSM pursued its public health policy to combat the misuse of medicines, notably by rolling out a large-scale communication campaign aimed at the general public.

For more information about public information:
https://ansm.sante.fr/qui-sommes-nous/nos-missions/informer-echanger-avec-notre-environnement/p/informer-nos-publics#title

Medicines are not ordinary products, and their use should not be taken lightly: the ANSM rolls out an information and awareness campaign to encourage the proper use of medicines

ANSM has been working for many years to improve the use, prescription and dispensing of medicines.[16] Each medicine has its own specific conditions of use, which must be respected to ensure its efficacy and safety. Improper use of medicines can have serious consequences, which may cause more undesirable effects, render the treatment ineffective, or even worsen the disease.

Since 2022, ANSM has led a public policy to combat misuse. As a key player in the safety of patients exposed to healthcare products, ANSM must be able to develop an overall understanding of the subject, while adopting an approach focused on a specific therapeutic class. Public health policy enables us to act upstream by establishing ourselves as a player in the prevention field. This policy, developed jointly with stakeholders, focuses both on identifying classes/molecules at risk and on educating the public and raising awareness of this issue.

"*Ensuring the proper use of medicines is a major public health issue that concerns us all, from healthcare professionals to patients*. *Everyone has a role to play at each stage in order to promote the proper use of medicines. Based on everyday situations, this campaign aims to raise awareness of the use of our medicines*." »
Dr Christelle Ratignier-Carbonneil
Director General of ANSM

Against this backdrop, in June 2023, the ANSM launched an information and awareness campaign to promote the proper use of medicines, targeting the general public. Based on four different situations, the campaign urges people to consider how they use medicines, and reminds them of the best practices to adopt, while conveying a key message: before taking any medicines or changing your treatment, always seek the advice of a healthcare professional.

[16] Also read the chapters on "Promoting proper use of medicines" and "Surveillance of non-compliant use", pages 43 and 45.

This campaign will continue in 2024.

Discover the campaign: www.lesmedicamentsetmoi.fr

Campaign facts & figures

- More than 3 million views of the campaign video
- More than 9 million people reached by Instagram and LinkedIn posts
- More than 550,000 people reached by the audio clips
- More than 1.7 million people reached by the campaign on the Internet

Oral vasoconstrictor medicines: ANSM recommends their avoidance by anyone with a cold

Vasoconstrictors are medicines designed to clear the nose.
Risks are associated with the use of medicines containing pseudoephedrine (oral vasoconstrictors), designed to relieve the symptoms of the common cold. These medicines are known to the general public as Actifed Rhume, Dolirhume, Humex Rhume, Rhinadvil Rhume, Nurofen Rhume and others.

Myocardial infarction, stroke and convulsions, as well as serious skin reactions, insomnia and other adverse events may be linked to the use of these vasoconstrictors.
In addition to these long-established risks of adverse reactions, other risks have been added on the basis of pharmacovigilance data and medical literature. These concern:

- posterior reversible encephalopathy syndrome (PRES);
- reversible cerebral vasoconstriction syndrome (RCVS).

All these adverse effects are likely to occur in patients with no medical history or risk factors, regardless of the dose and duration of pseudoephedrine treatment.
Although the frequency is low, ANSM considers that these risks are too serious given the non-essential nature of these products (people recover spontaneously from a cold in seven to 10 days). The persistence of cases – despite the measures already taken in France – combined with the non-essential nature of vasoconstrictors, led ANSM to advise against their use in October 2023.
The French College of General Practitioners (Collège de la médecine générale), the National Board of ENT Professionals (Conseil national professionnel d'ORL), the National Board of Pharmacists (Ordre national des pharmaciens) and the unions of dispensing pharmacists (Union de syndicats de pharmaciens d'officine and Fédération des syndicats pharmaceutiques de France) have endorsed this recommendation against using pseudoephedrine by the oral route to relieve cold symptoms.

In addition to its media interventions on this subject in the autumn of 2023, ANSM e-mailed this recommendation directly to the French pharmacists and prescribers concerned in March 2024.

Furthermore, in February 2023, in view of the latest risks to be identified (PRES and RCVS), ANSM requested the re-evaluation of medicines containing pseudoephedrine at European level, as these vasoconstrictors are also made available by our European neighbours. Following this evaluation, the European Medicines Agency (EMA) requested the addition of new contraindications and warnings to the package leaflets and summaries of product characteristics. ANSM considers this measure insufficient to reduce the risk of potentially serious adverse effects. This is why it sent a dissenting opinion to the EMA and regularly points out that the common cold can be cured in 7 to 10 days without medication.

https://ansm.sante.fr/actualites/en-cas-de-rhume-evitez-les-medicaments-vasoconstricteurs-par-voie-orale

Presenting the face of a committed agency

The Internal Communication and Strategic Project Support Strategy aims to:

- provide information about the Agency's internal activities and its external news in order to improve employee engagement;
- keep supporting the Agency's major transformation projects and key strategic issues;
- adopt and promote CSR policy
- encourage social activities to forge links in the age of hybrid working practices.

This strategy is based on:

- the intranet site which, with 3,320,000 visits in 2023 (averaging 276,000 views per month, up 11% on 2022), is the primary internal communication resource. Regular surveys of our teams show that this medium helps them to feel well informed.
- different kinds of events (conferences to improve understanding, events to raise awareness, social events to welcome people and create links, etc.), all working towards the same objective: promoting cross-functionality and enabling staff to work better together. 38 such events were organised in 2023.

- A programme of themed days designed to build closer relationships and develop a sense and pride of belonging (awareness-raising to instil best practices, commitment to solidarity and a sustainable future, opportunities to socialise for the pleasure of being together).

Here are four highlights of the many initiatives carried out in 2023:

1. The development of our Intranet site, with new editorial content and new social-network-like functionalities. This new, more modern and intuitive resource has seen an 11% increase in visits compared with the old site, peaking at a record-breaking 387,000 visits when it opened on 11 May 2023.
2. The organisation of the Agency's 30th anniversary on 18 September 2023, an event entirely dedicated to ANSM's teams. An opportunity to celebrate 30 years dedicated to serving patients' health. A happy birthday and a convivial moment shared by colleagues.
3. Support for or participation in causes, spearheaded by ANSM's involvement in the Odyssea race for Pink October and the distribution of Christmas chocolates to all teams, made by ESAT in Saint-Pée.
4. This is a first step towards promoting employee engagement and encouraging them to become ambassadors for the Agency by passing on information about the campaign to promote the Proper Use of Medicines and CSR-based initiatives on social networks.

ANSM's scientific publications in 2023[17]

In 2023, ANSM employees were authors or co-authors of **36** publications of scientific articles in international peer-reviewed journals, and of eight publications of presentations at conferences.
These publications covered various fields, such as pharmacovigilance, haemovigilance, clinical trials and medicinal product monitoring. This diversity reflects the breadth of the Agency's expertise and its contribution to all public health issues. These contributions reflect ANSM's ongoing commitment to scientific excellence and the promotion of a culture of transparency and knowledge-sharing.
To facilitate and harmonise this activity, the Agency introduced a scientific publication charter in December 2022. This charter defines ANSM's scientific publication principles, thereby helping to strengthen our approach to research and the dissemination of knowledge.

ACTIVE INVOLVEMENT OF USERS IN THE MANAGEMENT OF THEIR HEALTH

"The contribution of practices and citizens to decision-making in the health field has been enshrined in law since 2002. In reality, patient involvement has been a gradual process, and although things are improving, it is clear that much still needs to be done to fully recognise the role of patients in managing their own health. My actions and involvement in various bodies representing users and patients are totally consistent with this vision, which is both inclusive and in the general interest. I consider it normal that the people primarily affected by a system that has been created for them should be involved in decisions that will have a direct impact on their own or their loved ones' lives."

Jean-Philippe Plançon, Vice-Chair of the ANSM Management Board

Read his full interview on World Patient Safety Day:
https://www.linkedin.com/posts/ansm_patientsafety-santaezpublique-daezmocratiesanitaire-activity-7109467872543821824-PuxF?utm_source=share&utm_medium=member_ios

[17] Read the complete list in Appendix 2, page 128.

2023 DATA

- **111** news items published
- **50** newsletters sent out
- **4,404,626** unique visitors to ansm.sante.fr[18] and **10,772,274** page views, down 3.1% in one year
- **8** information and discussion webinars with health professionals, patient associations, commercial operators and manufacturers
- **14,582** media mentions
- **71** interviews given
- X (formerly Twitter): **43,765** subscribers (**1,255** new subscribers, up 2.95% compared with 2022)
- LinkedIn: **120,042** subscribers (**20,826** new subscribers, up **20.99%** compared with 2022)
- YouTube: **3,920** subscribers (**666** new subscribers, up **20.47%** compared with 2022)

[18] Read Appendix 2, page 127 for details of the visitor number trend for the ANSM website.

AN AGENCY THAT LISTENS TO ITS USERS

As part of its policy of transparency and openness towards civil society, ANSM established a User Reception Department in 2021. This department aims to centralise the management and processing of requests from all audiences in contact with ANSM (patients, health professionals, manufacturers, institutions, etc.), and to answer their enquiries without delay.

At the same time, the Agency contributes to the replies to letters and written questions submitted to the Minister for Health, or sent directly to the Agency.

In addition, to facilitate the reporting of alerts issued by whistle-blowers and improve follow-up measures, ANSM implemented a procedure in 2019 via a specific address posted on the home page of its website. This makes it easy for anyone who is personally aware of such an occurrence to report any serious violation of a law or regulation, or any serious threat to the general interest, concerning health products intended for human use or activities falling within the scope of ANSM's competence.

In January 2023, an AFNOR audit confirmed the ISO 9001 certification obtained by the User Reception Department during the previous year for its ability to “process user requests”.

2023 DATA

The User Reception Department

10,035 user requests were received, including:
- **6,877** requests processed at Level 1
- **3,158** requests processed at Level 2

The average processing time in 2022 was 9 days.

Level 1 requests are handled directly by the User Reception Department. The average processing time in 2023 was **2** days.
Level 2 requests require more in-depth expertise. They are handled in collaboration with the Agency's specialist divisions. The average processing time in 2023 was **25** days.

46% of enquiries came from individuals/patients, **35%** from health professionals, **14%** from manufacturers and **5%** from other categories of users.

For more information about the User Reception Department:
https://ansm.sante.fr/actualites/un-service-daccueil-des-usagers-a-lansm-pour-toujours-mieux-informer-nos-publics

Information for Members of Parliament

In 2023, the Agency answered **98** written questions and **3** letters sent by Members of Parliament.
The main questions submitted by Members of Parliament related to:
- stockouts of many medicines of major therapeutic interest, and supply problems,
- the presence of titanium dioxide and erythrosine in medicines;
- Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices;
- revision of Decree No 2008-841 on the sale to the public of medicinal plants listed in the pharmacopoeia.

Reporting of alerts issued by whistle-blowers

- **212 whistleblower reports were received** via the address posted on the ANSM website lanceur.alerte@ansm.sante.fr
- **185 of the alerts processed were followed up** and closed (the remainder are still being processed).

Product categories concerned by the reports received:

- **38%** medicines;
- **23%** MDs-IVDMDs;
- **7%** other (raw materials for pharmaceutical use, clinical trials)
- **23%** other (outside scope of ANSM: foodstuffs, miscellaneous)
- **5%** cosmetics.

Source of alerts:

- **55%** private individuals, anonymous;
- **22%** health professionals;
- **16%** employees, contractors, manufacturers;
- **7%** other.

For more information about reporting alerts:
https://ansm.sante.fr/actualites/lansm-met-en-place-ladresse-lanceur-alerte-ansm-sante-fr

PROACTIVE AND PROGRESSIVE PROVISION OF OUR DATA

Embodying its desire for openness, as set out in its Information Systems and Data Master Plan (SDSID), this policy concerns the proactive and progressive online publication of the Agency's data and documents, accompanied by educational items, in compliance with legal secrecy requirements, in order to raise awareness of its actions, make optimum use of its expertise and promote the use of its data.

Etalab (associated with Prime Minister's Office) and other institutions are helping ANSM with methodological aspects, while the French Data Protection Authority (CNIL) and the Commission for Access to Administrative Documents (CADA) are assisting with legal questions.

New "data.ansm" information platform

ANSM, with Etalab's "entrepreneurs of general interest" programme and in partnership with the Health Data Hub (HDH), has created https://data.ansm.sante.fr/, a new open-access information platform.

This platform is helping to improve the openness and transparency of healthcare data by providing access to detailed data on the history of declarations relating to pharmacovigilance, medication errors and stock shortages on a single platform. It is aimed at everyone, from private individuals to healthcare professionals and manufacturers.

data.ansm has been offering data from 5 databases since 2014:

- ANSM's national pharmacovigilance database (BNPV), containing reports of adverse reactions suspected to be due to medicines;
- the "Open Medic" database for the French national health insurance system (Assurance Maladie), containing information about medicinal product reimbursements (data from the National Health Data System);
- the ANSM "Codex" database containing information about marketing authorisations for medicines;
- the ANSM database of medication errors;
- the ANSM's "Trustmed" database of reports of stock-outs and risks of stock-outs of medicines.

https://ansm.sante.fr/actualites/data-ansm-une-plateforme-en-ligne-pour-en-savoir-plus-sur-les-effets-indesirables-des-medicaments-et-les-ruptures-de-stock

Transparency of the minutes of expert assessment bodies, especially standing scientific committees

The previous term of office of the fifteen standing scientific committees for the period from September 2019 to July 2023 was reviewed at the time of the renewal of the standing scientific committees in July 2023, paying particular attention to the time taken to publish the minutes of the 359 meetings of these committees. This revealed a steady rise in the rate of reports published in under four months, with 85.5% published in H1 2023.

The renewal of the standing scientific committees in July 2023 was accompanied by the updating of their rules of procedure. For greater transparency, the maximum period for publication of the minutes following meetings of the bodies has been reduced from four months to three months.

2023 DATA

Requests for access to the Agency's administrative documents

ANSM received 150 requests for the transmission of administrative documents received or produced by the Agency, in the following fields:

- **71**% marketing authorisations (MA) for medicines;
- **15%** pharmacovigilance for medicines;
- **5**% clinical trials;
- **2**% medical devices;
- **7%** miscellaneous (stock-outs, inspection reports, cosmetics, etc.).

ROBUST LEGAL AND REGULATORY ACTIVITY

ANSM carries out a significant amount of legal activity, producing more than 80,000 rulings each year, some of them of an individual or regulatory nature, which is exceptional for a public administrative body. It also participates in the drafting of texts relating to its field of competence in support of the French Ministry of Health and helps to improve legislation and regulations at national and European levels.[19]

ANSM is actively engaged in the environmental planning of the health system

The ANSM signed the environmental planning agreement for the healthcare system on 15 December 2023.
This agreement follows on from the activities launched by Prime Minister Elisabeth Borne under the "Green France" label, with a view to controlling the environmental impact and ensuring the long-term ecological transformation of the healthcare sector.

The Agency's main commitments are to:

- launch a trial on digitalisation of certain medicine package leaflets
- participate in the development of the unit-dose dispensation of medicines
- contribute to the establishment of a legal framework for the reuse of unused healthcare products and assist with increasing the reuse of reconditioned medical devices that are in good working order
- help promote the proper use of medicines and ensure that they are used as sparingly as possible
- define a list of variations that can reduce greenhouse gas emissions (such as significantly extending the stability of medicines)
- support technological innovations that reduce the carbon footprint of medicinal product design and production

ANSM participates in the implementation and monitoring of the environmental planning roadmap for the healthcare system in conjunction with the Ministry of Health and all associated institutions.

Watch the video on ANSM and the green transition, with Céline Mounier (Deputy Director General for Operations) and Valérie Salomon (Director of Scientific Affairs):
https://www.linkedin.com/posts/ansm_sedd-daezveloppementdurable-maezdicaments-activity-7110270162292850688-ysCH/

Reflection on the launch of an e-leaflet pilot phase and diversification of information media

Under current regulations, paper package leaflets are compulsory for all medicines. These leaflets are a major source of information for patients, presenting all the information needed to ensure the safely and effective use of medicines.
However, patients in hospitals do not have access to these leaflets because of the specific context of hospitalisation; moreover, in both hospital and non-hospital settings, they cannot be updated in real time to include the changes regularly made to marketing authorisations (MAs). As part of its policy of openness, ANSM is seeking to improve the information it provides to patients and healthcare professionals. This includes the development of computerised information tools (websites, social networks, professional software, production of electronic documents, etc.). This approach is also in line with the European Commission's review of pharmaceutical legislation, the discussions being conducted by the European Medicines Agency (EMA) and the introduction of comparable trials in other Member States. In this context, the production of electronic package leaflets (or e-leaflets) becomes an additional means of providing information to patients and can also help to promote the correct use of medicines and improve their safety. This has a double environmental impact, firstly in terms of reducing

greenhouse gases (GHGs), and secondly by promoting more appropriate and therefore more rational consumption. It will also provide effective support for the development of unit-dose dispensing. In 2023, ANSM therefore launched a consultation of stakeholders with a view to setting up an e-leaflet pilot phase of e-notices in the hospital and non-hospital sectors. This should enable the identification of the success factors and limitations of such an approach. The success of the electronic package leaflet production procedure depends on the adoption of a proactive, progressive and adaptive approach that enables the evaluation of each stage, the measurement of accessibility and impact both from public health and environmental perspectives, and the implementation of any measures that may be required. Its implementation is subject to the prior agreement of the European Commission. This pilot phase, which is expected to last two years, will be based on different arrangements for the hospital and non-hospital sectors. It has the following aims.

- In non-hospital settings: enabling patients and healthcare professionals to use a smartphone to access electronic package leaflets by scanning a QR code, which will be affixed to medicine boxes. The paper package leaflets will remain in each box. The Q/R code will link to the latest safety information in the leaflet, along with other content, including videos on proper use.
  For the non-hospital medical sector, the pilot phase is likely to involve the following medicines:
    - vaccines;
    - oral contraceptives;
    - homeopathic medicines granted a marketing authorisation;
    - paracetamol in dry oral forms;
    - proton pump inhibitors (PPIs);
    - statins.

- In the hospital sector (except for medicines prescribed on a retrocession basis [included on the “liste de rétrocession”] and those benefiting from early-access or compassionate-access authorisation): complete removal of the paper package leaflet (without the inclusion of a QR code on the boxes).

ANSM has drawn up a set of specifications (one on the operating procedures for the pilot phase, and the other on videos promoting proper use) with a view to implementing this pilot phase in 2024.

2023 DATA

Litigation and rulings

- **45** new applications (all courts combined) related to the Agency's decisions and activities.
- **31** rulings were handed down by the administrative tribunals.
- **93%** of the cases filed were decided in the Agency's favour.

Review of the financial sanctions imposed by ANSM

Pursuant to Article L. 5471-1 of the French Public Health Code, the Director General of ANSM may impose financial penalties on the perpetrators of breaches of the regulations, notably the rules governing the marketing, manufacture, pharmacovigilance and advertising of medicines, the anticipation and management of risks of stockouts of medicines, and the rules governing the marketing and advertising of medical devices and in vitro diagnostic medical devices.
These financial penalties are set out in Articles L. 5421-8, L. 5422-18, L. 5423-8, L. 5423-9, L. 5426-2 , L. 5438-1, L. 5461-9 and L. 5462-8 of the Public Health Code. Depending on the type of infringement in question, the amount of the fine may not exceed 30% of the turnover for the product or group of products concerned, or 10% of the turnover in the last financial year for which the accounts have been closed. These penalties are intended to be applied without prejudice to the adoption of health policy measures specific to each relevant activity and product sector.

In 2023, **6 financial penalties** were imposed by ANSM, totalling **€559,809.62**.

See the complete table showing changes in the financial penalties imposed by the ANSM in Appendix 3, page 135.

INCREASED INVOLVEMENT IN EUROPEAN AND INTERNATIONAL ACTIVITIES

European and international collaboration are essential to ensure that patients have access to high-quality, safe and effective medicines, medical devices and in vitro diagnostic medical devices, irrespective of where they are manufactured and how they are authorised. ANSM is actively involved in European and international activities, representing French expertise and ensuring that France's voice is heard in the discussions held and the decisions made at these levels.

The Agency is therefore a member of the European regulatory network of health agencies (HMA – Heads of Medicines Agencies), and of various committees at the European Medicines Agency (EMA). It is also a member of the European network of Competent Authorities for Medical Devices (CAMD) and of the Medical Device Coordination Group (MDCG). It is also a founding member of the International Coalition of Medicines Regulatory Authorities (ICMRA).

Find out more about ANSM's participation in European and international bodies:
https://ansm.sante.fr/qui-sommes-nous/nos-missions/informer-echanger-avec-notre-environnement/p/participer-aux-instances-internationales#title

ANSM leads the European "JAMS 2.0" project

In the context of the "EU4health" programme, ANSM is leading the European JAMS 2.0 project until the end of 2026. This project, intended to reinforce the market surveillance of medical devices (MD) and in vitro diagnostic medical devices (IVMD), brings together 24 European countries.
The objective of the JAMS 2.0 project is also to create training tools and facilitate the sharing of information between competent authorities.

On 14 and 15 November 2023, ANSM hosted a meeting of the work package leaders in charge of the eight working groups as part of the European JAMS 2.0 (Joint Action on Market Surveillance of medical devices) project, which was convened on the ANSM premises. This meeting, which was also attended by representatives from HaDEA (European Health and Digital Executive Agency) and the European Commission, marked the official launch of the project, which will run for three years.

JAMS 2.0 follows on from the first JAMS project (2016-2019), which ANSM began coordinating after the withdrawal of the UK agency MHRA. JAMS 1 resulted in improved mutual understanding, collaboration and cooperation between the 18 participating states. It reinforced the capacities of national competent authorities by providing them with technical guides, tools and training opportunities, and also helped to improve the general level of surveillance of medical devices in Europe.

Find out more: https://ansm.sante.fr/actualites/joint-action-on-market-surveillance-jams-2-0-leurope-a-lansm-les-14-et-15-novembre-2023

CHESSMEN and EU4H11 joint actions

As part of the EU4Health programme, the Inspection Division (ID) is actively involved in two joint actions. The EU4H11 Joint Action launched in December 2022 sets out to improve inspection systems and compliance with good manufacturing and distribution practices through closer cooperation between the competent authorities. The ID is leading two work packages in this Joint Action, concerning the qualification and training of auditors for the Joint Audit Programme (JAP) and Joint Reassessment Programme (JRP), on the one hand, and GMP inspectors (WP7), on the other. In 2023, a qualification process for JAP auditors was defined and implemented in cooperation with the European Medicines Agency (EMA), and an online training course was organised by ANSM on 5 October 2023, enabling the training of 150 European auditors and members of the international Pharmaceutical Inspection Co-operation Scheme (PIC/S).

ANSM is also contributing to the CHESSMEN Joint Action, which focuses on the European harmonisation of shortage management systems. The ID is actively involved in activities on best shortage notification and monitoring practices, as well as on digital information exchanges, notably via national shortage-reporting and management platforms. After the Joint Action was launched in February 2023, work in the first year consisted in taking stock of the different national practices. As part of the two work packages, questionnaires were transmitted to participants to identify existing practices and systems. Three reports were drawn up to identify the best practices that could be put in place in the Member States.

Assessment of the first year of twinning between ANSM and the Rwandan Medicines Agency

Since October 2022, ANSM has been helping to build the capacity of the Rwanda Food and Drugs Administration (RFDA), the authority established in 2018 to oversee the quality and safety of medicines and food. This mission will enable Rwanda, in the long term, to have an autonomous, stable, competent health agency.

In an initiative funded by the European Union and coordinated by Expertise France over a period of almost 900 days, ANSM has completed more than half of its twinning procedure with the RFDA. After 103 days working on site at 31 December 2023, the results of this first year are positive.

France is leading this twinning operation and participating in operational aspects with a consortium of European countries: mainly Germany, Belgium and Lithuania. Swedish and Austrian experts are also invited to contribute on specific topics. On the French side, ANSM, the French National Authority for Health (Haute Autorité de Santé – HAS) and the Regional Pharmacovigilance Centre (CRPV) in Bordeaux are involved. The twinning operation has three operational components. ANSM is leading the first and second components, which focus on the RFDA's structuring, organisation, regulations and partnerships, in addition to pharmacovigilance. It is supporting the final component, focusing on vaccine batch releases.

The next step will be to support the African Medicines Agency (project), alongside the European Medicines Agency (EMA).

Find out more: https://fr.linkedin.com/pulse/une-ann%C3%A9e-de-jumelage-avec-le-rwanda-un-retour-dexp%C3%A9rience-fructueux-iwfve

Other highlights

- **Appointment:** in September 2023, Thierry Sirdey, Head of Medical Devices and In Vitro Diagnostics at ANSM, was elected Chairman of the European group of Competent Authorities for Medical Devices (CAMD) and its Executive Committee (CEG) for a 2-year term.
- **ANSM's participation in the "Guideline on computerised systems and electronic data in clinical trials" within the framework of the GCP Inspection Working Group**
  https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guideline-computerised-systems-and-electronic-data-clinical-trials_en.pdf
- **New Article 120 transitional provisions and links with the application of Article 97.1 of Regulation (EU) 2017/745 on medical devices**
  https://ansm.sante.fr/evenements/webinaire-nouvelles-dispositions-transitoires-article-120-et-articulation-avec-lapplication-de-larticle-97-1-du-reglement-ue-2017-745-relatif-aux-dispositifs-medicaux
  https://ec.europa.eu/commission/presscorner/detail/en/qanda_23_24

ANSM's active involvement in CAMD

ANSM is a member of CAMD, the European Network of Competent Authorities for Medical Devices.
In 2023, CAMD held two face-to-face meetings, in Sweden and Spain. Discussions focused on the practices and organisation of medical device agencies in the host countries, as well as the governance of CAMD, a review of the objectives of the medical device and IVD regulations, the work of the "HMA Core Group on Medical Devices" and the "JAMS 2.0" project.
ANSM is actively involved in the "joint action on market surveillance" JAMS 2.0 project, with a view to contributing to and promoting the harmonisation of practices within the competent authorities in charge of medical devices and IVDMDs. Similarly, to consolidate the network and adapt it to changes in regulations, France has contributed to activities relating to the governance of the CAMD and its executive committee. Thierry Sirdey, Head of Medical Devices and In Vitro Diagnostics, was elected Chairman in September 2023.
Finally, ANSM is also contributing to the work carried out by the Irish Agency on the review of the objectives of the MD and IVD regulations.

Ensuring the safety of patients exposed to medicines and health products

2

FOCUS ON... STOCKOUTS

ANSM activated its 2023-2024 Winter Plan to monitor and manage stockouts and supply pressures on essential medicines as effectively as possible. The team at the Support Centre for Emergency Situations, Health Alerts and Risk Management (Centre d'appui aux situations d'urgence – CASAR), led by Pierre-Olivier Farenq, tell us about the resources and various initiatives implemented by ANSM, in conjunction with the various stakeholders, as part of this Winter Plan.

Can you explain the rise in stockout situations?

Medicine stockout situations are increasing for a number of reasons. Firstly, the stockout risk increases when the market is in a monopoly situation. Secondly, production-related problems such as manufacturing delays, production incidents or insufficient production capacities affect supplies. Thirdly, the complexity of the healthcare product manufacturing chain and the relocation of production sites for "mature" medicines to countries outside the European Union in recent years have increased the risk of production accidents. As a result, this autumn, ANSM rolled out its Winter plan drawn up with all the relevant stakeholders, in order to anticipate and limit the pressures on certain major winter medicines, secure their availability and thereby meet patients' needs.

What is ANSM's role in managing supply pressures?

ANSM plays a central role in coordinating the management of supply pressures on healthcare products. First of all, we have enhanced the surveillance of supply data. This includes monitoring manufacturers' and wholesaler-distributors' inventories and procurements, as well as sales by retail and hospital pharmacies. The challenge is to objectively assess the supply pressures and identify the causes. Secondly, in conjunction with the other health authorities, we coordinate the actions of the actors involved in the medicinal product supply chain to ensure the nationwide availability of treatments for patients on an equitable basis. We also notify patient associations and healthcare professionals about shortage situations, and are working closely with learned societies and other stakeholders to adapt the management measures. We support these measures by publishing information on our website. For example, the Winter Plan includes the generation of dedicated steering indicators, regular meetings with stakeholders, and weekly updates of the dedicated page on our website. In collaboration with teams from Santé Publique France, it also includes the expected timing of winter epidemics, in order to anticipate seasonal peaks in the consumption of medicinal products.

What resources can ANSM draw on to reduce the impact of supply pressures?

ANSM can implement several different measures according to the type of situation. Firstly, it can leverage supplies in order to secure available stocks by imposing quantitative quotas and banning exports, for example, or – in certain cases and as a last resort – by prioritising indications. Depending on the circumstances, pharmaceutical companies may also be asked to use imported products, or allow the network of subcontracted pharmacists to produce pharmacy-compounded preparations, for example. Measures to limit the use of proprietary medicinal products by healthcare professionals can also be envisaged, notably by working with the relevant learned societies to identify alternatives and by disseminating awareness-raising messages to healthcare professionals, patients and even the general public. Finally, we can also impose financial penalties if manufacturers fail to meet their obligations, whether in terms of ensuring adequate supplies to the national market or implementing shortage management plans.

In the framework of the Winter Plan, all these management measures have been identified in advance. They are evaluated and adapted once activated. Collaboration with the actors involved in this plan is essential to ensure compliance with these measures and their proper rollout. It must also be monitored: when the plan is in its active phase, fortnightly meetings, chaired by ANSM, are held with stakeholders.

How did the 2023-2024 Winter Plan help to alleviate these pressures?

This plan, supervised by ANSM, was of major importance last winter and will be rolled out again in the autumn:

- real-time monitoring of changes in the situation, using specific indicators to enable the adjustment of any measures taken, if necessary;
- weekly briefings at ANSM to benefit from the expertise of the majority of divisions and inform collegial decision-making;
- opening of a direct communication channel with stakeholders in the plan, to optimise coordination between players and facilitate rapid responses to problems;
- continuous improvement: feedback is gathered at the end of the season to identify aspects requiring improvement and adjust the plan for the following winter season.

The ANSM Winter Plan plays a key role in anticipating and managing supply pressures that arise during the winter season.

HIGH-RISK SITUATIONS (HRS): 34 NEW HIGH-RISK SITUATIONS IN 2023

An HRS is defined as the occurrence of an emerging event or a series of unusual or obscure events identified during the everyday management of incoming alerts and ongoing cases on the basis of the magnitude, seriousness, or treatment of the event(s) (proven or potential) in the media.

In 2023, around **40** HRS were monitored, **34** being new situations. Some of these concerned particularly sensitive issues such as the safe use of fluoroquinolones,[20] Dräger Carina ventilators,[21] and the stock-out of Eldisine 5 mg powder for injectable solution.[22]

By incorporating risk management into all of its decision-making processes, ANSM is exerting greater control over the risks associated with health products.
This risk management policy specifically involves the following actions:

- prioritising all activities on the basis of a risk analysis,
- coordinating responses to high-risk situations (HRS)
- developing a monitoring and planning strategy,

These situations are subject to a risk analysis, which includes criteria such as the severity and probability of occurrence, the population concerned, media impacts and societal consequences, acceptability and the internal/external control of the situation. Immediate risk-reduction measures are then established and an action plan is defined.

High-risk situations are categorised according to the level of risk. Occurrences posing the highest level of risk are classified as “exceptional health situations” (EHS) when the risk is assessed as being at the highest level.

Combating shortages of medicines: ANSM activates the first edition of its winter plan for 2023-2024

During the winter of 2022-2023, several medicines such as certain antibiotics, corticosteroids and paracetamol were subject to supply pressures in the context of an early triple epidemic of COVID-19, influenza and bronchiolitis.
Consequently, in conjunction with patient associations, representatives of healthcare professionals and all the players in the supply chain, ANSM rolled out a winter plan in October 2023. This plan set out to anticipate and limit the shortages of certain major “winter” medicines and thereby ensure the coverage of patients' needs.

The winter plan was designed to prevent and manage supply pressures, so as to avoid a repeat of the previous year's difficulties, and enable more effective anticipation of and responses to the supply pressures on medicines which are in particularly high demand in winter.

The plan is based on three types of indicators to assess the different dimensions of the situation:

- epidemiological data from the French Public Health Agency (Santé Publique France): monitoring of the number of medical consultations, visits to accident and emergency departments, and hospital admissions for certain diseases (COVID-19, influenza, bronchiolitis, etc.)
- ANSM data on supplies: monitoring of laboratory stocks and supplies, monitoring of wholesalers-distributors and pharmacy stocks, monitoring of sales to retail pharmacies, etc.
- data from the field: feedback on the difficulties encountered by healthcare professionals and patients.

[20] Read “Fluoroquinolone antibiotics administered systemically or by inhalation: reminder of restrictions on use”, page 45.
[21] Read “Masks equipped with magnets for ventilation equipment: risk of interference with implanted medical devices”, page 63.
[22] Read “Eldisine (vindesine): what to do in the event of a supply shortage”, page 51.

Depending on how the indicators evolve, ANSM may have to implement appropriate measures to limit the impact of stock-outs, such as importing medicines initially intended for other markets, imposing quotas, adjusting the distribution circuit or using pharmacy-compounded preparations, to enable patients to obtain their treatments throughout the winter period. To ensure that these measures are effective and properly dimensioned, they are closely monitored by dedicated committees (Winter Plan Monitoring Committees) in conjunction with the stakeholders concerned: stakeholders in the medicines chain, healthcare professionals and patient associations.

In practical terms, ANSM has stepped up its monitoring of certain major winter medicines, such as:

- antibiotics (e.g. amoxicillin / amoxicillin-clavulanic acid)
- fever medicines (e.g. paracetamol)
- oral corticosteroids (e.g. prednisone, prednisolone)
- asthma medicines: inhaled corticosteroids and bronchodilators (e.g. fluticasone, salbutamol).

In the interests of transparency and sharing with its audiences, ANSM published supply-related data on a weekly basis throughout the period in question.
To consult the supply data for these medicines: https://ansm.sante.fr/dossiers-thematiques/plan-hivernal.

In this context, for amoxicillin, the Agency is continuing to lead a group of volunteer pharmacies specialising in pharmacy-compounded preparations for children, enabling pharmacists to directly dispense a pharmacy-compounded preparation suitable for children under 12 on an exceptional and temporary basis, if their prescribed medicine is not available. More than 467,000 patients were treated in 2023 using such preparations.
ANSM has published a new version of the monograph on amoxicillin 125 mg, 250 mg and 500 mg capsules, including a shelf life for amoxicillin capsules in excess of one month, under certain conditions.

The Winter Plan is part of the activities undertaken jointly by the French Ministry of Health and Prevention and the Ministry of Industry in order to combat shortages. France is also involved in the work being carried out at European level to provide a global response to the difficulties in supplying healthcare products.

Find out more: https://ansm.sante.fr/actualites/lutte-contre-les-penuries-de-medicaments-lansm-active-son-plan-hivernal-2023-2024

Commitment charter for stakeholders in the medicines chain to ensure fair access to medicines for patients

When the indicators monitored as part of the 2023-24 Winter Plan showed that stocks of medicines were available but unevenly distributed across the country, at the request of the Minister for Health and Prevention, the ANSM and the French National College of the Board of Pharmacists (CNOP) proposed that all stakeholders in the pharmaceutical chain should sign a “Charter of stakeholders in the medicines chain on fair access to medicines for patients”. This redefined the responsibilities of each link in the medicines chain and strengthened their cooperation. To meet the public health challenge of combating supply pressures on medicines, the stakeholders in the pharmaceutical chain (manufacturers, stockists, wholesaler-distributors, dispensing pharmacists and hospital pharmacists) have joined forces to ensure compliance with the principles of professional ethics and to coordinate their activities, in conjunction with the health authorities, in order to guarantee the equitable availability of medicines nationwide in the event of supply pressures and enable all patients to receive the treatment they need. These commitments complement the initiatives undertaken to ensure the proper use of medicines, and especially of antibiotics. The commitments made under this charter were monitored at dedicated meetings with all the signatories (Supply Task Force meetings).

Read the charter of commitment: https://ansm.sante.fr/actualites/charte-dengagement-des-acteurs-de-la-chaine-du-medicament-pour-un-acces-equitable-des-patients-aux-medicaments

SURVEILLANCE OF MEDICINES

To ensure that patients benefit from high-quality, safe and effective medicines, ANSM starts monitoring these products during their development and continues to do so throughout their life cycle.

ANSM receives or detects potential signals from various sources (pharmacovigilance, medication error and misuse reports, addiction vigilance, articles from the monitoring of scientific literature, etc.). It categorises each signal according to its level of risk and analyses it by cross-referencing the data at its disposal in order to confirm or refute it. Discussions are organised with vigilance networks, patient representatives and health professionals throughout the signal-evaluation process.

In addition, the Agency establishes a reinforced surveillance programme for certain medicines based on a preliminary risk analysis of certain situations or products, without there necessarily being an identified signal.

In addition, via the EPI-PHARE scientific interest group[23] created in 2018 by ANSM and the French National Health Insurance Fund (Caisse Nationale de l'Assurance Maladie – CNAM), pharmaco-epidemiology studies are carried out using complex big data from the National Health Data System (Système National des Données de Santé – SNDS) in order to provide new knowledge on the real-life use, misuse, efficacy and risks of healthcare products.

ANSM is also responsible for securing supplies of medicines of major therapeutic interest (MITMs), and for processing and evaluating all medicine quality defect reports that it receives from pharmaceutical companies.

Lastly, ANSM carries out prior control of advertising for medicinal products, which concerns both advertising aimed at the general public (TV and radio adverts, public displays, social networks, etc.) and advertising aimed at healthcare professionals (stands at congresses, medical sales visits, promotional emails, etc.).

For more information about the surveillance of medicines:
https://ansm.sante.fr/qui-sommes-nous/nos-missions/assurer-la-securite-des-produits-de-sante/p/surveiller-les-medicaments#title

[23] For more information about EPI-PHARE: https://www.epi-phare.fr/

SIGNAL IDENTIFICATION AND PROCESSING

PHARMACOVIGILANCE

France's participation in the PRAC

France's contributions to the Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA) have stood out for a series of significant actions aiming to ensure the safety and efficacy of medical products available on the market. Here are its main contributions:

- triggering of Article 31 safety arbitration for pseudoephedrine-based products following a risk of posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS).
- triggering of Article 31 safety arbitration for hydroxyprogesterone-based products following a study demonstrating a link between a mother's exposure during pregnancy and the risk of cancer in her offspring, as well as a clinical trial demonstrating the absence of efficacy in preventing premature deliveries and neonatal morbimortality. France was co-Rapporteur to the PRAC for this procedure.
- triggering of the EPITT signal for risk of meningiomas with medroxyprogesterone.

Read PRAC opinions: https://ansm.sante.fr/actualites/?filter[categories][]=59

Lactic acidosis and metformin: an avoidable risk

Metformin is indicated for the treatment of type-2 diabetes. It is eliminated by the kidneys. Lactic acidosis is a known side effect of metformin. The risk increases if renal function deteriorates, and can lead to death if treatment is delayed.

In May 2023, ANSM, the CNP-MIR (National Board for Intensive Care Medicine – Resuscitation), the CMG (College of General Practitioners), the French Diabetics Federation, the CRPV network and the SFAR (French Anaesthesia/Resuscitation Society) alerted healthcare professionals and patients to the existing risk of lactic acidosis with metformin, particularly in patients with impaired renal function, cardio-respiratory disease or sepsis (serious infection).

This risk of a serious adverse reaction can be limited by the following measures:

- monitoring the patient's renal function and prescribing a dose of metformin adapted to the renal function;
- assessment of the risk of aggravating renal function by taking account of nephrotoxic drugs and/or possible dehydration, which may increase the risk of lactic acidosis;
- discontinuation of metformin and increased monitoring of renal function in the case of the injection of iodinated contrast products, and ensuring correct hydration when they are used;
- temporary cessation of metformin in the event of acute dehydration (diarrhoea, severe vomiting, fever or reduced fluid intake) and resumption once dehydration has been corrected and if renal function has not deteriorated;
- vigilance in the event of unbalanced diabetes and/or the onset of acute illnesses likely to impair renal function, and/or decompensation of a chronic illness (recent myocardial infarction, acute heart failure, respiratory failure, shock, etc.), all of which are situations associated with a risk of lactic acidosis.

Find out more: https://ansm.sante.fr/actualites/acidose-lactique-et-metformine-un-risque-evitable

Other highlights

- **Chemotherapy based on 5-FU or capecitabine: testing for DPD (dihydropyrimidine dehydrogenase) deficiency is mandatory before starting any treatment**
  https://ansm.sante.fr/actualites/chimiotherapies-a-base-de-5-fu-ou-capecitabine-la-recherche-dun-deficit-en-dpd-dihydropyrimidine-deshydrogenase-est-obligatoire-avant-tout-debut-de-traitement
- **Chlorhexidine: beware of the risk of an immediate serious allergic reaction**
  https://ansm.sante.fr/actualites/chlorhexidine-attention-au-risque-de-reaction-allergique-immediate-grave
- **Crizotinib: vision disorders including a risk of severe vision loss and the need to monitor paediatric patients**
  https://ansm.sante.fr/informations-de-securite/xalkori-crizotinib-troubles-de-la-vision-incluant-un-risque-de-perte-de-vision-severe-et-necessite-de-surveillance-des-patients-pediatriques
- **Clomid (clomiphene citrate): treatment should be stopped if vision is impaired**
  https://ansm.sante.fr/actualites/clomid-citrate-de-clomifene-le-traitement-doit-etre-arrete-en-cas-dalteration-de-la-vision
- **Finasteride 1 mg (Propecia and generics): addition of warnings on boxes to reinforce information about adverse reactions, and a QR code link to the special report on Finasteride 1mg and hair loss**
  https://ansm.sante.fr/actualites/finasteride-1-mg-propecia-et-generiques-ajout-de-mentions-dalerte-sur-les-boites-pour-renforcer-linformation-sur-les-effets-indesirables
- **Lamotrigine: beware of the risk of severe skin eruption, particularly at the start of treatment**
  https://ansm.sante.fr/actualites/lamotrigine-attention-au-risque-deruption-cutanee-grave-en-particulier-au-debut-du-traitement
- **Medicinal products containing tenofovir disoproxil: ANSM and the EMA ask pharmaceutical companies to reduce the concentration of an impurity (CMIC)**
  https://ansm.sante.fr/actualites/medicaments-contenant-du-tenofovir-disoproxil-lansm-et-lema-demandent-aux-laboratoires-de-reduire-la-concentration-dune-impurete-cmic
- **Pralsetinib (Gavreto): increased risk of tuberculosis, and associated risk-reduction measures**
  https://ansm.sante.fr/informations-de-securite/gavreto-pralsetinib-augmentation-du-risque-de-tuberculose-et-mesures-de-reduction-du-risque-associees
- **Treatment of varicose veins: reminder of the steps to be taken to reduce the cardiovascular risks associated with the use of venous sclerosants (SmPC/package leaflets and risk-management plans)**
  https://ansm.sante.fr/actualites/traitement-des-varices-rappel-des-conduites-a-tenir-pour-reduire-les-risques-cardiovasculaires-lies-a-lutilisation-des-sclerosants-veineux
- **Zolgensma (onasemnogene abeparvovec): case of acute liver failure with fatal outcome**
  https://ansm.sante.fr/informations-de-securite/zolgensma-onasemnogene-abeparvovec-cas-dinsuffisance-hepatique-aigue-dissue-fatale
- **ANSM suspends the marketing of Trex Tea, Trex Caps and Trex Plus products**
  https://ansm.sante.fr/actualites/lansm-suspend-la-commercialisation-des-produits-trex-tea-trex-caps-et-trex-plus
- **Oral vasoconstrictor medicinal products: ANSM recommends their avoidance by anyone with a cold**[24]
  https://ansm.sante.fr/actualites/en-cas-de-rhume-evitez-les-medicaments-vasoconstricteurs-par-voie-orale

For more information about pharmacovigilance:
https://ansm.sante.fr/qui-sommes-nous/nos-missions/assurer-la-securite-des-produits-de-sante/p/organiser-les-vigilances#pharmacovigilance

All our pharmacovigilance statistics (French, European and international) can be found in Appendix 4, page 138.

[24] Read the highlight on page 20.

MEDICATION ERRORS

The Ferrostrane pipette should be used with caution with very young children

Ferrostrane 0.68% syrup (sodium feredetate) is indicated notably for low-weight babies as a curative or preventive treatment for iron deficiency.

The dosing pipette currently supplied with Ferrostrane 0.68% syrup is unsuitable for low-weight infants because its graduations do not enable very small volumes to be administered.

To avoid any risk of medication errors, particular attention must be paid to the volume prescribed, which may be between two graduations of the current pipette (0.7 mL/day or 1.3 mL/day, for example), or even less than the 0.5 mL marked on the first graduation (0.3 mL/day).

An overdose of iron can cause digestive problems such as diarrhoea, constipation, nausea, vomiting and even digestive haemorrhaging. In infants, these adverse reactions can be particularly severe.

In the second half of 2024, a pipette adapted to small volumes will be supplied with the syrup, in new packaging, different from the current version. As a result, two distinct presentations of Ferrostrane 0.68% containing the same syrup will be available:

- one with the current pipette with 0.5 mL graduations, starting at 0.5 mL, for most patients and most infants;
- the other with a pipette featuring smaller graduations, suitable for the small volumes that may be prescribed for low-weight babies.

A letter has been sent to the healthcare professionals concerned to inform them of this situation.

Find out more: https://ansm.sante.fr/actualites/la-pipette-de-ferrostrane-est-a-utiliser-avec-precaution-chez-les-plus-petits

MEOPA (Actynox, Antasol, Entonox, Kalinox, Oxynox, Placynox): changes to labelling to reduce the risk of confusion with oxygen cylinders

Erroneous administration of MEOPA (an equimolar mixture of oxygen and nitrous oxide) has been reported as a result of confusion between MEOPA cylinders and oxygen cylinders. In the most serious cases, when MEOPA is administered instead of oxygen, such an error in administration can lead to respiratory distress through desaturation.

To reduce this risk, ANSM has asked pharmaceutical companies that market MEOPA to modify their labels to distinguish it more clearly from medical oxygen. The new label has been rolled out gradually since the beginning of November 2023:

- the brand name of each of the proprietary medicinal products has been enlarged to cover a larger surface area of the bottle;
- the international non-proprietary name (INN) on MEOPA bottles has been harmonised and is now presented as follows: nitrous oxide/oxygen – 50%/50%.

A document has been produced for use by healthcare services, setting out the distinctive features enabling the clear identification of the bottles.

Find out more: https://ansm.sante.fr/actualites/meopa-actynox-antasol-entonox-kalinox-oxynox-placynox-modification-de-letiquetage-pour-reduire-le-risque-de-confusion-avec-les-bouteilles-doxygene

Injectable potassium chloride: preventing avoidable medicinal errors ("never events") and improving information for healthcare professionals

The use of injectable potassium chloride (KCl) must comply with strict precautions for use: especially, injection by slow intravenous infusion, and only after dilution. Incorrect use can pose a risk to the patient's life.
Despite a series of measures put in place to reduce the risk of serious adverse reactions linked to the incorrect use of injectable KCl (changes to ampoule labelling, SmPC and package leaflet information, distribution of a poster on proper use), cases of medication errors continue to be reported to ANSM.
Additional new tools have been designed to further reinforce this information in healthcare institutions. They provide a reminder of the precautions to be taken when using injectable KCl: a presentation reminding people of the correct procedures for use; a new information poster to encourage proper use, distributed in the departments concerned; and a training aid for healthcare professionals, setting out the key messages and specifying the different types of medicinal errors encountered between 2017 and 2020.

To find out more:
- https://ansm.sante.fr/dossiers-thematiques/prevenir-les-erreurs-avec-le-chlorure-de-potassium-injectable
- https://ansm.sante.fr/actualites/renforcer-linformation-des-professionnels-de-sante-pour-une-utilisation-securisee-du-chlorure-de-potassium-kcl-injectable

Other highlights

- **Neofordex 40 mg (dexamethasone): beware of the risk of medication errors with the new unscored tablet**
  https://ansm.sante.fr/actualites/neofordex-40-mg-dexamethasone-attention-au-risque-derreur-medicamenteuse-avec-le-nouveau-comprime-sans-barre-de-secabilite
- **Theralene: beware of the risk of medication errors with the new pipette**
  https://ansm.sante.fr/informations-de-securite/attention-au-risque-derreur-medicamenteuse-de-surdose-accidentelle-avec-la-nouvelle-pipette-de-theralene
- **Gencebok 10 mg/mL solution for infusion (caffeine citrate):**
  https://ansm.sante.fr/informations-de-securite/gencebok-10-mg-ml-solution-pour-perfusion-citrate-de-cafeine-attention-au-risque-derreur-medicamenteuse
- **Stockout of Arsenic Trioxide Accord 1 mg/mL: beware of the risk of a medication error if Trisenox 2 mg/mL is substituted**

https://ansm.sante.fr/informations-de-securite/rupture-de-stock-darsenic-trioxide-accord-1mg-ml-attention-au-risque-derreur-medicamenteuse-en-cas-de-remplacement-par-trisenox-2mg-ml

2023 DATA

- **3,075** reports were submitted to ANSM, including **2,990** proven errors, **32** potential errors and **53** potential medication errors (or latent errors);
- **2,210** reports of proven errors were associated with an adverse reaction (**744** of which were considered serious in terms of pharmacovigilance criteria);
- **780** reports of proven errors were not associated with an adverse reaction.

Changes in medication error reporting

2019	2020	2021	2022	2023
2,180	2,365	1,815	1,926	3,075[25]

For more information about managing medication errors:
https://ansm.sante.fr/page/la-gestion-des-erreurs-medicamenteuses

[25] A new process for transmitting reports received by poison control centres was introduced in 2023, which has led to this increase.

PROMOTING THE PROPER USE OF MEDICINES

ANSM publishes recommendations for the proper use of antibiotics

Antibiotics are a major resource in human and veterinary medicine. Improving how they are used is essential to maintaining their effectiveness and combating the resistance mechanisms developed by bacteria. In December 2023, ANSM published recommendations for patients, parents and healthcare professionals, highlighting the importance of using antibiotics correctly. These recommendations were drawn up with representatives of healthcare professionals, after consultation with patient associations.

In June 2023, the Agency, in conjunction with EPI-PHARE, published a report on antibiotic consumption between 2000 and 2020. The data shows that the consumption of antibiotics in France is still too high (France is the fifth-largest consumer of antibiotics in Europe), and is accompanied by misuse that encourages the emergence of resistant bacteria. This poses a threat to the effectiveness of antibiotics. Antibiotic resistance is a phenomenon that has existed for many years and is growing at an alarming rate worldwide, prompting the World Health Organisation to raise the alarm about this situation, describing it as a "silent pandemic".
This loss of antibiotic efficacy can lead to therapeutic "dead ends" where infections cannot be effectively treated by any antibiotic.

It is therefore essential to take stronger steps to reduce this over-consumption. This also helps to reduce shortages, particularly during winter epidemics, and prevent the development of resistant bacteria.
In this context, the correct prescription and judicious use of antibiotics form a winning partnership serving public health.

Maintaining the efficacy of antibiotics remains a priority and a major public health issue for current populations and future generations.

Find out more:

- **Read the recommendations**: https://ansm.sante.fr/actualites/recommandations-pour-le-bon-usage-des-antibiotiques
- **Read the report on antibiotic consumption between 2000 and 2020**: https://ansm.sante.fr/actualites/lansm-publie-un-rapport-sur-la-consommation-des-antibiotiques-entre-2000-et-2020

ANSM provides a reminder of the correct use of ketamine

Ketamine, a narcotic drug used in anaesthesia, has been used for several years to treat intractable pain in palliative care, and even chronic pain, in accordance with recommendations drawn up by ANSM and learned societies, respectively. The psychotropic properties of ketamine also lead to it being used for non-medical, "recreational" purposes.

The Agency is closely monitoring the use of ketamine, notably in conjunction with pharmacovigilance centres (CRPV) and addiction vigilance centres (CEIP-A). For several years now, an overall increase in the use of ketamine-based medicinal products has been observed for the long-term treatment of chronic pain (off-label use, not approved by recommendations), including fibromyalgia. An increase in the illegal consumption of ketamine, used as a party drug or in a chemsex setting, has also been observed by CEIP-A centres.

Serious complications following the administration of ketamine are regularly reported, in both medical and non-medical settings, i.e. serious damage to the liver, biliary tract and urological system, with possible kidney repercussions, which are most commonly the result of prolonged and/or repeated use, which can also lead to dependence.

There are also regular reports of medication errors due to confusion between the different dosages of ketamine-based medicinal products.

In this context, ANSM has issued a reminder of the precautions to be taken, particularly when ketamine is used for prolonged periods to treat intractable or chronic pain:

- follow the recommended dosage and do not prescribe or administer ketamine for prolonged periods;
- conduct regular monitoring of liver and kidney function, as well as urine cytology;
- watch out for blood in the urine or pelvic pain, which are warning signs of damage to the urinary tract;
- consider discontinuing treatment in the event of liver or uronephrological disorders, with the help of an addictologist if necessary.

And in the case of addiction, it mentions the need to consult addiction specialists (CSAPA, CAARUD, etc.).

Find out more: https://ansm.sante.fr/actualites/lansm-rappelle-le-bon-usage-de-la-ketamine

Other highlights

- **Promoting the correct use of medicines: launch of an information and awareness campaign**[26]
  https://ansm.sante.fr/page/les-medicaments-et-moi
- **Non-steroidal anti-inflammatory drugs (NSAIDs) and serious infectious complications: a reminder of the rules for proper use**
  https://ansm.sante.fr/actualites/anti-inflammatoires-non-steroidiens-ains-et-complications-infectieuses-graves
- **Mydriatic eye drops: how can we reduce the occurrence of side effects in children?**
  https://ansm.sante.fr/actualites/comment-limiter-la-survenue-des-effets-indesirables-des-collyres-mydriatiques-chez-les-enfants
- **Mianserin-based medicines: reminder of correct use and the risk of serious adverse reactions, particularly in elderly patients**
  https://ansm.sante.fr/informations-de-securite/medicaments-a-base-de-mianserine-rappel-du-bon-usage-et-des-risques-deffets-indesirables-graves-notamment-chez-les-patients-ages
- **Treatment of gout with colchicine: a new lower dosage and a warning message on boxes to reduce the risk of overdose**
  https://ansm.sante.fr/informations-de-securite/prise-en-charge-par-colchicine-de-la-goutte-une-nouvelle-posologie-plus-faible-et-un-message-dalerte-sur-les-boites-pour-reduire-le-risque-de-surdosage

Understanding the benefit/risk balance

A medicine, irrespective of whether it is available on prescription, contains one or more active substances that act on the body. These substances are expected to have beneficial effects in diagnosis, prevention, treatment and cure. They may also have undesirable effects. All medicines have benefits and risks: this is known as the “benefit/risk balance”.
The benefit/risk balance is assessed by the health authorities before a medicine is marketed, and throughout its life cycle, by monitoring adverse reactions. This scale is evaluated for a specific indication, for a specific population, and for specific conditions of use (dosage, frequency, etc.). Using a medicine properly means complying with this framework, which guarantees a favourable benefit/risk balance for the medicine.

Video presentation by Isabelle Yoldjian, Director of Medical Division 1: https://www.youtube.com/watch?v=p2izy8wa40s

[26] Read “ANSM rolls out an information and awareness campaign to encourage the proper use of medicines”, page 18.

SURVEILLANCE OF NON-COMPLIANT USE

Ozempic (semaglutide): therapeutic indications for the treatment of type-2 diabetes

Ozempic (semaglutide) is a prescription-only medicine indicated for the treatment of inadequately controlled type-2 diabetes. Reports from the field indicate misuses by non-diabetics who are using the medicine to lose weight, which could exacerbate supply pressures, depriving patients who need this essential treatment.

In this context, ANSM and the French National Health Insurance Fund (CNAM) have implemented active surveillance of its use by monitoring sales and reimbursement data from the National Health Data System (SNDS), reports of non-compliant use, and adverse reaction reports sent to regional pharmacovigilance centres.

ANSM and the CNAM regularly convene meetings of representatives of patient associations (FFD, FAS) and healthcare professionals (CMG, CNOM, CNOP, CNP, FFN, SFD, USPO, FSPF) to discuss the subject and inform them about the actions taken.

At the same time, ANSM has been warned of severe supply pressures in the GLP-1 analogue (aGLP-1) class, due to a significant increase in global demand and overstretched production capacities. The medicines concerned in France are Ozempic (semaglutide) and Trulicity (dulaglutide). These pressures, which began in the autumn of 2022, continued throughout 2023.
To enable the patients concerned to keep benefiting from appropriate treatment, ANSM has drawn up recommendations for prescribing physicians, in consultation with the French-language Diabetes Society (Société francophone du diabète – SFD) and the French Diabetics Federation (Fédération française des diabétiques – FFD). These recommendations change according to the situation.

Finally, **a temporary scientific committee on "Analysis of the use of GLP-1 analogues"** was formed in December 2023, with the aim of:

- taking stock of the use of GLP-1 analogues, both within and outside the scope of their marketing authorisation (MA);
- determining the risks associated with taking these medicines;
- drawing up recommendations for their use in the event of supply difficulties.

Find out more:

- https://ansm.sante.fr/actualites/ozempic-semaglutide-un-medicament-a-utiliser-uniquement-dans-le-traitement-du-diabete-de-type-2
- **on what to do in the event of supply pressures:** https://ansm.sante.fr/actualites/diabete-de-type-2-et-tensions-dapprovisionnement-conduite-a-tenir-pour-la-prescription-des-analogues-de-glp1
- **on the creation of the temporary scientific committee:** https://ansm.sante.fr/actualites/creation-dun-comite-scientifique-temporaire-pour-analyser-lusage-des-analogues-du-glp-1

Fluoroquinolone antibiotics administered systemically or by inhalation: reminder of restrictions on use

Fluoroquinolones are a class of antibiotics that can be used to treat severe bacterial infections. Like all medicines, they may cause undesirable effects.

Given the severity of some of these effects, such as damage to the nervous system (peripheral neuropathies), neuro-psychiatric disorders, musculoskeletal system disorders (joint pain and swelling, inflammation and even ruptured tendons, muscle pain and/or weakness), and their long-term, disabling and potentially irreversible nature, these medicines should only be prescribed for their approved indications, and after careful assessment of the benefits and risks for each patient.

In June 2023, ANSM issued a reminder to healthcare professionals and learned societies, as well as patient associations, about the restrictions on the use of fluoroquinolone antibiotics. The data from a

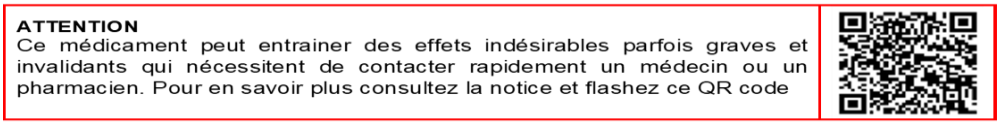
recent study conducted by the EMA suggests that fluoroquinolones continue to be prescribed outside their recommended uses.

Fluoroquinolones administered systemically and by inhalation must not be prescribed:

- to patients who have experienced serious adverse reactions with a quinolone or fluoroquinolone antibiotic;
- for treating non-severe or self-limiting infections (such as pharyngitis, angina and acute bronchitis);
- for treating infections of mild to moderate severity (including uncomplicated cystitis, acute exacerbation of chronic bronchitis and chronic obstructive pulmonary disease (COPD), acute bacterial rhinitis and acute otitis media), unless the other antibiotics usually recommended for these infections are considered inappropriate;
- for treating non-bacterial infections, such as non-bacterial (chronic) prostatitis;
- for preventing traveller's diarrhoea or recurrent lower urinary tract infections.

A letter was sent to all healthcare professionals.

In addition, in order to better inform patients about the adverse reactions to fluoroquinolones and what to do in the event of symptoms indicating such effects, we have had the marketing authorisations for all fluoroquinolones amended to include a warning message printed on the boxes of these medicines. It is associated with a QR code linked to the special report published on our website in October 2022. This warning message, printed on all boxes distributed from December 2023 onwards, was developed in conjunction with healthcare professionals and patient and victim associations.



To find out more: https://ansm.sante.fr/dossiers-thematiques/fluoroquinolones

2023 DATA

- A total of **125 reports of off-label use** (OLU) were reported, including the identification of **54** cases of use contrary to the terms of the marketing authorisation, which exposed users to an actual or potential risk. These reports are mainly identified via the “significant case reporting” procedure used by the Regional Pharmacovigilance Centres (CPRV).
- During the year, risk reduction measures or actions were implemented for **50%** of these cases.
- **24%** of situations were undergoing assessment, and no action was deemed to be necessary in **26%** of the cases.

PHARMACO-EPIDEMIOLOGY

Study examining the increased risk of serious cardiovascular events with bivalent COVID-19 mRNA vaccines compared with monovalent vaccines

As part of the enhanced monitoring of COVID-19 vaccines, EPI-PHARE has carried out a new pharmaco-epidemiological study to assess the increased risk of a serious cardiovascular event (myocardial infarction, ischaemic and haemorrhagic stroke, or pulmonary embolism) in people aged 50 or over who received a booster dose of one of the bivalent Comirnaty mRNA vaccines, compared with people who received the monovalent Comirnaty mRNA vaccine.

Since the end of 2022, in France, three mRNA vaccines developed by Pfizer/BioNtech can be used as a booster in people aged 12 and over who have previously received at least one primary vaccination against COVID-19:

- a monovalent vaccine targeting only the original SARS-CoV-2;
- a bivalent vaccine targeting the original SARS-CoV-2 and the Omicron BA.1 sublineage;
- a bivalent vaccine targeting the original SARS-CoV-2 and the BA.4 and BA.5 sub-variants.

In January 2023, the US Food and Drug Administration (FDA) and the Vaccine Safety Datalink at the Centers for Disease Control and Prevention (CDC) announced the possibility of an increased risk of ischaemic stroke within 21 days of administration of the Comirnaty bivalent vaccine in people aged 65 and over.

Based on this signal, EPI-PHARE conducted a pharmaco-epidemiological study using data from the French National Health Data System (SNDS). The aim of the study was to assess whether the risk of serious cardiovascular events was different in people aged 50 or over depending on whether they had received a booster dose of the Comirnaty bivalent vaccine or the Comirnaty monovalent vaccine.

Between 6 October and 9 November 2022, 1,148,036 people aged 50 and over in France received a booster dose of either the monovalent Comirnaty vaccine or one of the bivalent Comirnaty vaccines.

The results of this study, published in the New England Journal of Medicine (NEJM) in March 2023, show no increase in the risk of ischaemic stroke, haemorrhagic stroke, myocardial infarction, pulmonary embolism, or of the four events combined, in the 21 days following administration of the Comirnaty bivalent vaccine compared with administration of the monovalent vaccine.

Find out more: https://ansm.sante.fr/actualites/epi-phare-publie-dans-le-nejm-les-resultats-dune-etude-qui-montre-quil-ny-a-pas-daugmentation-du-risque-devenement-cardiovasculaire-grave-avec-les-vaccins-bivalents-contre-le-covid-19 and https://www.epi-phare.fr/rapports-detudes-et-publications/nejm-vaccins-bivalents/

IUDs containing the most hormones are more likely to pose a higher risk of depressive disorders

As with all hormonal contraceptives, the use of a levonorgestrel intrauterine device (IUD) may be associated with a low risk of depression or mood disorders (depressed mood).

To assess whether these risks depend on the levonorgestrel dosage, EPI-PHARE studied the use of psychotropic drugs (antidepressants, anxiolytics and hypnotics) during the two years following insertion of an IUD with a levonorgestrel dosage of either 52 mg or 19.5 mg.

The results of this pharmaco-epidemiological study, conducted on reimbursement data from the French National Health Insurance (SNDS) and published in the Journal of the American Medical Association (JAMA), show that women have a very slightly increased risk of using antidepressants in the two years following insertion of an IUD with a higher dosage of levonorgestrel (52 mg) compared with an IUD with a lower progestin dosage. However, the study showed no increase in the use of anxiolytics or hypnotics.

This study is the first to show that the risk of depressive disorders depends on the dose of levonorgestrel contained in the IUD. This risk is low and still needs to be determined.

Find out more: https://ansm.sante.fr/actualites/les-sterilets-contenant-le-plus-dhormone-presenteraient-davantage-de-risque-de-troubles-depressifs and https://www.epi-phare.fr/rapports-detudes-et-publications/association-entre-dispositifs-intra-uterins-au-levonorgestrel-et-lusage-ulterieur-de-psychotropes-en-france/

Other highlights

- **Booster doses of monovalent mRNA vaccines are effective against the risk of hospitalisation for COVID-19 in cases of infection with the Omicron BA.4 and BA.5 sub-variants**
  https://ansm.sante.fr/actualites/les-doses-de-rappel-des-vaccins-monovalents-a-arnm-sont-efficaces-contre-le-risque-dhospitalisation-pour-covid-19-en-cas-dinfection-par-les-sous-variants-omicron-ba-4-et-ba-5
- **Progestins and meningioma: no increase in risk with levonorgestrel IUDs but confirmation of the risk for three new substances**
  https://ansm.sante.fr/actualites/progestatifs-et-meningiome-pas-daugmentation-du-risque-avec-les-diu-au-levonorgestrel-mais-confirmation-du-risque-pour-3-nouvelles-substances
- **MRNA vaccines do not increase the risk of Guillain-Barré syndrome, unlike adenoviral vector vaccines**
  https://www.epi-phare.fr/actualites/communique-de-presse-11-10-2023/

2023 DATA

- **4 reports published** on the EPI-PHARE website
- **27 articles published** in international peer-reviewed journals[27]

For more pharmaco-epidemiological information:
https://www.epi-phare.fr/

[27] Read the complete list in Appendix 2, page 128.

ENHANCED SURVEILLANCE OF MEDICINES

HPV vaccination campaign: ANSM rolls out an enhanced surveillance system

Human papillomavirus (HPV) infections are amongst the most common sexually transmitted infections, usually contracted at the very beginning of sexual life. They affect half of all young people aged between 15 and 24, and 80% of women and men will be exposed to these viruses during their lives. These infections can be the cause of certain cancers, such as those of the cervix, vulva, vagina, anus, penis and ENT sphere (particularly throat cancers). The vaccine is highly effective in preventing HPV infections, preventing up to 90% of HPV infections that cause cancer. Both men and women can be vaccinated to prevent cancers linked to these infections.
In the autumn of 2023, a national HPV vaccination campaign began in secondary schools to improve vaccination coverage of girls and boys with the Gardasil 9 vaccine.

In this context, ANSM has implemented a reinforced surveillance system to complement that already in place since 2006, when HPV vaccines were first used in France. This system, in conjunction with the French network of regional pharmacovigilance centres (CRPV) and EPI-PHARE, is largely based on the collection and ongoing analysis of adverse reactions reported by healthcare professionals and patients to the national and European pharmacovigilance systems.
Particular attention is paid to serious and unexpected adverse reactions (not listed in the summary of product characteristics (SPC) or package leaflet) and certain autoimmune diseases of interest, although the data has not identified any increased risk.

Since October 2023, ANSM has been publishing monthly key figures on adverse effect reports, vaccination and any potential signals identified. In addition, two periodic summaries of the pharmacovigilance survey will be published at the end of the first and second vaccination phases (in the spring and summer of 2024), and a detailed pharmacovigilance report will be published in the autumn of 2024.

Data at 31 December 2023

Since 14 September 2023, 58 cases of adverse events have been reported following vaccination with Gardasil 9, 36 of which were related to vaccination carried out as part of the campaign, while, according to provisional and fragmentary feedback from the Regional Health Agencies, just over 92,000 pupils had been vaccinated in secondary schools by 23 December 2023.
To date, the ongoing analysis of reported adverse events has not identified any safety signals.
ANSM reiterates that, due to a risk of malaise, vaccinated people should be carefully supervised for 15 minutes after the injection and remain lying down (on floor mats or blankets) or sitting on the floor with their back against a wall in an open space, to avoid any injury that might occur after a fall.
No specific signals were identified over the past period.

To find out more: https://ansm.sante.fr/dossiers-thematiques/vaccins-contre-les-infections-a-papillomavirus-humains-hpv

National COVID-19 vaccination campaign: what can be learned from the enhanced surveillance system?

As part of the national COVID-19 vaccination campaign, which began on 27 December 2020, ANSM had implemented a specific enhanced surveillance system in conjunction with the French network of Regional Pharmacovigilance Centres (CRPV) and the EPI-PHARE Scientific Interest Group.

This scheme was a major public health issue. It has enabled their efficacy in the vaccinated population to be guaranteed and any undesirable effects that may not have been observed during the clinical trials to be identified.

More than three years after the launch of the campaign and almost 157,000,000 injections, the monitoring carried out and the international data confirm the safety and efficacy of the COVID-19 vaccines.

Key messages

- Efficacy against severe forms of COVID-19 is around 90%, which means that vaccinated people are nine times less likely to be hospitalised or die from COVID-19 than unvaccinated people.
- The first booster dose was 83%-effective in reducing the risk of hospitalisation for COVID-19.
- The majority of the reported adverse reactions are known and not serious.
- Pharmacoepidemiological studies conducted by EPI-PHARE confirm the major impact of vaccination in protecting against severe forms of the disease. These studies, conducted on the entire French population, confirmed the efficacy observed in clinical trials involving tens of thousands of people. International studies also attest to their effectiveness.

The monitoring carried out by ANSM shows that most of the adverse reactions reported are not serious and were observed during clinical trials. It has also enabled the identification of rare adverse events, such as myocarditis and pericarditis with mRNA vaccines and atypical thrombosis with adenoviral vector vaccines. The new adverse reactions identified as a result of our monitoring do not call into question the safety profile of the vaccines.
However, this new data has enabled the health authorities to make changes to the recommendations as the national vaccination campaign progresses.

Based on international data, including information from our own surveillance, the European Medicines Agency (EMA) has extended the Conditional Marketing Authorisations (CMA) for the Comirnaty, Jcovden, Nuvaxovid, Spikevax and Vaxzevria vaccines to “standard” MAs.

In this context, the enhanced surveillance system has evolved. These vaccines are now monitored through a continuous analysis of significant cases by experts from the CRPVs and the Agency. ANSM is also continuing its surveillance activities, and now relies on its Standing Scientific Committee on “Pharmaco-Surveillance and Proper Use” for the collegial analysis of any new potential safety signals detected.
If a safety signal is confirmed, measures appropriate to the nature and level of the risk will be implemented, in association with the EMA, to prevent or reduce the likelihood of the risk occurring in vaccinated people.

Find out more:https://www.ansm.sante.fr/Declarer-un-effet-indesirable/Votre-declaration-concerne-un-medicament/Votre-declaration-concerne-un-medicament/Votre-declaration-concerne-un-medicament-Vous#defaut

Prevention of lower respiratory tract infections caused by the respiratory syncytial virus

Beyfortus (nirsevimab) is indicated in newborns and infants for the prevention of lower respiratory tract infections caused by respiratory syncytial virus (RSV) during their first season of RSV circulation. Beyfortus has had marketing authorisation since 30 October 2022. It has been available in France since mid-September 2023.
A pharmacovigilance survey has been implemented to monitor known adverse reactions to Beyfortus (nirsevimab) and, if necessary, to detect any new adverse reactions not identified in the clinical trials. Within this framework, if a safety signal is validated, measures adapted to the nature of the risk will be put in place, in liaison with the European Medicines Agency, to prevent or reduce the probability of the risk occurring in treated newborns and infants.

For more information about the enhanced surveillance of medicinal products:
https://ansm.sante.fr/page/la-surveillance-renforcee-des-medicaments

SURVEILLANCE OF THE COVERAGE OF PATIENTS' HEALTH NEEDS

SECURING THE SUPPLY OF MEDICINAL PRODUCTS OF MAJOR THERAPEUTIC VALUE

Eldisine (vindesine): what to do in the event of a supply shortage

Vindesine is a medicine used in acute lymphoblastic leukaemia, non-Hodgkin's lymphoma and neuroblastoma.

In July 2023, the EG LABO pharmaceutical company informed ANSM of a risk of disruption to Eldisine supply due to the identification of a non-conformity in two batches of active substance. The release, initially announced for October 2023, has been postponed several times by the company as its planned measures to make the product available again have not been successful.

At the beginning of November 2023, the ANSM referred the matter to the French National Cancer Institute (INCA) to define urgently, with the help of experts, the therapeutic alternatives to vindesine and the criteria for prioritising indications. Their opinion was published in December 2024.

To find out more and consult the experts' opinion on alternatives to treatment with vindesine: https://ansm.sante.fr/actualites/eldisine-vindesine-conduite-a-tenir-dans-un-contexte-de-rupture-dapprovisionnement

Other highlights

- **Combating shortages of medicines: ANSM activates its 2023-2024 winter pla**[28]
  https://ansm.sante.fr/actualites/lutte-contre-les-penuries-de-medicaments-lansm-active-son-plan-hivernal-2023-2024
- **Type 2 diabetes and supply tensions: how to prescribe GLP1 analogues**[29]
  https://ansm.sante.fr/actualites/diabete-de-type-2-et-tensions-dapprovisionnement-conduite-a-tenir-pour-la-prescription-des-analogues-de-glp1
- **Tensions in the supply of Corgard 80 mg (nadolol): easing of dispensing conditions**
  https://ansm.sante.fr/actualites/tensions-dapprovisionnement-en-corgard-80-mg-nadolol-ce-medicament-doit-etre-reserve-a-certains-patients-atteints-de-troubles-du-rythme-dorigine-genetique
- **Supply pressures on adrenaline auto-injectors (Emerade, Anapen, Epipen and Jext): recommendations for patients and doctors**
  https://ansm.sante.fr/actualites/tensions-dapprovisionnement-sur-les-auto-injecteurs-dadrenaline-emerade-anapen-epipen-et-jext
- **Supply difficulties for corticosteroids (prednisone and prednisolone): recommendations for pharmacists**
  https://ansm.sante.fr/actualites/difficultes-dapprovisionnement-en-corticoides-prednisone-et-prednisolone-lansm-publie-une-recommandation-pour-les-pharmaciens
- **Extended-release flecainide: what to do in a context of supply pressures**
  https://ansm.sante.fr/actualites/flecainide-a-liberation-prolongee-conduite-a-tenir-dans-un-contexte-de-tensions-dapprovisionnement
- **Integrilin discontinuation: recommendations for healthcare professionals**
  https://ansm.sante.fr/informations-de-securite/arret-de-commercialisation-dintegrilin-recommandations-de-lansm

[28] Read about this highlight in the "HRS" chapter on page 36.
[29] Read about this highlight in the chapter entitled “Surveillance of non-compliant use” on page 45.

2023 DATA

Changes in stockout and stockout-risk reports	2018	2019	2020	2021	2022	2023
	871	1,504	2,446	2,160	3,761	**4,925**

Our data on changes in stockout-risk and stockout reports per therapeutic class can be found in Appendix 4, page 138.

For more information about the securing of the supply of medicines of major therapeutic interest
https://ansm.sante.fr/qui-sommes-nous/nos-missions/assurer-la-securite-des-produits-de-sante/p/assurer-la-disponibilite#title

MANAGEMENT OF QUALITY DEFECTS

ANSM also processes and assesses all reports of medicine quality defects that it receives from pharmaceutical companies. These quality defects can occur during the manufacture of medicines and/or active substances.

Highlights

- **One ampoule of Clopixol Depot in a box of Fluanxol LP 100 mg/1 ml**
  https://ansm.sante.fr/informations-de-securite/fluanxol-lp-100-mg-1-ml-solution-injectable-im-lundbeck-sas
- **WFI water vials present in certain blood-derived medicines (BDMs)**
  https://ansm.sante.fr/informations-de-securite/ne-pas-utiliser-les-flacons-deau-ppi-100-ml-et-200-ml-presents-dans-certains-medicaments-derives-du-sang-mds
- **Naprosyne 1,000 mg: recall of batches following identification of an error in the transcription of the dosage in Braille on the box**
  https://ansm.sante.fr/actualites/naprosyne-1000-mg-rappel-de-lots
- **Rixubis 500 IU, 1000 IU, 2000 IU, 3000 IU nonacog gamma for the treatment and prevention of haemorrhage in Haemophilia B: replacement of certain reconstitution devices due to a quality defect**
  https://ansm.sante.fr/informations-de-securite/remplacement-du-dispositif-de-reconstitution-contenu-dans-certaines-boites-de-rixubis-500-ui-1000-ui-2000-ui-3000-ui-de-nonacog-gamma

2023 DATA

- **1,968** reports in 2023
- **25%** were thoroughly investigated
- **34** batch recalls were carried out

Change in the number of quality-defect reports	Number of reports	Number of batch recalls
2019	2102	70
2020	1854	62
2021	1798	46
2022	1890	33
2023	**1968**	**34**

For more information about quality-defect management:
https://ansm.sante.fr/qui-sommes-nous/nos-missions/assurer-la-securite-des-produits-de-sante/p/assurer-la-disponibilite#title

CONTROL OVER ADVERTISING

Advertising to the general public and on social networks

One highlight of 2023 was the promulgation of the **Law of 9 June 2023**, which is intended to regulate commercial influence and combat abuses by influencers on social networks, known as the "**Influencers Law**", whose provisions include a ban on influencers promoting medicines on social networks.

Pursuant to this law and the Articles L.5122-2 and R.5122-4 of the French Public Health Code, sponsored content promoting a medicine on social networks may not originate from "scientists, healthcare professionals or from persons who, although they are neither scientists nor healthcare professionals, may, by virtue of their reputation, encourage the consumption of the medicine concerned".

Consult the legislative text: https://www.legifrance.gouv.fr/jorf/id/JORFTEXT000047663185

At the same time, in view of the significant increase in applications for GP (general public) advertising approvals for media intended for distribution on social networks, ANSM has issued recommendations concerning the presentation of these media to the professional organisations representing healthcare industries.
These are designed to ensure that the public immediately notices the promotional nature of the publication.

Read the minutes of the Interface Committee's Advertising working group: https://ansm.sante.fr/evenements/comite-dinterface-avec-les-representants-des-industries-du-medicament-groupe-de-travail-publicite-information-communication-1

Advertising aimed at professionals: end of the alternative system enabling the distribution of guides to the proper use of vaccines and medicines indicated for COVID-19

In view of the constant and rapid changes in the epidemiology, safety data and therapeutic strategies of the vaccines and medicinal products indicated for COVID-19 during the pandemic phase, the dissemination of advertising was incompatible with the obligation to provide healthcare professionals with accurate and up-to-date information.
An alternative system enabling the distribution of guides to information and proper use distributed under the authority of the ANSM according to a predefined framework was put in place in April 2022.

With effect from July 2023, ANSM considered that the epidemiological situation and the conditions for the use of the above-mentioned treatments and vaccines, which had stabilised, were compatible with promotional activity and the distribution of advertising material for these proprietary medicinal products. Applications for advertising approvals for medical professionals (MP approvals) could therefore be submitted by pharmaceutical companies from the July 2023 submission period (from 06/07 to 27/07) onwards.

Find out more: https://ansm.sante.fr/dossiers-thematiques/covid-19-vos-demarches-durant-la-pandemie/covid-19-communications-pour-le-bon-usage-des-vaccins-et-des-medicaments-indiques-dans-la-covid-19

2023 DATA

In 2023, pharmaceutical companies submitted the following applications to ANSM:

- **9,986 applications for advertising approvals for medical professionals (MP approvals)**, an **increase of 5.7%** compared with 2022 (9,440 applications).
  Of these applications:
  - 875 (8.8%) were subject to requests for corrections,
  - 436 (4.4%) were subject to refusals of approval.

  This corresponds to an overall intervention rate of 13.1%.

- **1,207 applications for advertising approvals targeting the general public (GP approvals)**, up 18.1% compared with 2022 (1,022 applications).
  Of these applications:
  - 488 (40.4%) were subject to requests for corrections,
  - 136 (11.3%) were subject to refusal of approval.

  This corresponds to an overall intervention rate of 51.7%.

A total of **11,193** applications (GP and MP combined) were submitted.
Over a five-year period – excluding 2020 and 2021 due to exceptional measures linked to the COVID-19 pandemic – **a steady increase in the number of advertising approval applications (+14% compared with 2017)** was observed, despite the updating of recommendations intended to reduce them, in 2019 and 2022.

For more information about control over the advertising of medicines:
https://ansm.sante.fr/page/le-controle-de-la-publicite-des-medicaments

MEDICINES AND PREGNANCY

Anti-epileptic medicines and pregnancy: better understanding of the risks for the unborn child

Following an initial report published in 2019, ANSM conducted a new review of the data on the use of anti-epileptic medicines during pregnancy and the main risks that these medicinal products may pose to the unborn child: malformative risks and risks of neurodevelopmental disorders. This report classifies anti-epileptic medicines according to the level of risk of major malformations and neurodevelopmental disorders.

What can we learn from this report?

- This update confirms the level of risk already known for valproate, both the malformative risk and the risk of neurodevelopmental disorders if taken by the mother during pregnancy.
- The risk of major malformation associated with pregabalin has been confirmed.
- An increased risk of neurodevelopmental disorders has been identified for topiramate and possibly for carbamazepine.

At the same time, to make the report easier to understand, an information sheet has been designed for use in the framework of a dialogue between the prescriber and the patient.

To consult the report and the information sheet: https://ansm.sante.fr/actualites/antiepileptiques-et-grossesse-mieux-connaitre-les-risques-pour-lenfant-a-naitre

In the light of the newly available data, ANSM has launched a number of initiatives at national and European level to ensure the safe use of anti-epileptic medicines:

- **Topiramate (Epitomax and generics): changes to prescribing and dispensing conditions for girls, adolescents, women of childbearing age and pregnant women**

  To limit exposure to topiramate during pregnancy, in view of the recently revealed risks of neurodevelopmental disorders for the unborn child and in addition to the already known malformative risks, the prescribing and dispensing conditions for topiramate-based medicinal products have been modified.

  For girls, teenagers and women of childbearing age, the initial annual prescription is now reserved for neurologists and paediatricians. This must be accompanied by the patient's (or her legal representative's) agreement to treatment by these doctors after the patient has been fully informed. Dispensation by pharmacies will be subject to presentation of an annual treatment agreement form co-signed by the patient and the specialist doctor (neurologist or paediatrician), and an annual prescription by the neurologist or paediatrician.

  Finally, and at the request of ANSM, all of the available data has been examined at European level in order to reassess the benefit/risk balance of these medicines for patients. Following this re-evaluation, the EMA has decided to contraindicate topiramate-based medicines for the treatment of epilepsy in girls, adolescents and women of childbearing age who are not using an effective method of contraception, and in pregnant women, except in exceptional cases where there is no therapeutic alternative. Topiramate was already contraindicated for migraine in pregnant women and women of childbearing age not using a highly effective method of contraception.

  Find out more: https://ansm.sante.fr/actualites/topiramate-et-risques-chez-les-enfants-exposes-pendant-la-grossesse-modification-des-conditions-de-prescription-et-de-delivrance-aux-femmes-concernees-5
  https://ansm.sante.fr/actualites/topiramate-epitomax-et-generiques-et-troubles-neurodeveloppementaux-mise-en-place-de-mesures-en-europe-pour-limiter-lutilisation-pendant-la-grossesse

- **Carbamazepine: changes to prescribing and dispensing conditions for girls, adolescents, women of childbearing age and pregnant women**
  Given the persistence of a large number of pregnancies exposed to carbamazepine, the ANSM has decided to modify the prescribing and dispensing conditions for these medicines by proposing to introduce an annual certificate of shared information. This certificate would be co-signed by the prescriber and the patient once a year, and the dispensation of carbamazepine would be subject to its presentation to a pharmacist.
  This project has been drawn up with representatives of healthcare professionals and patient associations to ensure that patients and prescribers are fully informed about the risks associated with the use of this medicinal product.
  A consultation of all parties with the pharmaceutical companies concerned began in October 2023.
  In addition, an analysis of recent data from the scientific literature points towards an increased risk of neurodevelopmental disorders, which cannot yet be fully characterised, in children exposed to carbamazepine during pregnancy. In October 2023, ANSM therefore requested a European-level assessment of this new data. However, the rapporteur country did not consent to this assessment.

Valproate: European evaluation of the potential risk of neurodevelopmental disorders in the offspring of fathers treated in the months prior to conception

The results of a study commissioned from pharmaceutical companies as part of the European monitoring of medicines containing valproate and its derivatives suggest an increased risk of neurodevelopmental disorders in children whose fathers were treated with valproate in the three months prior to conception. This study has limitations and the EMA has requested additional data from the pharmaceutical companies.
As soon as the results of this study were known, ANSM sent an information letter to all the healthcare professionals concerned in order to alert them to this potential risk. A patient information sheet has also been made available on the Agency's website, to be given to patients when a valproate-based product or one of its derivatives is prescribed or dispensed to them.
At the same time, ANSM has asked the pharmaceutical companies marketing these medicines to submit an application to amend their marketing authorisations to enable the inclusion of this potential risk in the summary of product characteristics and the package leaflets for these medicines. ANSM has also asked them to submit additional documents to better inform patients and healthcare professionals about this risk and how to reduce it.

Find out more: https://ansm.sante.fr/actualites/evaluation-europeenne-du-risque-potentiel-de-troubles-neurodeveloppementaux-chez-les-enfants-dont-le-pere-a-ete-traite-par-valproate-dans-les-mois-precedant-la-conception

Other highlights

- **Treatment of severe acne: raising awareness of the risks associated with oral isotretinoin: a special report and educational videos accessible on the ANSM website via a QR code on patient cards, brochures and medicine boxes**
  https://ansm.sante.fr/actualites/traitement-de-lacne-severe-mieux-faire-connaitre-les-risques-associes-a-lisotretinoine-orale
- **Reassessment of the pictogram on the outer packaging of teratogenic or foetotoxic medicinal products: creation of a temporary scientific committee**
  https://ansm.sante.fr/actualites/evolution-du-pictogramme-grossesse-creation-dun-comite-scientifique-temporaire

2023 DATA

- **130** evaluation applications concerning the amendment of section 4.6 (pregnancy, breastfeeding, fertility) and/or section 5.3 (non-clinical – reproductive toxicity) of SmPCs and package leaflets
- **52** potential signals transmitted by the Regional Pharmacovigilance Centres, 21 of which required action or measures to be taken
- **16** potential signals from the literature detected and evaluated, 11 of which are subject to specific monitoring
- **30** analyses of paediatric investigation plans
- **61** requests for evaluations of marketing authorisation applications
- **11** participations in meetings of the Non-clinical Working Party (NcWP - CHMP/EMA)

For more information about medicines and pregnancy:
https://ansm.sante.fr/dossiers-thematiques/medicaments-et-grossesse

ANSM'S ROLE IN THE PREVENTION OF ADDICTIVE BEHAVIOURS

ANSM classifies hexahydrocannabinol (HHC) and two of its derivatives as narcotics

HHC and its derivatives are obtained by chemical synthesis from natural cannabinoids, producing psychotropic effects comparable to those experienced when THC is consumed. Sold mainly on the Internet and in CBD shops, HHC comes in the form of oil, resin, smoking herb, spray, gummies (sweets), e-liquid, jelly, etc. The concentration of HHC in these products varies and can be as high as 99%, depending on the form and brand.

Consumption of HHC or its derivatives exposes users to risks such as tremors, vomiting, anxiety, "bad trips", mental confusion, malaise, tachycardia, chest pain and high blood pressure, the intensity of which seems to vary according to the HHC content, which is not always specified or accurate.

In this context, ANSM has decided to place hexahydrocannabinol (HHC) and two of its derivatives, HHC acetate (HHCO) and hexahydroxycannabiphorol (HHCP), on the list of narcotics. As a result, since 13 June 2023, their production, sale and use have all been banned in France.

This decision follows studies carried out at the Agency's request by the drug dependence and addiction vigilance information and assessment centres (CEIP-A), which reported that HHC presents a risk of abuse and dependence equivalent to that of cannabis. Moreover, the chemical structure of these products is close to that of delta-9 tetrahydrocannabinol (delta-9 THC), which is classified as a narcotic.

In Europe, other countries have banned the sale of HHC, including Austria, Belgium, Denmark and the United Kingdom.

Enhanced monitoring of HHC and cannabinoids in general is continuing.

Find out more: https://ansm.sante.fr/actualites/lansm-classe-lhexahydrocannabinol-hhc-et-deux-de-ses-derives-sur-la-liste-des-stupefiants

Antarene Codeine (codeine-ibuprofen): prolonged use, in the event of abuse or dependence, can lead to renal and intestinal toxicity, which may result in death

Antarene Codeine is a combination of two painkillers, ibuprofen and codeine. Several cases of renal, gastrointestinal and metabolic toxicity have been reported in countries where it is available without a prescription. In France, all medicines containing codeine have been subject to compulsory medical prescription since 2017.
The reported cases of toxicity, which sometimes led to the death of the patient, occurred in situations of prolonged use, at higher-than-recommended doses, in a context of abuse and dependence on codeine. Prolonged use of this medicine causes kidney damage (renal failure) and a significant drop in potassium levels in the blood (hypokalaemia), which can lead to muscle weakness and impairment of consciousness. Perforations and haemorrhages in the stomach or intestines and severe anaemia have also been observed.
In this context, the European Medicines Agency (EMA) requested the addition of these adverse reactions to the summary of product characteristics (SmPC) and the package leaflet.

Find out more: https://ansm.sante.fr/actualites/antarene-codeine-codeine-ibuprofene-la-prise-prolongee-en-cas-dabus-et-de-dependance-peut-entrainer-une-toxicite-renale-et-intestinale-pouvant-conduire-au-deces

Other highlights

- **Non-medicinal nitrous oxide: ANSM publishes a diagnosis- and treatment-support document for healthcare professionals**
  Link to news article: https://ansm.sante.fr/actualites/intoxication-au-protoxyde-dazote-lansm-publie-un-document-daide-au-diagnostic-et-a-la-prise-en-charge-pour-les-professionnels-de-sante
- **Pregabalin/Gabapentin: close monitoring in addiction vigilance**
  Find out more: https://ansm.sante.fr/evenements/comite-psychotropes-stupefiants-et-addictions-formation-restreinte-expertise-1

2023 DATA

- **10,614** import and export authorisations for narcotics and psychotropic drugs
- **887** authorisations for activities relating to narcotics and psychotropic drugs

Total number of spontaneous reports of abuse, drug dependence and misuse reported by the CEIP-A network*

2019	2020	2021	2022	2023
6,705	7,275	5,159	6,314	**7,225**

Number of national addiction vigilance survey reports

2019	2020	2021	2022	2023
26	24	21	21	**21***

*Of these 21 investigations, the ANSM is continuing to monitor cases of abuse, dependence and misuse:

- of **nitrous oxide** in the form of capsules or cylinders;

Analysis of the data collected by the addiction vigilance network over the last few years shows an exponential increase in the number of cases associated with increasingly severe clinical consequences (in descending order: use/addiction disorders, neurological, psychiatric and thrombo-embolic disorders). Nitrous oxide continues to be monitored on an annual basis.
To find out more: https://ansm.sante.fr/evenements/comite-psychotropes-stupefiants-et-addictions-formation-restreinte-expertise

- of transmucosal fentanyl (fast-acting, buccal and nasal forms)

These proprietary medicinal products have been monitored for many years because of the risks of abuse, dependence and misuse associated with medicinal products in the opioid class. Analysis of addiction vigilance data for 2023 shows that non-compliant use (non-cancer indications and/or insufficient or non-existent background treatment) continues to occur, leading to cases of abuse/addiction and overdose.
Find out more: https://ansm.sante.fr/evenements/comite-psychotropes-stupefiants-et-addictions-formation-restreinte-expertise-1

For more information about addiction vigilance:
https://ansm.sante.fr/qui-sommes-nous/nos-missions/assurer-la-securite-des-produits-de-sante/p/organiser-les-vigilances#addictovigilance

For more information about the regulation of flows of narcotic and psychotropic substances:
https://ansm.sante.fr/vos-demarches/industriel/demande-dautorisation-relative-aux-stupefiants-et-psychotropes-pour-les-industriels

SURVEILLANCE OF BLOOD PRODUCTS

ANSM is the pilot organisation for the haemovigilance system and is involved in the collection, monitoring and analysis of adverse effects and incidents concerning both recipients and donors of these blood products. This surveillance concerns the entire transfusion chain, from the collection of blood and its components to transfusion.

In 2023, ANSM published the 2022 Haemovigilance Activity Report and decided to change the procedures for reporting adverse reactions involving blood donors, in order to bring them into line with European and international procedures.

Haemovigilance: ANSM changes the reporting of adverse reactions by blood donors

Since 2007, healthcare professionals working in blood transfusion centres have been obliged to report any adverse reactions graded as 2 to 4 in severity that occur in blood donors to the national haemovigilance system. The reporting of minor or “grade-1” adverse reactions has not been necessary, but they have been collected, analysed and monitored by the blood transfusion clinics of the French National Blood Service (EFS) and the Army Blood Transfusion Centre (CTSA). Blood donors, for their part, have been able to report adverse reactions to blood transfusion clinics, regardless of the severity of the reaction.
After many years of collecting and analysing these reports, and in the light of European studies of the subject, the scope of the reporting adverse reactions occurring in blood donors to the national haemovigilance system has been simplified to focus on the most serious adverse reactions (grades 3 and 4). The majority of grade-2 reports (87%) have related to vasovagal syncope and haematomas at the puncture site, with no signs of seriousness and no subsequent complications.
Donors and healthcare professionals will continue to report these reactions, as well as grade-1 reactions, to the haemovigilance unit for blood transfusion clinics, which will assess and analyse them. This decision by the Director General of the ANSM, which came into force on 2 January, 2024, will harmonise European and international procedures, facilitating the comparison of data between countries, and particularly between EU Member States. It also harmonises the French and European definitions of serious adverse drug reactions. This change will enable the inclusion of the clinical and/or biological manifestations observed in the donor during or after the donation, as well as any complications and possible impacts on the donor's daily life post-donation.

Find out more: https://ansm.sante.fr/actualites/hemovigilance-lansm-fait-evoluer-la-declaration-des-effets-indesirables-donneurs-de-sang

ANSM publishes the Haemovigilance Activity Report for 2022

As it does every year, ANSM has published a summary of national haemovigilance data relating to the monitoring of the entire transfusion chain (from blood collection to recipient monitoring). Its analysis shows that the majority of adverse events, whether in recipients or donors, were not severe and were similar to previous years, both in terms of the type of event observed and the frequency. No new signals were identified in 2022.

Read the report and its summary: https://ansm.sante.fr/actualites/lansm-publie-le-rapport-dactivite-dhemovigilance-2022

For more information about the surveillance of blood products:
https://ansm.sante.fr/qui-sommes-nous/nos-missions/assurer-la-securite-des-produits-de-sante/p

All our statistical data on haemovigilance reports of adverse transfusion events, serious transfusion chain incidents, and post-donation haemovigilance information, can be found in Appendix 5, page 142.

SURVEILLANCE OF MEDICAL DEVICES AND IN VITRO DIAGNOSTIC MEDICAL DEVICES

ANSM is the competent authority in France for medical devices (MD) and in vitro diagnostic medical devices (IVDMD). According to the applicable regulations, one of its main missions is to carry out the market surveillance of these devices. Unlike for medicinal products, it does not authorise the marketing of medical devices and IVDMDs: “notified” bodies are responsible for carrying out the necessary assessments prior to the marketing of such devices in order to ensure that they comply with the applicable requirements. The manufacturer manages and bears responsibility for this compliance. The regulations therefore require manufacturers to affix a CE Mark to devices prior to their marketing, which guarantees their compliance.

As part of its market surveillance remit, ANSM ensures that the MDs and IVDMDs available in France are safe, effective and properly used. In this capacity, it authorises clinical trials, inspects manufacturing sites, conducts market-control activities and also carries out significant regulatory activities in France and at also at European level. It also has a key role to play in ensuring access to these health products and their availability, with the aim of avoiding disruption to services to ensure that patients receive the most appropriate care.

In 2023, against a backdrop of regulatory changes and increased safety and performance requirements, ANSM was particularly active in ensuring the continued availability of medical devices and IVDMDs, within a secure regulatory framework. This active involvement led to:

- the pursuit and intensification of work on implementing and adjusting tools and procedures for managing the unavailability of medical devices and IVDMDs;
- the consideration and establishment of a policy on the application of Article 59 of the MD regulation and Article 54 of the IVDMD regulation, under which the Director General of ANSM may grant exemptions from the CE marking requirement, in the interest of public health; the key issue here is to ensure the availability of medical devices or IVDMDs that have not met the requirements of the regulations, on the basis of an established and proven favourable benefit/risk ratio for the patient(s), first and foremost in terms of safety of use; information on these procedures will be provided, including notices to applicants on the Agency's website, during 2024;
- one-off regulatory support for the transitional phase between the old provisions stemming from the now repealed directives and the new regulations.

All of these activities are taking place in a European environment, which involves exchanges and sharing of information on these various subjects with all the competent authorities and the European Commission.

For more information about MDs and IVDMDs:
https://ansm.sante.fr/qui-sommes-nous/nos-missions/assurer-la-securite-des-produits-de-sante/p/surveiller-les-dispositifs-medicaux-et-autres-produits#title

SURVEILLANCE OF INCIDENTS AND RISKS OF INCIDENTS

Nidek and Staar intraocular lenses: what to do about the risk of ocular hypertonia

ANSM has been informed of a quality defect affecting certain batches of preloaded intraocular lenses surgically implanted in the eye during cataract operations. These lenses, manufactured by Nidek Co Ltd (Eyecee One model) and Staar Surgical Japan (KS-SP model), may be the cause of ocular hypertonia. Batches of lenses for these two models began to be used in France after 10 December 2021.
Nidek and Staar have recalled all the lenses concerned from implant centres in France. They are therefore no longer available or used on the French market.

To monitor the risk of hypertonia in the patients concerned, ANSM, in conjunction with the French Ophthalmological Society (Société française d'ophtalmologie – SFO) and the French Glaucoma Society (Société française du glaucome – SFG), has drawn up recommendations for patients, surgeons and ophthalmologists in the implant centres concerned. These recommendations were published on the ANSM website on 6 October 2023 after discussions with patient associations.

In this communication, ANSM asked implanting centres to plan a follow-up visit for all patients fitted with implants, and subsequently monitor them on an annual basis.

ANSM has also asked them and their patients to report any adverse effects reported following the implantation of these lenses. Since the publication went online, there has been no significant increase in the number of reports of adverse reactions with these lenses.

Find out more: https://ansm.sante.fr/actualites/lentilles-intraoculaires-nidek-et-staar-conduite-a-tenir-face-au-risque-dhypertonie-oculaire

Masks equipped with magnets for ventilation equipment: risk of interference with implanted medical devices

At the end of 2022, ANSM was informed, firstly by Philips and then a few months later by the manufacturers Dräger and Resmed, of a risk of electromagnetic interference between masks with magnets for ventilation devices (continuous positive airway pressure or CPAP devices) and implanted medical devices made of metal (e.g. pacemakers). Such interference might occur when patients themselves or members of their household are equipped with metal implanted devices and are in the vicinity of these masks containing magnets (at a distance of less than 15 cm). This interference could cause these implanted devices to malfunction.

Patients using these masks with magnets from these three manufacturers were informed by their home health care providers (HHCPs) about the implanted medical devices concerned and what they should do.

Any patients who are personally fitted with metallic implanted medical devices that are contraindicated with their magnetic masks, or are in close contact with people fitted with such devices, have been invited by ANSM to contact their home health care providers (HHCPs) in order to discuss alternatives and have their masks replaced by a non-magnetic model, and to contact their doctor to determine what action to take pending the replacement.

Find out more: https://ansm.sante.fr/actualites/masques-avec-aimants-philips-pour-appareils-de-ventilation-contre-lapnee-du-sommeil-risque-dinterferences-avec-des-dispositifs-medicaux-implantes

Accompanying safety information for pacemakers and implantable defibrillators

In 2023, ANSM provided safety information about models of implantable pacemakers and implantable defibrillators manufactured by Abbott, Microport, Medtronic and Boston Scientific, in order to inform healthcare professionals about what to do with implanted patients. This safety information gave rise to

discussions with the Association of Wearers of Electric Cardiac Prostheses (Association des Porteurs de Prothèses Électriques Cardiaques – APODEC) and with the French Cardiology Society (Société Française de Cardiologie – SFC) and its Rythmology and Pacemaker Group. These communications also led to the dissemination of an information letter to patients.

Specific conditions set by ANSM for the marketing, wholesale distribution and use of Fresenius Exelia infusion systems

Persistent multifactoral malfunctions observed in Exelia infusion systems, manufactured and marketed by Fresenius, prompted ANSM to take a public health decision on 10/07/2023 setting specific conditions for the marketing, wholesale distribution and use of these devices.
Exelia infusion systems include syringe pumps (Exelia SP) and infusion pumps (Exelia VP), in addition to pump and syringe pump management units (Exelia Combox and Exelia Therapy Manager). These medical devices enable the administration of injectable medicines to hospitalised patients, particularly those in intensive care. These patients may not survive without these “critical medicines”. In some cases, disturbances during infusion may cause treatment to be interrupted, with potentially serious clinical consequences depending on the type of medicinal product infused (e.g. catecholamines).
Since 2020, Fresenius had issued 11 safety notices relating to malfunctions in its infusion systems, with different types of consequences (stoppage of infusion, stoppage of line relays, inability to start the pump or infusion, etc.). These malfunctions, which have interrupted or are likely to interrupt treatment, represent a loss of opportunity for the patient. They are also a source of stress for healthcare professionals, which may impact patient care. The series of corrective solutions implemented by Fresenius had failed to ensure a sufficient level of security for its devices.
After several discussions with users and learned societies (French Anaesthesia and Resuscitation Society – SFAR and the French-Language Resuscitation Society – SRLF) to determine the conditions to ensure continuity of care within hospital departments, ANSM imposed specific conditions for the marketing and use of Exelia infusion systems marketed in 2023, for a period of 12 months. If, at the end of this 12-month period, Fresenius should fail to demonstrate that its product complies with the applicable regulations, its marketing, importation, wholesale distribution, holding for sale or free distribution, commissioning and use will be suspended until compliance is established.
Therefore, from the roll-out of the next software version (1.2.1) of the device in July 2023 and for a period of at least six months, ANSM has asked Fresenius to collect and evaluate the data from all voluntary user healthcare institutions, according to an evaluation plan implemented by Fresenius, and then to forward its analysis to ANSM. At the end of this period, the available data will be studied by ANSM to determine what action should be taken.

Find out more: https://ansm.sante.fr/actualites/lansm-fixe-des-conditions-particulieres-de-mise-sur-le-marche-de-distribution-en-gros-et-dutilisation-des-systemes-de-perfusion-exelia-de-la-societe-fresenius

ANSM suspends the importation, marketing, distribution, advertising and use of medical devices manufactured by BioIntegral Surgical

In April 2022, following the identification of a potential risk of contamination of these medical devices by *Mycobacterium chelonae* , which could cause endocarditis in implanted patients, the Canadian company BioIntegral Surgical (BIS) quarantined all its heart valves and biological valve conduits of porcine origin.
ANSM asked for the devices to be quarantined immediately in all French healthcare institutions that use them, and drew up recommendations for use by healthcare institutions in the management of implanted patients, outlining what to do in the event of suspected endocarditis.
In June 2023, these recommendations were updated in conjunction with the institutions concerned (the French Ministry of Health, the National Reference Centre for Mycobacteria and Mycobacterial Resistance to Anti-Tuberculosis Drugs (CNR-MyRMA), the French Public Health Agency (Santé publique France), the New Aquitaine Regional Health Agency (Agence régionale de santé) and the New Aquitaine Support Centre for the Prevention of Healthcare-Associated Infections (Centre d’appui pour la prévention des infections associées aux soins), as well as two learned societies for thoracic and cardiovascular surgery.
At the same time, ANSM continued its investigations. In conjunction with its German counterpart (BfArm), ANSM, in agreement with BIS, commissioned coordinated analyses by the German and French

Mycobacteria Reference centres (CNR), which showed that 11 of the 12 devices tested were positive for *Mycobacterium chelonae*. Even though the cultures were negative (no bacterial growth), the risk of contamination could not be ruled out, according to the French-Language Infectious Pathology Society (Société de pathologie infectieuse de langue française – SPILF) and the Dutch Society of Medical Microbiology. In addition, a market surveillance survey was carried out among eight competing manufacturers, two of whom used porcine tissues from the same source. No mycobacteria were observed on any of the eight devices tested by CNR-MyRMA. ANSM also conducted a survey of all implanting centres, via the regional medical device vigilance and reagent vigilance coordinators, in order to gather data on the clinical status of patients implanted with BIS-validated bioconduits (n=372, 96% response rate), for the period between 2015 and 14 April 2022. A total of one non-severe case of endocarditis linked to *Mycobacterium chelonae* was reported in France between 2015 and 2022. As of 1st July 2023, no new cases of *Mycobacterium chelonae* endocarditis had been reported in France.

As a safety measure and to prevent any return of these products to the French market following the lifting of the quarantine by Italy, ANSM issued a public health decision on 2 August 2023, suspending the importation, marketing, distribution, advertising and use of aortic conduits (NRAC), pulmonary conduits (NRPC and NRIP), mitral valves (NRM), aortic valves (NRA) and pericardial patches (NRPP) manufactured by BIS until they are brought into compliance with the provisions applicable to them.

Find out more: https://ansm.sante.fr/actualites/lansm-suspend-limportation-la-mise-sur-le-marche-la-distribution-la-publicite-et-lutilisation-des-dispositifs-medicaux-fabriques-par-la-societe-biointegral-surgical
https://ansm.sante.fr/actualites/lansm-suspend-limportation-la-mise-sur-le-marche-la-distribution-la-publicite-et-lutilisation-des-dispositifs-medicaux-fabriques-par-la-societe-biointegral-surgical

Other highlights

- **Philips ventilation devices: ANSM takes legal action**
  https://ansm.sante.fr/actualites/appareils-de-ventilation-philips-lansm-saisit-la-justice
- **Philips DreamStation 2 PPC: watch out for any signs of overheating**
  https://ansm.sante.fr/actualites/ppc-dreamstation-2-philips-surveiller-tout-signe-de-surchauffe
- **Dräger Carina ventilators must no longer be used in paediatrics**
  https://ansm.sante.fr/actualites/les-ventilateurs-drager-carina-ne-doivent-plus-etre-utilises-en-pediatrie
- **ANSM is asking manufacturers of medical devices who issue a safety advisory to include the barcode of the devices concerned**
  https://ansm.sante.fr/actualites/lansm-demande-aux-fabricants-de-dispositifs-medicaux-qui-envoient-un-avis-de-securite-dy-apposer-le-code-barres-des-dispositifs-concernes

All our statistical data on medical device vigilance and reagent vigilance can be found in Appendix 6, page 144.

For more information about medical device vigilance and reagent vigilance:
https://ansm.sante.fr/qui-sommes-nous/nos-missions/assurer-la-securite-des-produits-de-sante/p/organiser-les-vigilances#title

AVAILABILITY OF MEDICAL DEVICES AND IN VITRO DIAGNOSTIC MEDICAL DEVICES

Pressures on the supply of trisomy 21 screening tests

In August 2023, ANSM was informed by the distributor PerkinElmer France of a supply shortage of reagents for the dosage of free beta HCG used for the prenatal screening of trisomy 21 in the AutoDelfia, Delfia Xpress and Delfia manual/VICTOR automated systems manufactured by the Finnish company PerkinElmer/Wallac Oy.

The Finnish company PerkinElmer/Wallac Oy took steps to ensure that the pressures did not impact the performance of screening tests conducted in France: a delivery quota was introduced and users were informed that the AutoDELFIA Free hCGß and AutoDELFIA hAFP/Free hCGβ Dual reagent kits temporarily had only one vial of tracer instead of two, with the quantity being sufficient to perform the required tests. The company issued instructions to users on how to optimise the use of the bottle.

At the same time, in conjunction with the French Ministry of Health and Prevention and the Biomedicine Agency (Agence de Biomédecine), ANSM has been closely monitoring developments in the situation in order to reduce the potential impact. In this context, it has been striving to find alternatives in order to alleviate the pressures and guarantee access to screening for all pregnant women in France.

Normal availability has been effective since 15 November 2023.

Find out more: https://ansm.sante.fr/actualites/tensions-dapprovisionnement-en-tests-de-depistage-de-la-trisomie-21

Supply shortage of HLS, HIT and PLS extracorporeal circulation circuits at Maquet cardiopulmonary GmbH (MCP) / Getinge

Following a suspension of the CE certificate on 1st March 2023 by the notified body for the manufacturer MCP due to non-conformities linked to packaging, the circuits of three commercial ranges – “HLS”, “HIT” and “PLS” – were no longer covered by a CE certificate enabling them to be marketed.
They are respectively used with the MAQUET CARDIOHELP and ROTAFLOW consoles, for cardiac and/or pulmonary assistance; these consumables are captive to the dedicated consoles. Given the number of Maquet consoles involved, this situation meant that alternative solutions could not be rolled out to cover the market needs.

This situation, affecting all European Union member states, has been discussed with the relevant authorities in other countries and with the European Commission.

In March 2023, considering that the benefit linked to the use of the medical devices affected by the suspension of CE certification remained greater than the risk induced by their possible unavailability, ANSM authorised the marketing of these devices in France under a derogation, for a six-month period, subject to compliance with certain conditions, pursuant to Article 59.1 of Regulation (EU) 2017/745.[30] Other competent authorities have also granted a derogation on their territory.

[30] **Article 59.1 of Regulation (EU) 2017/745:**
By way of derogation from Article 52, any competent authority may authorise, on a duly justified request, the placing on the market or putting into service within the territory of the Member State concerned, of a specific device for which the procedures referred to in that Article have not been carried out but use of which is in the interest of public health or patient safety or health.

At the same time, a European Union-wide derogation was adopted by the European Commission on 31/03/2023, in application of Article 59.31,[31] enabling HLS, HIT and PLS circuits to be placed on the European market by the manufacturer MCP, subject to certain conditions being met.
Find out more: https://ansm.sante.fr/informations-de-securite/circuit-ou-pack-pour-ecmo-packs-hls-et-pls-maquet-getinge

Other highlights

- **Rüsch endotracheal intubation probes from Teleflex following a major batch recall:** https://ansm.sante.fr/disponibilites-des-produits-de-sante/dispositifs-medicaux/sonde-endotracheale-rusch-plusieurs-references-teleflex
- **Swan-Ganz catheter for measuring continuous cardiac output by thermodilution, with no satisfactory alternative solution available**
  https://ansm.sante.fr/disponibilites-des-produits-de-sante/dispositifs-medicaux/catheter-de-mesure-du-debit-cardiaque-continu-par-thermodilution-swan-ganz-catheter-cco-svo2-cedv-et-catheter-cco-svo2-cedv-vip-edwards-lifesciences-sas
- **Integra neurosurgical devices**
  Linkhttps://ansm.sante.fr/disponibilites-des-produits-de-sante/dispositifs-medicaux/sondes-licox-catheter-neuroballoon-valve-osv-ii-integra-neurosciences-implants
- **Medtronic temperature sensors not RoHS compliant**
  Linkhttps://ansm.sante.fr/disponibilites-des-produits-de-sante/dispositifs-medicaux/sonde-de-temperature-a-usage-general-et-stethoscope-oesophagien-avec-capteur-de-temperature-mon-a-therm-medtronic
- **MedComp/Hemotech paediatric haemodialysis catheters**
  https://ansm.sante.fr/disponibilites-des-produits-de-sante/dispositifs-medicaux/sonde-de-temperature-a-usage-general-et-stethoscope-oesophagien-avec-capteur-de-temperature-mon-a-therm-medtronic
- **Belzer storage solution**
  https://ansm.sante.fr/disponibilites-des-produits-de-sante/dispositifs-medicaux/belzer-mps-uw-machine-perfusion-solution-bridge-to-life-europe-ltd
  https://ansm.sante.fr/informations-de-securite/dispositif-de-transport-ou-conservation-dorganes-belzer-mps-uw-machine-perfusion-solution-1l-belzer-uw-cold-storage-solutionl-university-of-wisconsin-solution-1l-storeprotect-1l-carnamedica-1

[31] **Article 59(3) of Regulation (EU) 2017/745**: the Commission, in exceptional cases relating to public health or patient safety or health, may, by means of implementing acts, extend for a limited period of time the validity of an authorisation granted by a Member State in accordance with paragraph 1 of this Article to the territory of the Union and set the conditions under which the device may be placed on the market or put into service.

MARKET CONTROL

Update of the July 2020 market control report on oro-pharyngeal rapid diagnostic tests (RDTs) for group A Streptococcal angina.

At the end of 2022, reagent vigilance incidents were reported concerning oro-pharyngeal RDTs for group A Streptococcus angina. The tests in question gave falsely negative results, with potentially serious clinical consequences. In addition to the investigations conducted during the processing of these reagent vigilance reports, it was decided to update the data in the July 2020 report on oro-pharyngeal RDTs for group A Streptococcus angina. The analytical sensitivity of 19 devices was assessed by the ANSM control laboratories, suggesting that these tests have a similar and consistent analytical sensitivity (detection threshold) of around 1 × 10 5 CFU/test, or even 1 × 10 4 CFU/test for the 5 strains of *Streptococcus pyogenes* tested.

Find out more: https://ansm.sante.fr/uploads/2023/10/16/20231016-controle-du-marche-trod-angine-strep-a-2023.pdf

Decision of 28/02/2023 establishing the quality control procedures in respect of external teletherapy and radiosurgery

On 17 March 2023, the decision of 28/02/2023 setting out the quality control procedures for external radiotherapy and radiosurgery facilities was published on the ANSM website.
This decision is a revision of the decision of 27 July 2007. This revision has enabled the inclusion of all techniques used in radiotherapy today and the adaptation of the tests in the 2007 decision to the linear accelerators currently in service, while ensuring compliance with the regulations in force: in practice, the internal quality control decision and the internal quality control audit decision have been merged, and the external quality control audit has been abolished. A select group of the Standing Scientific Committee on the Quality Control of Medical Devices, dedicated to external radiotherapy facilities, worked on the drafting of this decision. The draft text was put out to public consultation and then submitted to the French Nuclear Safety Authority (Autorité de Sureté Nucléaire – ASN) for its opinion before publication. Its publication is accompanied by an application guide, which was updated on 20 October 2023.

Find out more: https://ansm.sante.fr/actualites/decision-du-28-02-2023-fixant-les-modalites-du-controle-de-qualite-des-installations-de-radiotherapie-externe-et-de-radiochirurgie

New data on breast implants

In January 2023, ANSM published new data on breast implant market surveillance in France.

In particular, ANSM has published a report on medical device vigilance covering the years 2014-2020. The primary objective of this medical device vigilance report is to raise the profile and inform the general public about the medical device safety data reported to ANSM in relation to breast implants, and more specifically to ruptures and shells. An update on reported cases of anaplastic large-cell lymphoma (ALCL) associated with breast implants, is also available on the website. ANSM is also closely monitoring reports of adverse reactions suggestive of ASIA syndrome (autoimmune syndrome of induced adjuvant). According to the medical literature, this syndrome has been described in people fitted with silicone breast implants. The term “breast implant illness” (BII) is sometimes used. It can include a range of symptoms of varying intensity, such as fatigue, memory loss, skin rash or joint pain...

Finally, as part of its monitoring of new breast implants, ANSM has also updated the list of implants marketed in France with their texturisation level, in line with the various standards monitored by ANSM.

Find out more: https://ansm.sante.fr/actualites/lansm-publie-de-nouvelles-donnees-sur-la-surveillance-des-implants-mammaires

Implants for the treatment of urinary incontinence and pelvic organ prolapse

Implantable medical devices for the treatment of urinary incontinence and prolapse, a condition in which organs drop down from their original position, also called “mesh implants”, are manufactured in the form of implantable strips and pelvic reinforcement implants. ANSM has been monitoring these implantable devices for several years: a thematic page describing the monitoring activities carried out by ANSM, European monitoring and key dates in France and abroad is available on the ANSM website. In March 2023, the report on the Review of Vigilance Data between January 2017 and December 2022 for suburethral slings and pelvic reinforcement implants was published online. In May 2023, an update of the market situation with sales data for 2020 and 2021 was published online.
At European level, ANSM has maintained its involvement in a **“task force”**, dedicated to the **procedures for assessing medical device vigilance incidents** linked to the use of these medical devices (a guide for market operators is currently undergoing validation).

ESSURE permanent contraceptive devices

Although the Essure medical device for tubal sterilisation has not been marketed in France since August 2017, ANSM is maintaining the surveillance it had implemented for this device, by monitoring the monthly trend for incidents reported in medical device vigilance. In addition, a thematic page describing the surveillance activities carried out by ANSM in France, and key dates in France and worldwide is available on the ANSM website. In August 2023, the results of medical device vigilance reports received by ANSM between 01/01/2013 and 31/07/23 were published online.
In addition, on 1st April 2023, a national register of practices was opened by the National Professional Council for Gynaecology-Obstetrics and Medical Gynaecology (Conseil national professionnel de gynécologie-obstétrique et de gynécologie médicale – CNP GO-GM) as part of the action plan rolled out by the Ministry of Health and Prevention with all stakeholders.

Other highlights

- **Los Deline body fillers: withdrawal of all products from the market**
  https://ansm.sante.fr/actualites/produits-de-comblement-du-volume-de-corps-los-deline-retrait-du-marche-de-lensemble-des-produits
- **ANSM suspends the installation of medical gas distribution systems by Technique Médicale du Centre (TMC)**
  https://ansm.sante.fr/actualites/lansm-suspend-linstallation-des-systemes-de-distribution-des-gaz-medicaux-de-la-societe-technique-medicale-du-centre-tmc
- **Prion standard protocol:** the transitional period to PSP v.2018 has been extended to 31 December 2026.
  https://ansm.sante.fr/actualites/publication-de-la-nouvelle-version-du-protocole-standard-prion-psp
- **ANSM has requested the recall of “ERG Dencott” disposable scleral electrodes following an unannounced inspection finding**
  https://ansm.sante.fr/informations-de-securite/electrodes-sclerales-pour-electroretinogramme-coques-erg-dencott-dencott-ocellus
- **Market situation for non-hormonal intrauterine devices**
  https://ansm.sante.fr/uploads/2023/07/17/20230717-controle-marche-diu-2021.pdf
- **Digitisation of the process for receiving advertising requests**
  https://www.demarches-simplifiees.fr/commencer/ansm-demande-autorisation-prealable-de-publicite
- **Clarification of the documents accompanying hearing aids**
  https://ansm.sante.fr/uploads/2023/02/13/20230213-reco-dm-aides-auditives.pdf

All our statistical data on market control can be found in Appendix 6, page 144.

For more information about market control:
https://ansm.sante.fr/qui-sommes-nous/nos-missions/assurer-la-securite-des-produits-de-sante/p/surveiller-les-dispositifs-medicaux-et-autres-produits#title

SURVEILLANCE OF OTHER HEALTH PRODUCTS

As for medical devices, these products are marketed within a European regulatory framework. This marketing is carried out under the responsibility of the manufacturer or its representative, without prior authorisation, provided that they are not harmful to human health under normal conditions of use and that their composition is mentioned for the purpose of informing consumers.

The regulations applicable to tattooing products are similar to those for cosmetics. They are not subject to prior marketing authorisation. The person in charge of placing the product on the market is responsible for ensuring that the product meets legislative and regulatory requirements and poses no danger to health. Tattoo products are examined by the Council of Europe's Committee of Experts on Cosmetic Products.

Until 31 December 2023, ANSM, together with the French Department for Fair Trading, Consumer Affairs and Fraud Control (Direction générale de la consommation, de la concurrence et de la répression des fraudes – DGCCRF), monitored the market for cosmetics and tattoo products. Since 1st January 2024, the DGCCRF and the French Agency for Food, Environmental, and Occupational Health & Safety (Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail – ANSES) have been responsible for monitoring these products.

Nuud deodorant: the manufacturer withdraws all batches of this deodorant from the market

Users of Nuud deodorant have reported adverse reactions such as painful underarm cysts, sometimes accompanied by infection treated with antibiotics. In most of the reported cases, the cysts disappeared after people stopped using the product or took the prescribed treatment. ANSM conducted investigations. They showed that the dosage form of this deodorant, a predominantly oily ointment, is likely to block underarm pores, with the possibility of microbial superinfection as a result of its occlusive effect. The ingredients in Nuud deodorant are not individually considered to be the cause of the adverse reactions reported.

Consequently, to protect consumers, the manufacturer, in conjunction with ANSM, has decided to withdraw all available batches of the product from the market at the various points of sale and on distributors' premises.

Find out more: https://ansm.sante.fr/actualites/deodorant-nuud-retrait-du-marche-par-le-fabricant-de-lensemble-des-lots-de-ce-deodorant

Cosmetics and tattoo market surveillance missions entrusted to the DGCCRF

Since 1st January 2024, the Department for Fair Trading, Consumer Affairs and Fraud Control (DGCCRF) has been the sole authority responsible for inspecting establishments that manufacture and packaging cosmetic products and tattoos, a task it previously shared with ANSM. As part of the reform, it has also taken over the management of declarations of establishments, which were previously the Agency's responsibility.
The French Agency for Food, Environmental, and Occupational Health & Safety (ANSES) is now responsible for cosmetic product vigilance, tattoo product vigilance and risk assessment.

However, ANSM remains responsible for:

- verifying the compliance with Good Laboratory Practice (GLP) of non-clinical studies on cosmetic and tattoo products and the test facilities that carry them out;
- issuing certificates of conformity with good manufacturing practice for exports of cosmetic and tattoo products outside the European Union;
- issuing authorisations for clinical trials involving cosmetic and tattoo products.

Find out more: https://ansm.sante.fr/actualites/les-missions-de-surveillance-du-marche-des-cosmetiques-confiees-a-la-dgccrf

Other highlights

- **ANSM suspends the marketing of Joëlle Ciocco Paris cosmetic products**
  https://ansm.sante.fr/actualites/lansm-suspend-la-commercialisation-de-produits-cosmetiques-de-la-marque-joelle-ciocco-paris
- **ANSM issues a public health decision concerning Perma Blend tattooing products (permanent make-up)**
  https://ansm.sante.fr/actualites/lansm-prend-une-decision-de-police-sanitaire-concernant-les-produits-de-tatouage-perma-blend-maquillage-permanent

2023 DATA

- **479** cosmetic product vigilance reports processed by ANSM (compared to 280 in 2022), 152 (32%) of which were classified as “serious”. The market withdrawal of the deodorant Nuud contributed significantly to the increase in the number of reports in 2023.

INSPECTION TO ENSURE QUALITY COMPLIANCE

ANSM helps to ensure the quality, safety and availability of health products on the market, through inspections that assess the compliance of operators' practices in the field. These inspections, both announced and unannounced, concern all health products throughout their life cycle. They are carried out in France or abroad, as part of an annual programme or on request. ANSM also manages the authorisations, approvals and declarations of activity required by the regulations. For each of these missions, ANSM is involved at national, European and international levels in order to contribute to the development and definition of regulatory frameworks, share best practices and collaborate in crisis management. It may also initiate administrative, criminal or regulatory proceedings, as well as financial penalties.

For more information about inspection:
https://ansm.sante.fr/qui-sommes-nous/nos-missions/assurer-la-securite-des-produits-de-sante/p/inspecter-les-produits-et-les-pratiques#title

ANSM maintains its commitment to combating the falsification of medicines

On 17 November 2023, ANSM organised a webinar on medicine fraud and falsification for the manufacturers concerned. Over 400 participants attended the seminar, which can be replayed on the ANSM website.
The aim of this seminar was to remind all stakeholders of the importance of close collaboration between the public sector, professional organisations and pharmaceutical companies in order to combat this global scourge effectively.
This webinar covered the following topics:

- the risk of falsified medicines on a global and European scale;
- the legislative, regulatory and criminal context, including reminders of:
    - manufacturers' obligations to report any falsification or suspected falsification of medicinal products to ANSM,
    - the obligation to report any theft of narcotics and psychotropic drugs to the police, ANSM and the regional health agencies (ARS);
- the role of ANSM and the general framework for combating drug trafficking in France;
- a review of inspection discrepancies relating to this topic;
- the means of combating falsification and the Qualified Person's role in preserving the legal medicine distribution chain.

Find out more: https://ansm.sante.fr/evenements/webinaire-dinformation-sur-les-fraudes-et-falsifications-des-medicaments

ANSM in contact with representatives from the advanced therapy medicinal products (ATMP) sector

Established in 2020, the Advanced Therapy Medicinal Products (ATMP) Interface Committee, coordinated by the Inspection Division in partnership with the Europe and Innovation Division, brings ANSM together with representatives of the sector from the academic world, public institutions, start-ups, small businesses and pharmaceutical companies, at meetings held three or four times a year.

The ATMP Committee met four times in 2023, culminating in a seminar attended by some forty participants on 21 December 2023.
This session set out to summarise the issues addressed in 2023 and prepare for the 2024 programme. To this end, the members were assigned to three workshops (one for each theme: Quality/Preclinical/Clinical), each with the following objectives:

- describing the theme and what it covers;
- identifying aspects to be improved and points to be developed;
- proposing opportunities, ideas and/or actions that need to be developed in 2024 or in the years to come.

These activities enabled technical and regulatory advances to be summarised and shared with players in the sector. Through these workshops, we also identified ways to strengthen regulations, along with the need to include other institutions in our discussions and to perpetuate this dialogue and feedback. These issues will be the focus of new initiatives in 2024 designed to support the development of ATMP in France.
Lastly, ANSM also seized this opportunity to continue its efforts to facilitate operational exchanges and encourage the sharing of information between players in the private, public and voluntary sectors.

Changes in the regulations on micro-organisms and toxins

ANSM exercises its authority in the field of micro-organisms and toxins (MOTs) by overseeing the assessment, inspection, monitoring and management of establishments where MOT operations are authorised.

ANSM is also responsible for proposing legislative and regulatory changes to the standards in this field. In particular, under the French Public Health Code, the Agency is responsible for proposing the list of MOTs to which the regulations apply. It also stipulates that the content of the technical documentation on which the application for authorisation is based shall be determined by a decision of the Director General of ANSM.

2023 saw changes in several regulatory frameworks.

The publication of the Order of 26 April 2023 establishing a new list of MOTs marked the end of the work begun in 2019 with the formation of a Scientific Committee and continued with successive consultations of the French High Council for Biotechnology (Haut conseil des biotechnologies), the National Biosafety Advisory Council (Conseil national consultatif pour la Biosécurité), the relevant national reference centres, several ministries and ANSES, whose opinion is required by the Public Health Code. On 29 June 2023, ANSM organised a webinar dedicated to the new list of MOTs, with the participation of the Ministry of Health.

At the same time, four decrees relating to threshold doses and concentrations for toxins, the information stated on authorisations, the special register and the training and professional experience of operators were revised and published in 2023.

All these measures to update the standards were intended to shift the focus of the provisions to the highest-risk activities and to simplify the application of the regulations for operators in the field.

ANSM is participating in the “Mutual Reliance” and “US-FDA Third Country Inspections Recognition” pilot programmes, managed by the European Medicines Agency (EMA)

To promote international collaboration between European inspectorates and those belonging to the PIC/S (Pharmaceutical Inspection Co-operation Scheme), the European Medicines Agency (EMA) has proposed that competent authorities in the European Union take part in a pilot programme designed to assess the impact of using the results of inspections carried out by the regulatory authorities of third countries that are members of the PIC/S in their own territories. This programme sets out to measure the degree of confidence in the verification of compliance with Good Manufacturing Practices (GMP) on manufacturing sites producing medicinal products and active substances, which are located in these countries.
The Inspection Department is participating in the “Mutual Reliance” pilot programme launched by the EMA in October 2022, which will run until December 2024.
In practice, the period of validity of the GMP compliance certificates for these sites may be extended on the basis of a documented assessment of the inspection process implemented by the PIC/S member agencies concerned by this project.

A similar pilot programme concerning the recognition of the results of inspections carried out by the US-FDA on sites manufacturing chemical medicinal products and their raw materials located in countries outside the European Union has been launched by the EMA, in which ANSM is also participating.

ANSM's continued involvement in the Global Action Plan for Poliovirus Containment (GAPIV)

Since 2018, ANSM has been providing technical support to the French Ministry of Health (DGS) as part of the global polio eradication initiative coordinated by the World Health Organization (WHO), on the implementation of the Global Action Plan for Poliovirus Containment.
This plan aims to ensure the perfectly safe containment of all poliovirus stockpiles in order to minimise the risk of reintroducing these viruses into the population following a global interruption of wild poliovirus and vaccine-derived poliovirus transmission.
In 2023, ANSM inspectors continued their audits of essential establishments authorised to hold stocks of type-2 poliovirus: three initial audits and one follow-up audit were carried out. As a result of these audits, the WHO issued three provisional containment certificates – the first in Europe.
In collaboration with the DGS, ANSM also contributed, through support meetings and the verification and compilation of submission dossiers, to the granting of five new certificates of participation for the last establishments identified as holding type-2 poliovirus stocks.
Finally, in line with the WHO timetable, 2023 marked the launch of activities relating to type-1 and type-3 polioviruses. ANSM has helped to identify establishments possessing this type of equipment and is working with the DGS to help them participate in the certification process.

Find out more:

- https://iris.who.int/bitstream/handle/10665/350556/9789240035300-fre.pdf
- https://polioeradication.org/wp-content/uploads/2024/03/Containment-table-March-2024-scaled.jpg

Another highlight

- **Recall of "Dencott ERG Shell" scleral electrodes for electroretinograms following an inspection**
  https://ansm.sante.fr/informations-de-securite/electrodes-sclerales-pour-electroretinogramme-coques-erg-dencott-dencott-ocellus

2023 DATA

	2019	2020	2021	2022	2023
Inspections	660	441	623	562	**553**
• unannounced in France	10%	3%	3%	8%	**9%**
• conducted abroad	6%	2%	2%	4%	**6%**
Injunctions	50	40	33	29	**21**
Animal health decisions relating to inspection activities	8	3	2	5	**2**
Cases transmitted to judicial authorities	12	2	2	1	**1**

All our inspection and administrative management data for the various domains can be found in Appendix 7, page 146.

LABORATORY-BASED QUALITY CONTROL OF HEALTHCARE PRODUCTS

For the purposes of providing independent technical and scientific expert assessments, ANSM has its own testing laboratories in which it carries out a variety of tests (biochemical, immunological, physicochemical, biological, microbiological, immuno-haematological) on all healthcare products (already on the market or awaiting authorisation) to ensure their quality and safety of use.

These checks are carried out in accordance with the criteria and analysis methods of the Pharmacopoeia. This regulatory document defines the purity criteria for raw materials or preparations used in the manufacture of medicinal products (for human and veterinary use), and even their containers, as well as the analysis methods used to ensure their control. The Pharmacopoeia includes the texts of the European Pharmacopoeia, as well as those of the French Pharmacopoeia.

European collaborative study on medicines packaged in glass ampoules

ANSM took part in market surveillance organised at European level (by the European Directorate for the Quality of Medicines and Healthcare – EDQM), following evidence of the presence of small fragments of glass after opening medicinal products presented in glass ampoules for oral or parenteral use. 138 samples (2,190 ampoules) were analysed by nine Official Medicines Control Laboratories (OMCLs). The 28 products tested by ANSM were selected mainly on the basis of recent Quality Defect reports and sales volumes. The tests focused on searching for visible and invisible particles in the solution after opening (according to the methods of the European Pharmacopoeia, Ph. Eur.) as well as looking for glass particles on the operator's hands, the ampoule itself or on the work surface. Overall, the formation of glass particles was observed in a high percentage of ampoules tested (31% of all types) and 24% of filtered solutions revealed the presence of particles generated when the ampoule was opened. Pointed and sharp (potentially dangerous) openings were also observed in 32% of ampoules. This extensive European survey showed that this issue affects many different manufacturers and types of ampoules to varying degrees. Letters were sent to MA holders asking them to carry out a risk analysis and define the actions to be taken to ensure the safe use of these products. In addition, a number of actions are planned at European level, especially in order to inform the Ph. Eur. with a view to the possible revision of the general chapter concerned, as well as users (hospital practitioners, nurses, patients, etc.).

Survey of plant-based oral health products for weight-loss purposes

As part of the 2023 market surveillance programme, and following the in-house development of a molecular biology methodology (DNA research and amplification) for identifying Ephedra, a regulated plant, a survey of herbal health products for weight loss was organised. It should be noted that this validated methodology will soon be extended to other regulated plants that may be subject to adulteration. These products have been selected for their indications in weight loss in the broadest sense (treatment of constipation, digestive disorders, urinary or digestive elimination, adjuvants for slimming/weight-loss diets, etc.). Only plant-based products (powder, whole or fragmented) were considered, not extracts. Twelve proprietary medicinal products with marketing authorisation and 10 products in the oral medical device category were included in the study. For all these products, the following analysis strategy was adopted: control of labelling (for medicines only), microbiological quality control and search for chemical and botanical adulterants. The results of this study are expected in H2 2024.

For more information about the laboratory-based quality control of health products:
https://ansm.sante.fr/qui-sommes-nous/nos-missions/assurer-la-securite-des-produits-de-sante/p/controler-la-qualite-des-produits#title

All our data on the laboratory-based quality control of health products can be found in Appendix 8, page 152.

Participation in the development of standards relating to the quality of medicines and their components within the framework of the French and European pharmacopoeias

ANSM participates in the development of quality standards within the framework of the French and European Pharmacopoeias.
It sits on the European Pharmacopoeia committees, monitors their work and can conduct analyses in its control laboratory. It is responsible for transmitting French commentaries and their analyses, with the support of three French pharmacopoeia committees, in the framework of public enquiries into monographs and chapters of the pharmacopoeia. For the patient, these specifications are one of the fundamental guarantees of the safe use of the medicine.

Pharmacopoeia		2019	2020	2021	2022	2023
Studies for the French Pharmacopoeia		65	66	25	27	38
Studies for the European Pharmacopoeia	Pharmeuropa[32] COM - other	456	424	384	415	418
	European surveys	42	52	39	33	70
Total		563	542	448	475	526

Work on the cannabis (flower) monograph has continued and will lead to its publication in the European Pharmacopoeia in 2024. This monograph becomes the binding reference for all cannabis-based medicinal products and preparations.
Find out more: https://www.edqm.eu/fr/-/ph.-eur.-pre-publishes-cannabis-flower-monograph-on-the-edqm-website

[32] Pharmeuropa: public enquiry into the monographs and chapters of the Ph. Eur, 4 times/year

Facilitating patient access to innovative treatments

3

FOCUS ON...ANSM'S EUROPEAN STRATEGY

ANSM continues to strengthen its role within European bodies in all matters relating to health products: medicinal products, medical devices and in vitro diagnostic medical devices. Working as a team with the 27 Member States, the Agency is maintaining its commitment by sharing its expertise with its European neighbours. Vincent Gazin, Deputy Director of the Europe and Innovation Division, and Thierry Sirdey, Director of Medical Devices and In Vitro Diagnostic Medical Devices, explain the ANSM's European strategy.

Which European bodies are responsible for medicines and health products, and what role does ANSM play in them?

Vincent Gazin: For medicines, the European Medicines Agency (EMA) is the equivalent, at European level, of the national regulatory agencies in the sense that its missions are described in legislative texts and the decisions it generates apply to the whole of Europe. One major difference, however, concerns the provision of expertise: for this activity, the EMA collaborates with the medicine regulatory agencies of the 27 European Union Member States, and with those of the European Economic Area (EEA), which also includes Iceland, Liechtenstein and Norway. Working closely with this network of agencies, the EMA evaluates and ensures the safety of medicines products eligible for centralised procedures. In addition, the informal Heads of Medicines Agencies (HMA) network brings together the heads of the national medicine regulatory agencies. This network coordinates the regulatory and strategic activities of national agencies and works closely with the EMA to harmonise processes and ensure the consistency of rules throughout Europe. This is a decentralised network, and certain procedures depend on the HMA, via the CMDh committee. The EMA and the HMA are complementary and form the European Medicines Regulatory Network (EMRN). ANSM is an active member of both networks. Its management takes part in the governance committees and a large number of staff members participate in the groups and committees, giving the Agency a say in the decisions and votes taken by the collegial bodies.[33]

Thierry Sirdey: Medical devices (MDs) and in vitro diagnostic medical devices (IVDMDs) are regulated by other collegial bodies in Europe: the Medical Device Coordination Group (MDCG) and the Competent Authorities for Medical Devices (CAMD). The MDCG is a regulatory committee chaired by the European Commission. It plays a central role in consensus-building activities undertaken by the 27 Member States on the implementation of regulations relating to DM/DIV. Thirteen technical working groups are attached to it. The CAMD network is an informal, voluntary network of competent national authorities in the EU. It aims to strengthen inter-agency cooperation with a view to improving the surveillance and safety of medical devices. By sharing information and best practices, CAMD is helping to improve harmonisation and coordination between Member States. Effective collaboration with the European Commission and the MDCG helps to coordinate work and support discussions and decisions. In 2023, ANSM was actively in the CAMD's governance.[34]

This undoubtedly requires a great deal of energy and resources, so why is it important for ANSM to be involved in European bodies?

T.S.: In the case of MDs/IVDMDs, the regulations governing the marketing of devices are different from those governing medicinal products. This is a European regulation, based on Regulations 2017/745 and 746, which applies in the same manner and is mandatory in all 27 Member States for all DM and IVDMDs. ANSM actively participates in the MDCG, the governance body, and its technical groups. This network enables the Agency to influence decisions taken at European level, always in the interests of patients and healthcare professionals. The MDCG helps to maintain consistency between the actions taken on IVDs and IVDMDs at European level. ANSM continues to take the lead in revising the regulatory texts relating to the clinical evaluation and marketing conditions for MDs/IVDMDs, a process which

[33] Also read: “Participation in international bodies” https://ansm.sante.fr/qui-sommes-nous/nos-missions/informer-echanger-avec-notre-environnement/p/participer-aux-instances-internationales#title
[34] Also read: “ANSM’s active involvement in CAMD”, page 32.

began in 2010. The results of these consultations and assessments led to the proposal of two new regulations in 2012, which were adopted in 2017. Since their publication, France has continued to play a leading role in developing and strengthening these common regulations, which guarantee the safety and effectiveness of authorised devices.

V.G.: Over the last 30 years, the regulation of medicines has increasingly been carried out at European level. It is at this supranational level that the marketing of innovative medicines is authorised or refused. European decisions are the fruit of consensus reached within the committees, which are collegiate bodies, ensuring a certain robustness of decisions. As in the case of MDs/IVDMDs, working with other European countries facilitates the optimisation and harmonisation of practices. Operating at the European level enables the principle of “worksharing” to be put into practice, with agencies pooling their expertise.

What are ANSM's ambitions/strategies at European level?

V.G.: The European strategy extends our French ministerial plans on to the European level and reflects our national medical and pharmaceutical expertise. One aim is to use local experience to inform high-level regulatory decisions. This means listening to healthcare professionals and patients and supporting projects through to European level. Promoting our expertise by providing support for project leaders, as with our scientific opinions, increases the ANSM's credibility and power in European decision-making, for medicines as well as MDs/IVDMDs, thereby fostering a virtuous process from experience in the field through to decision-making.

Does ANSM differ from other national agencies in certain respects?

V.G.: ANSM has a robust, long-established pharmacovigilance network, with its 30 regional centres, from which our European neighbours can benefit. As far as early access to innovative treatments is concerned, French regulations authorise exceptional access, thereby helping to organise follow-up. This generates useful real-life data for new indications and enables patients to access treatments. European collaboration is being further strengthened, particularly on clinical trials with the new European regulations, and on simultaneous national scientific advice (SNSA), in which the ANSM continues to play a major role by sharing its expertise.

T.S.: ANSM has adopted a strategic position in the MDCG coordination group, as well as in its 13 working groups on new technologies, software, clinical investigations, and so on. For example, the Agency is working with its counterparts to improve the clinical evaluation of medical devices by encouraging manufacturers to submit better quality dossiers. We are also trying to take the lead in networks such as CAMD, in order to provide forums to enrich discussions between countries with a view to harmonising decisions taken in the management of MDs/IVDMDs. Finally, and still within these coordination groups, ANSM also plays an important role in stockouts of MDs/IVDMDs. In fact, the Agency was one of the countries in 2023 that had developed the most advanced MD stockout management and monitoring systems among all the various Member States. In this context, we have managed to obtain support for the passage of a provision in a proposal for a regulation, currently being voted on by the European Parliament, which obliges manufacturers to notify their competent authority as soon as they become aware of a disruption to supplies of one of their MDs/IVDMDs that may have an impact on patients.

EARLY ACCESS TO HEALTH PRODUCTS

To offer patients rapid access to innovations representing a major therapeutic advance or meeting an unmet medical need, various procedures enable ANSM to supervise and support early, safe and fair access to innovative products.

In 2023, ANSM coordinated 85 scientific opinions within the Scientific Advice Working Party (SAWP) of the European Medicines Agency (EMA).
In response to the increase in the number of advanced therapy medicinal products, the ANSM's Innovation and Referral Service (Guichet innovation et orientation – GIO) has also stepped up its support for research and provision of scientific advice and regulatory support.

For more information about early access to health products:
https://ansm.sante.fr/qui-sommes-nous/nos-missions/faciliter-lacces-a-linnovation-therapeutique/p

THE INNOVATION AND REFERRAL SERVICE

The Innovation and Referral Service's role vis-à-vis advanced therapy medicinal products

With the number of advanced therapy medicinal products (ATMPs) under development rising steadily, and the EMA expecting to be required to assess a significant number of centralised marketing authorisation applications for this type of medicinal product by 2025, the Innovation and Referral Service is confirming its role and expertise in support for translational and clinical research targeting start-ups and the academic centres involved in France. The number of scientific opinions on these topics increased by almost 50% in 2023. The Innovation and Referral Service also provides regulatory support for this type of product and acts as the competent authority for the use of GMOs on research sites (hospitals, research centres, etc.).

ANSM's participation in the Committee for Advanced Therapy Medicinal Products (CAT) and the Scientific Advice Working Party (SAWP)

The European Medicines Agency (EMA), drawing on the expertise of the Committee for Advanced Therapies (CAT), has recommended the approval of the first gene therapy medicinal product using the new CRISPR/Cas9 ex vivogene-editing technology. Casgevy (exagamglogene autotemcel) is indicated for the treatment of transfusion-dependent beta-thalassaemia and severe sickle cell disease in patients aged 12 and over for whom haematopoietic stem cell transplantation is appropriate but no donor is available.

ANSM has coordinated 85 scientific opinions for the EMA's Scientific Advice Working Party (SAWP), a multidisciplinary EMA group that coordinates scientific advice and assistance on study protocols for stakeholders. It is composed of representatives from the Committee for Orphan Medicinal Products (COMP), the Paediatric Committee (PDCO), the Committee for Advanced Therapies (CAT) and a member of the Pharmacovigilance Risk Assessment Committee (PRAC). A fair representation of areas of expertise such as non-clinical safety, pharmacokinetics, methodology and statistics, therapeutic fields such as cardiology, oncology, diabetes, neurodegenerative disorders and infectious diseases, is ensured amongst the members.

Find out more:
- https://www.ema.europa.eu/en/scientific-advice-working-party
- https://www.ema.europa.eu/en/committees/committee-advanced-therapies-cat

2023 DATA

- From January to December 2023, **377** requests for regulatory and scientific support were received via the Innovation and Referral Service.
- **35%** of the requests were for scientific opinions, and **65%** were for regulatory guidance.
- In **73%** of cases, the scientific opinions and regulatory guidance were issued for start-ups and micro-companies.
- **27%** were requests from large companies, mainly in relation to complex pre-submissions. This share is increasing.
- **44%** of requests related to medical devices (a quarter of which concerned digital MDs), primarily MD classification/qualification requests, but also requests for regulatory guidance. Requests for scientific opinions were also submitted for MDs, but to a lesser degree compared to medicines.
- 36% of requests concerned medicinal products, primarily requests for scientific opinions (36 of which related to advanced therapy medicinal products, up 50% in one year).
- Lastly, **20%** of requests concerned issues relating to the implementation of research in France (for example, when the research does not relate directly to the health product but concerns activities involving biological and toxic risks falling within ANSM's remit).

Number of requests for regulatory and scientific support received via the Innovation and Referral Service

2020 (September to December)	2021	2022	2023
124	277	337	**377**

European scientific opinions issued for medicines

	2019	2020	2021	2022	2023
European opinions issued by the EMA	674	766	853	833	**717**
number of these opinions coordinated by ANSM	76	66	73	101	**85**
	11.3%	8.6%	8.6%	12.12%	**11.9%**

For more information about the Innovation and Referral Service:
https://ansm.sante.fr/vos-demarches/industriel/guichet-innovation-et-orientation-gio

EXCEPTIONAL ACCESS DECISIONS: COMPASSIONATE ACCESS, EARLY ACCESS AND THE COMPASSIONATE PRESCRIPTION FRAMEWORK

Authorisation for early access to medicines: a positive two-year review

Introduced on 1 July 2021, early access authorisation (autorisation d'accès précoce – AAP) gives patients rapidly reimbursed access to medicines that are not yet authorised or covered under ordinary law. These early access authorisations are granted by the French National Authority for Health (HAS), after ANSM has given its assent on the presumed efficacy and safety of the products or a marketing authorisation. They concern presumably innovative medicines that meet unmet therapeutic needs and are intended for patients suffering from serious, rare or disabling diseases whose treatment cannot be postponed.

The early access authorisation scheme, from which more than 100,000 patients have already benefited, is in demand from manufacturers, with the number of applications submitted to the HAS increasing every quarter. This increase is mainly due to post-authorisation applications.

For ANSM, a drop of around 15% in pre-authorisation applications has been observed. In 2023, ANSM issued its opinions within an average of 60 days, in line with its commitment to the HAS.
In the context of pre-MA early access authorisations, of the 65 opinions issued by ANSM since July 2021, 74% of applications have also received a positive opinion from the HAS, enabling innovative products to benefit from this exemption mechanism.

As part of the development of these proprietary medicinal products, it should be noted that following early access, 79% of applications received marketing authorisation.

It has also been found that early access authorisation enables patients to receive coverage for treatment on average nine months before it is included on the reimbursement lists.

Find out more: https://ansm.sante.fr/actualites/autorisation-dacces-precoce-aux-medicaments-un-bilan-a-deux-ans-positif

Compassionate access: a new version of e-saturne

A new version of the e-saturne application was published on 18 April 2023. With enhanced security, broader access and a revamped graphical interface, the application has been adapted to simplify its use and make it easier for healthcare professionals to apply for compassionate access authorisation (autorisation d'accès compassionnel – AAC). This new version also enables better management of the tool and improved monitoring of indicators.

These changes resulted from comments and requests reported directly by e-saturne users.

Here are the main new features:

- simplified access thanks to the e-CPS login system. The e-CPS login system also improves security and allows pharmacy interns to log in;
- a quicker and easier search function to facilitate the finding of information on products in the exceptional access database, such as brand name, INN, indication, etc.;
- notification of healthcare professionals by email to provide notice of renewals of compassionate access authorisations;
- alert issued during applications for compassionate access authorisation indicating that a product has been granted early access authorisation or marketing authorisation (MA), directly via e-saturne;
- rapid identification of the actions to be taken by professionals by means of the folders shown on the home page ("tray"-based system): applications to be processed, renewed, in draft form or being processed by the ANSM, in addition to responses to be provided, etc.

Various user support tools (guides and videos) have been provided for pharmacists and hospital prescribers.

Since the 2021 reform, the number of compassionate access authorisation applications seems to have stabilised, with a relative drop of around 10% in 2023, probably linked to the granting of marketing authorisations for COVID-19 products which were in high demand under the compassionate access authorisation scheme.
The number of proprietary medicinal products made available on a compassionate access basis has remained relatively constant, with 373 proprietary medicinal products subject to compassionate access authorisations in 2023.
In the new version of e-saturne, thanks to the automated processing of applications meeting the granting criteria set out in the standard, 86% of authorisations were issued immediately, thereby facilitating the work of prescribers and pharmacists in hospital pharmacies (pharmacies à usage intérieur – PUI).
For the other applications that did not meet these criteria, i.e. almost 9,000 compassionate access authorisation applications in 2023, a decision was made within an average of three days.

For more information and to consult the tools: https://ansm.sante.fr/actualites/acces-compassionnel-une-nouvelle-version-de-saturne-lapplication-de-demande-dautorisation-pour-les-professionnels-arrive-courant-avril

Early access for Jemperli in endometrial cancer

Since 23 October 2023, the medicinal product Jemperli (dostarlimab) has been available on an early access basis for women with newly diagnosed or recurrent advanced endometrial cancer.
This release follows the decision by the HAS to grant early access authorisation on 27 September for a period of 12 months, following a positive opinion from ANSM, which was in favour of a strong presumption of efficacy and safety for Jemperli in this indication.

Specifically, Jemperli is indicated in combination with platinum-based chemotherapy in endometrial cancer patients over 18 years of age who are candidates for systemic therapy.

Jemperli may only be prescribed for these specific indications by specialists in oncology and doctors with expertise in cancer. They then give the patient a “patient card”, which she must keep for the duration of her treatment. This patient card contains important information on the medicine from the package leaflet and details of what to do in the event of symptoms suggesting an adverse reaction of immunological origin, such as: inflammatory pneumonitis, colitis, hepatitis, endocrinopathy (hypo- or hyperthyroidism, thyroiditis, hypophysitis, type-1 diabetes mellitus, diabetic ketoacidosis, adrenal insufficiency), nephritis, skin reactions, arthralgia or others. A detailed list is provided in the leaflet.

Find out more: https://ansm.sante.fr/actualites/acces-precoce-pour-jemperli-dans-le-cancer-de-lendometre

A compassionate prescription framework for Kaftrio and Kalydeco in the treatment of cystic fibrosis

Since 1st June 2023, the compassionate prescribing framework (cadre de prescription compassionnelle – CPC) for Kaftrio and Kalydeco has been extended to cystic fibrosis patients without an F508del mutation, from the age of 6, regardless of the severity of the disease. Treatment is not indicated for patients with two mutated genes predictive of a lack of CFTR protein synthesis.

It is still recommended that the prescription of the treatment be submitted to the coordinating centre of the Rare Disease Reference Centre (CRMR) for cystic fibrosis and disorders linked to a CFTR anomaly, in accordance with current clinical practice, and that patients treated under this compassionate prescribing framework be registered in the French Cystic Fibrosis Register.

To find out more and access the Therapeutic Use and Patient Monitoring Protocol (PUT-SP): https://ansm.sante.fr/actualites/mucoviscidose-de-nouveaux-patients-vont-pouvoir-beneficier-de-lassociation-des-medicaments-kaftrio-75-mg-50-mg-100-mg-et-kalydeco-150-mg

For more information about early access and compassionate access authorisations:
https://ansm.sante.fr/page/faire-une-demande-dacces-derogatoire

All our data on compassionate access, early access and the compassionate prescribing framework can be found in Appendix 9, page 154.

MEDICAL CANNABIS TRIAL

Evaluation of the trial, submission of reports to Parliament

The medical cannabis trial began on 26 March 2021, with the main aim of assessing the feasibility of the patient-access circuit. It will enable cannabis-based medicines to be made available to 3,000 patients on an active list in a secure, controlled environment, in order to test the conditions of use in real life and collect efficacy and safety data.
This trial has been the subject of several evaluation reports.
In 2022, the first evaluation focused on the feasibility of the medical cannabis access circuit and the first real-life efficacy data. This evaluation was carried out at using an electronic register that collected data on all patients (prescription data, dispensing data and clinical assessment scales). It confirmed the suitability and feasibility of the circuit and that the efficacy data for the various indications was encouraging, despite a moderate level of participation by general practitioners was moderate ( ).
The second evaluation, a pharmacovigilance and addiction vigilance survey, showed an expected safety profile, with few serious cases and no problems of addiction, abuse or misuse with medical cannabis.
The third evaluation, a survey of patient pathways and perceptions, showed that 93% of the patients involved in the trial were in favour of generalisation, and gave a satisfaction score of 8.2/10.

In 2023, an additional evaluation covering a longer period and an extended cohort of patients was submitted to the French Ministry of Health and then to Parliament.
It confirmed the efficacy of medical cannabis in all the indications tested, and also that this efficacy continued for more than 18 months after the introduction of treatment in some patients. The number of referrals from general practitioners remains limited, even though more GPs took part (10%). The addiction vigilance and pharmacovigilance data collected confirmed the safety profile assessed in 2022, as well as the absence of misuse or abuse of these medicines.

Future widespread use of medical cannabis

The Social Security Financing Act for 2024 of 26 December 2023 sets out the procedures for including medical cannabis-based medicinal products under ordinary law. They will have a specific status, with an authorisation for use for a temporary period of five years, issued by ANSM no later than 31 December 2024. In particular, this authorisation will be accompanied by an obligation to implement a system for collecting follow-up data on the patients treated, for which the procedures will be defined by ANSM. A Council of State decree will specify the various elements relating to this status.

A transitional period, from 27 March to 31 December 2024 at the latest, will ensure continuity of treatment for patients included in the trial. It will be limited to patients already included on 26 March 2024, and to medicines already used during the trial, with the exception of cannabis flowers.

Find out more: https://ansm.sante.fr/actualites/cannabis-medical-point-detape-sur-la-derniere-annee-de-lexperimentation-et-larrivee-de-medicaments-a-base-de-cannabis
And:
https://ansm.sante.fr/dossiers-thematiques/cannabis-a-usage-medical

2023 DATA

3,027 patients have been included since the start of the trial, with **1,828** still being treated:

- 1,077 patients for refractory neuropathic pain;
- 255 patients for painful spasticity caused by multiple sclerosis (MS);
- 158 patients for drug-resistant epilepsy;
- 141 patients in palliative care situations;
- 133 oncology patients;
- 64 patients for painful spasticity due to pathologies of the central nervous system excluding MS.

1,132 patients have left the trial since it began: 362 for ineffectiveness of treatment and 288 for adverse reactions. a further 482 patients have left the trial for another reason,159 of whom who died.

2,157 healthcare professionals have been trained, including 522 doctors from referral structures, 465 hospital pharmacists, 907 retail pharmacists, 76 advisors from pharmacovigilance centres (CRPV) and addiction vigilance centres (CEIP-A), and 187 liaison doctors in the non-hospital sector.

339 reference structures are involved in the experiment.

For more information about the medical cannabis trial:

https://ansm.sante.fr/dossiers-thematiques/cannabis-a-usage-medical

CLINICAL TRIALS

To ensure the safety of patients needing to use a new healthcare product or a new treatment strategy, the efficacy and safety of this product or treatment must be assessed on a limited cohort before it is made more widely available. These studies are known as clinical trials. They help determine the best conditions for the use of health products. They may also be conducted to assess a new way of using a known treatment.
ANSM is the competent authority in France to evaluate and authorise clinical trials.

For more information about clinical trials:
https://ansm.sante.fr/qui-sommes-nous/nos-missions/faciliter-lacces-a-linnovation-therapeutique/p/encadrer-les-essais-cliniques#title

All our data on clinical trials can be found in Appendix 10, page 156.

CTIS portal: review and outlook

On 31 January 2023, the CTIS (Clinical Trial Information System) portal became the single entry point for new applications for clinical trial authorisations in all 27 European Union (EU) Member States.
This portal was launched by the European Medicines Agency (EMA) in January 2022 to centralise on a single platform all submissions of applications for clinical trials carried out in the European Union, as well as evaluations and authorisations by the Member States.

Directive 2001/20/EC will be definitively repealed on 31 January 2025. Clinical trials that still have an operational centre in France on this date, approved under the previous directive, will need to be brought into line with the new regulation (CTIS portal). As a result, sponsors will be required to re-file their clinical trial documentation on the CTIS platform in order to comply with the regulations, or risk suspension on 31 January 2025. These are “transition trials”. By 2023, almost 300 transition trials had been submitted.

Find out more: https://ansm.sante.fr/documents/reference/reglementation-relative-aux-essais-ou-investigations-cliniques/faq-entree-en-vigueur-du-reglement-europeen-sur-les-essais-cliniques-de-medicaments-ndeg-536-2014

ANSM involved in the CTCG

ANSM is a member of the Clinical Trial Coordination Group (CTCG), and has been appointed to its Steering Committee. This group, operating under the authority of the HMA, is to reinforce the harmonisation, coordination and transparency of clinical trials in Member States.

In 2023, the CTCG worked on various issues, including the transition and decentralisation of clinical trials, the optimisation of the CTIS database, a pilot phase for coordinating scientific advice, and the updating of best practices. Contributions to the COMBINE (combined Medicines-MD/IVDMD trials), CTR Collaborate (continued implementation of the Clinical Trials Regulation), ACT-EU (acceleration of clinical trials in the EU) projects, in addition to the CT-CURE (harmonised and accelerated assessment of multinational clinical trials) joint actions, were also discussed.

Vigilance for clinical trials of medicines: simplified reporting procedures for sponsors

On 22 May 2023, the procedures for reporting vigilance data from clinical trials conducted under the Jardé Law changed, and the process has been simplified.
From now on, serious unexpected adverse reactions (SUSARs) during clinical trials must be reported solely by electronic transmission to the European Eudravigilance database. The simultaneous reporting of SUSARs to ANSM by email has been abolished, except for clinical trials conducted on healthy volunteers in France. In this case, the reporting procedures via the declarationsusars@ansm.sante.fr email address and via Eudravigilance remain unchanged.

For further information: see *Notice to sponsors of clinical trials of medicinal products - Volume 2 RIPH1 Vigilance (Jardé Law)* https://ansm.sante.fr/vos-demarches/industriel/declaration-devenements-et-deffets-indesirables-graves-de-faits-nouveaux-avec-ou-sans-mesures-urgentes-de-securite-rapport-annuel-de-securite

The Annual Safety Reports (ASR) and Development Safety Update Report (DSUR) for clinical trials conducted under the Jardé Law must be submitted via a simplified form.

To find out more: https://ansm.sante.fr/actualites/vigilance-des-essais-cliniques-de-medicaments-des-modalites-de-declaration-simplifiees-pour-les-promoteurs

Review and outlook for clinical trials since the entry into force of Regulations (EU) 2017/745 on medical devices and (EU) 2017/746 on in vitro diagnostic medical devices

Following the entry into force on 26 May 2021 of the requirements relating to clinical investigations (CI) under European Regulation 2017/745 on medical devices, and on 26 May 2022 of the requirements relating to performance studies (PS) under European regulation 2017/746 on in vitro diagnostic medical devices (IVDMDs), ANSM continued in 2023 to implement the new process for managing these CI and PS, with a ramping-up of PS submissions for IVDMDs in 2023. ANSM played an active role in drafting the European Questions & Answers on performance studies (PS).
In addition, “combined” or “mixed” clinical trials involving a medicinal product and a medical device or an IVDMD, are frequently carried out in the European Union, especially with a view to making innovative treatments available to patients. These tests must comply with the three regulations (medicines, MD and IVDMD), which makes them complex to implement.
ANSM has played an active role in the European Combine project. The first phase, carried out in 2023, developed an understanding of the challenges and obstacles encountered in combined studies, when applying the three overlapping regulations. The aim of the next phase is to develop solutions to streamline procedures. This project has involved the competent authorities of 15 Member States, covering three types of products, i.e. around fifty participants, for some forty meetings held in 2023.

Find out more: https://health.ec.europa.eu/medical-devices-topics-interest/combined-studies_en#the-combine-project

MARKETING OF MEDICINES

The marketing of a medicine in France means that it has undergone an assessment and been granted a marketing authorisation by ANSM or by the European Commission (following an opinion issued by the European Medicines Agency (EMA)).

There are four marketing authorisation procedures for medicines: three European procedures (centralised, decentralised, mutual recognition), and one national procedure.

For France, ANSM issues MAs for medicines authorised under the national procedure and medicines authorised under European decentralised and mutual recognition procedures. The decisions specify the prescribing and dispensing conditions for the medicine, which are specific to each country.
In addition, the Agency also issues registration decisions: these are simplified authorisation procedures that may apply to certain herbal and homeopathic medicines in accordance with specific conditions.

For more information about the marketing of medicines:
https://ansm.sante.fr/page/autorisation-de-mise-sur-le-marche-pour-les-medicaments

All our data on marketing authorisations for medicines can be found in Appendix 11, page 163.

MARKETING AUTHORISATION AND REGISTRATION APPLICATIONS FOR MEDICINES

Centralised authorisation procedure: France is the third-ranked evaluating country

ANSM is a member of the CHMP (Committee for Medicinal Products for Human Use), the committee responsible for evaluating medicinal products as part of the centralised authorisation procedure.[35] In 2023, the Agency was rapporteur or co-rapporteur for 15 of the 99 procedures evaluated, making it the third largest evaluator, behind the Netherlands and Germany (18 and 16 MA procedures, respectively). Of the 99 marketing authorisation procedures evaluated by the CHMP, 77 received a positive opinion, three received a negative opinion and 19 were withdrawn while undergoing examination. The four most frequently represented therapeutic areas among the dossiers receiving a positive opinion are:

- oncology 32%
- immunology 14%
- cardiology 8%, and dermatology 8%

ANSM acted as rapporteur mainly on products used in oncology (46%), infectious diseases, rare diseases, dermatology and companion in vitro diagnostic tests.

In 2023, France was appointed rapporteur or co-rapporteur for 19 marketing authorisation applications to be submitted in the coming months or years:

Centralised procedures	2019	2020	2021	2022	2023
Number of dossiers assigned to France (rapporteur, co-rapporteur)[36]	19	19	18	19	**19**

[35] Also read the interview entitled “ANSM's European strategy”, page 78.
[36] Including Companion & PRIME test procedures.

To consult CHMP opinions:
https://ansm.sante.fr/actualites/?filter[categories][]=33

Creation of the European Specialised Expert Communities (ESEC), new European expert groups

The CHMP consults its working groups on scientific issues falling within their area of expertise and delegates certain tasks to them as part of the scientific assessment of marketing authorisation applications or the drafting and revision of scientific guidance documents.

These working groups can now be supported by new specialist expert groups: the European Specialised Expert Communities (ESEC). These ESECs may be dedicated to a particular therapeutic area or expertise. To date, eight ESECs have been created, with others to follow in the coming months. ANSM experts intervene in each of these communities.
Existing ESCOs:

- Non-clinical ESEC (Non-Clinical and New Approach Methodologies European Specialised Expert Community)
- Methodology / Statistics ESEC (Methodology European Specialised Expert Community)
- Biological Quality ESEC (Biological Quality European Specialised Expert Community)
- Chemical Quality ESEC (Chemical Quality European Specialised Expert Community)
- Haematology ESEC (Haematology European Specialised Expert Community)
- Oncology ESEC (Oncology European Specialised Expert Community)
- Neurology ESEC (Neurology European Specialised Expert Community)
- Radiopharmaceutical ESEC (Radiopharmaceutical European Specialised Expert Community)

Find out more: https://www.ema.europa.eu/en/committees/working-parties-other-groups/chmp-working-parties-other-groups

France's participation in the CMDh...

ANSM has been a member of the CMDh (Coordination Group for Mutual Recognition and Decentralised Procedures - Human) since its creation in October 2005.
In 2023, the Agency was the reference Member State for nine MAs under the mutual recognition procedure and five MAs under the decentralised procedure.
ANSM also initiated an arbitration procedure at the CMDh under Article 29(1) of Directive 2001/83/EC for a marketing authorisation application under the mutual recognition procedure in which France is one of the Member States concerned. This procedure resulted in an agreement between the reference Member State and ANSM.

ANSM also participates in various CMDh working groups, such as the ASMF Working Party, the Pharmacovigilance Working Party, the Variations Working Party and the CMDh/GCP working party.

Through the CMDh and its various working groups, ANSM participates in the drafting of regulations and recommendations on procedures for registering and modifying medicinal products under mutual and decentralised recognition procedures.

In 2023, ANSM took part in the creation or updating of various documents, including:

- recommendations on Informed Consent Applications in Mutual Recognition and Decentralised Procedures;[37]

[37] Recommendations concerning applications for a medicinal product with the same qualitative and quantitative composition in active substances and the same pharmaceutical form as an authorised medicinal product, for which the holder has consented to the use of the pharmaceutical, pre-clinical and clinical documentation contained in the file for that medicinal product, subject to the mutual recognition and decentralised procedures.

- CMDh SOP on the decision-making process for new active substance status or extension of marketing protection or data exclusivity;[38]
- Decentralised Procedure Members States' Standard Operating Procedure;[39]
- Applicant's Response document in Mutual Recognition and Decentralised Procedures for Marketing Authorisation Applications.[40]

In liaison with the European Commission and the EMA, the CMDh also participated in the revision of Regulation (EC) 1234/2008 on changes to marketing authorisations (via a delegated act, published in March 2023).
Through its various working groups, the CMDh is also involved in the revision of European legislation on medicinal products.

The CMDh is also involved in issues relating to the presence of nitrosamine impurities in certain medicinal products; it draws up recommendations and guidelines on the subject, which are regularly updated, in collaboration with the EMA and the other European working groups concerned.

For more information about the CMDh: https://ansm.sante.fr/qui-sommes-nous/nos-missions/informer-echanger-avec-notre-environnement/p/participer-aux-instances-internationales#title

... and the HMPC

In 2023, after carrying out a systematic review of new monographs or monographs under revision, and analysing comments from public enquiries, the Committee on Herbal Medicinal Products (HMPC) adopted:

- Ten Union monographs;
- A concept paper on new techniques for preparing plant extracts;
- Two updated Q&A documents on the quality requirements for herbal medicinal products, as well as updated Q&A documents on the regulatory framework for traditional herbal medicinal product registrations and marketing authorisations.

For more information about the HMPC: https://ansm.sante.fr/qui-sommes-nous/nos-missions/informer-echanger-avec-notre-environnement/p/participer-aux-instances-internationales#title

Tenofovir disoproxil and CMIC impurity

Tenofovir disoproxil is an active substance widely used in the treatment of infection by human immunodeficiency virus (HIV) or hepatitis B virus (HBV), or for HIV prevention (pre-exposure prophylaxis).
In March 2023, ANSM and the European Medicines Agency (EMA) asked laboratories manufacturing medicines containing tenofovir disoproxil to reduce the concentration of a substance called CMIC (chloromethyl isopropyl carbonate).
CMIC, which is essential in the manufacturing process for medicines containing tenofovir disoproxil, is classified as a mutagenic substance. These substances are known to increase the probability of cancer when their concentration is above a certain threshold. However, the mutagenic effect of CMIC has only been demonstrated in the laboratory (in vitro tests). The risk of this impurity actually causing cancer in humans has not been demonstrated. The request to reduce the concentration of CMIC is therefore a precautionary measure.

Find out more: https://ansm.sante.fr/actualites/medicaments-contenant-du-tenofovir-disoproxil-lansm-et-lema-demandent-aux-laboratoires-de-reduire-la-concentration-dune-impurete-cmic

[38] CMDh standard operating procedure for the decision-making process relating to the status of a new active substance or the extension of market exclusivity or data protection.
[39] Member States' standard operating procedure for the decentralised procedure.
[40] Response document from the applicant for a marketing authorisation subject to the mutual recognition and decentralised procedures.

ACCESS TO ORPHAN AND PAEDIATRIC MEDICINES

Early access to dabrafenib-trametinib for paediatric gliomas

Since 28 August 2023, the combination of dabrafenib and trametinib has been available on an early-access basis in a formulation adapted to children aged at least one year old who are suffering from BRAF V600E mutation-positive gliomas.
This release follows the HAS' decision to grant early access authorisation (AAP) on 29 June 2023 for a period of 12 months, based on the opinion of ANSM. This supports a strong presumption of the efficacy and safety of the dabrafenib-trametinib combination for this indication.

Specifically, the combination of dabrafenib and trametinib is indicated for paediatric patients aged at least one year old, who are suffering from:

- low-grade glioma (LGG) with a BRAF V600E mutation, requiring systemic treatment;
- or high-grade glioma with a BRAF V600E mutation, who have received at least one previous course of radiotherapy and/or chemotherapy

Only oncology specialists and doctors qualified in oncology may prescribe dabrafenib-trametinib for these specific indications.

Find out more: https://ansm.sante.fr/tableau-acces-derogatoire/dabrafenib ; https://ansm.sante.fr/tableau-acces-derogatoire/trametinib

France's participation in the PDCO

France was rapporteur or co-rapporteur for **99** cases, including 39 PIP cases, 44 PIP modifications and 16 PIP completion checks.
The year 2023 was marked by France's vice-presidency of the EMA's Paediatric Committee (PDCO), with the aim of better promoting general paediatric issues in Europe (stepwise PIP, development of medicinal products per indication and mode of action, training in paediatrics, therapeutic recommendations, paediatric networks, regulation).
In Europe, France is still raked third in terms of evaluating PIP paediatric developments. This confirms the national commitment to making paediatrics a public health priority.

	2019	2020	2021	2022	2023
Number of Paediatric Investigation Plan (PIP) applications for which France was the rapporteur or peer-reviewer	88	87	100	107	**99**
Percentage relative to the total number of PIPs	7.3%	6.7%	7.2%	8.1%	**7.6%**

For more information about the PDCO: https://ansm.sante.fr/qui-sommes-nous/nos-missions/informer-echanger-avec-notre-environnement/p/participer-aux-instances-internationales#title

For more information about access to orphan and paediatric medicines:
https://ansm.sante.fr/qui-sommes-nous/notre-perimetre/les-medicaments/p/medicaments-en-pediatrie#title

RELEASE OF BATCHES OF VACCINES AND BLOOD-DERIVED MEDICINES

Vaccines and blood-derived medicinal products are sensitive biological products since their production uses starting materials of human or animal origin, and involves a complex process, subject to variability. While they meet the same requirements as other medicines in terms of safety of use and monitoring, their marketing conditions are reinforced via a national-authority release process.

This system requires control by an independent national authority of 100% of vaccine and blood-derived medicinal product batches before they are marketed. Batches released in this manner may circulate freely within the European area.

This release, conducted by ANSM in its capacity as the official national control laboratory, involves a documentary review of the manufacturer's production and control data and controls carried out in independent laboratories relating to the identity, efficacy and safety of vaccine and blood-derived medicinal product batches. For each batch, the critical parameters to be controlled are defined jointly by all the European laboratories within the European Directorate for the Quality of Medicines and Healthcare in Strasbourg (EDQM – Council of Europe). This harmonisation work also enables mutual recognition between Member States and avoids unnecessary duplication of tests.

For more information about the release of batches of vaccines and blood-derived medicines:
https://ansm.sante.fr/qui-sommes-nous/nos-missions/assurer-la-securite-des-produits-de-sante/p/controler-la-qualite-des-produits#liberation_lots_vaccins

All our data on batch releases for vaccines and blood-derived medicines can be found in Appendix 12, page 168.

Implementation of the release of the VRS Abrysvo vaccine

Abrysvo is a vaccine designed to protect adults aged 60 and over against lower respiratory tract infections (LRTI, lung diseases such as bronchitis or pneumonia) caused by the respiratory syncytial virus (RSV). A special feature of this RSV vaccine is that it can also be used in mothers during pregnancy to protect their infants against RSV from birth to six months of age. Abrysvo contains the two proteins present on the surface of the virus, known as RSV F proteins of subgroup A and subgroup B, stabilised in prefusion form. To enable the release of batches, ANSM introduced various controls on the finished product in 2023 in order to verify the quality of the batches. These controls are: a slot-blot (to identify the two proteins), an ELISA test (to determine the amount of F protein present) and a SEC-HPLC test (to check purity). At the same time, the manufacturer was asked to provide all the important production information that needs to be included in the test protocol required for batch release. The implementation of this release has strengthened ANSM's standing at European level concerning the release of innovative vaccines. This is one of the first vaccines to be marketed for this disease. This product has been released in collaboration with the official Belgian medicines control laboratory (Sciensano OMCL).

AUTHORISATION OF BLOOD PRODUCTS AND OTHER BIOLOGICAL PRODUCTS

Products derived from the human body cover a multitude of products: labile blood products (LBPs) used in blood transfusions, organs, tissues and cells used for transplants, and breast milk for therapeutic use.

All these products (with the exception of breast milk and organs transplanted in routine practice) are subject to assessment and authorisation by ANSM. Their assessment is based on the same essential benefit and risk criteria as those applied to medicinal products: therapeutic benefit, efficacy, safety of use, and quality.

Due to the origin of these products (derived from living organisms), the risk of viral or microbiological contamination or contamination by other infectious biological agents is monitored very closely. ANSM therefore assesses the viral safety with regard to transmission risk. For tissues (corneas, bones, parts of the locomotor system, valves, etc.) and cell therapy preparations, ANSM also assesses their preparation and preservation processes.

ANSM also authorises the importation and exportation of tissues and cell therapy preparations to third countries.

For more information about the authorisation of blood products and other biological products:
https://ansm.sante.fr/page/autorisation-des-produits-sanguins-et-des-autres-produits-biologiques

All our data on the authorisation of blood products and other biological products can be found in Appendix 13, page 169.

Moving forward, drawing on our resources

4

FOCUS ON...THE OFFICE OF TOMORROW

ANSM's 2023 Social Barometer Survey highlights some encouraging results, notably showing that staff are adapting well to the hybrid mode (face-to-face and remote). To maintain the team spirit, Hélène Boissin-Jonville, Deputy Director of Human Resources, and François Le-Né, Deputy Director of Finance and Administration, explain how ANSM is developing the office of the future, especially by creating flexible, user-friendly environments.

What can we learn from the 2023 Social Barometer Survey?

Hélène Boissin-Jonville: A response rate of 50% was recorded for the 2023 Social Barometer Survey – identical to that in 2021. This is a satisfactory rate and the profile of respondents was sufficiently representative to measure the social climate at ANSM. The results show significant improvements compared with the 2021 Barometer Survey, particularly in terms of understanding how the Agency is organised and confidence in relations between staff and managers. However, the results show that efforts need to be maintained and that particular attention needs to be paid, for example, to improving the understanding of the Agency's strategy and managing staff workloads. Staff and teams feel that they are adapting well to the hybrid mode, although challenges remain in terms of maintaining team spirit in this configuration.

François Le-Né: In activities with significant flows of information, it is essential to ensure that all our resources encourage collaboration in order to maintain cohesion and team spirit. Communication channels and the adaptation of premises are key issues in this transition to a hybrid model.

Why are changes being made to premises at the Saint-Denis Pleyel site?

F.LN: The aim is to optimise the available space and the location of the departments. The aims are, firstly, to accommodate all the staff at Saint-Denis on the same site, in order to accommodate all the teams working for a single division on the same floor and to house divisions that work together or perform a common activity in the same building, and secondly, to provide environments that are better suited to our new hybrid way of working, taking account of the needs expressed by staff and divisions during surveys, workshops and interviews.

H.BJ: Creating user-friendly spaces, redesigning our offices and optimising our meeting areas are also ways of encouraging informal meetings, facilitating links between staff from different divisions and making the Agency more attractive to the outside world and to job applicants. 94% of ANSM staff work from home three days a week, so it's important to make coming to work at the office a meaningful experience.

What progress has been made in this work? What are the final objectives?

F.LN: We are currently halfway through the redevelopment of the Pleyel premises. A joint review was carried out with all the divisions in 2023 in order to determine the new types of spaces required and to consider the layout of the offices. Following a functional and technical review, a schedule for the works and relocations was drawn up, and work began in the second half of 2023. By early 2025, the relocation phase should be complete, giving way to the refurbishment phase scheduled for 2025/2026.

Are any changes planned for Vendargues?

F.LN: Absolutely. Following an energy audit, we identified waterproofing, roofing and façade work that needs to be carried out as a matter of urgency. However, we are also thinking about reorganising our spaces, adopting an approach similar to that used at Pleyel, including the development of equipment and facilities that are better suited to the hybrid work mode, in addition to new, user-friendly spaces.

H.BJ: These reorganisations will also make it possible to accommodate a number of employees who have historically been based in Saint-Denis and who, for personal reasons in particular, would like to relocate to the South of France. We are proposing to assign employees or future employees whose team is based in Saint-Denis to the Vendargues site, and to implement an organisational procedure that will allow them to return to the Saint-Denis site on a regular basis for face-to-face sessions. Offering our employees a better quality of life and attractive working conditions enhances our attractiveness as an employer. The aim of this opportunity is also to extend our employment pool, across all activities, beyond the Paris region.

In Lyon, why are a joint ANSM/ANSES building and laboratories still planned for 2024?

F.LN: Over and above our scientific interests, this shared building will allow us to share certain facilities and services with ANSES, such as shared meeting rooms and catering facilities, the building reception desk and grounds maintenance. Purchases and services not related to the building have already been identified as being suitable for pooling. Others could be envisaged after a period of joint operations.
The move to these premises is scheduled for the beginning of the fourth quarter of 2024. We are currently working with ANSES on the service contracts required to occupy this new building.

OUR ORGANISATION

New appointments to the ANSM's Senior Management and Divisions were made in 2023, presented in chronological order of arrival:

- Céline Mounier, appointed Deputy Director General for Operations in January 2023
- Mehdi Benkebil, appointed Director of Surveillance in February 2023
- Alexandre de la Volpilière, appointed Deputy Director General for Operations in June 2023
- Elodie Massé, appointed Director of Communication and Information in June 2023
- Christelle Ratignier-Carbonneil, reappointed as Director General of the ANSM in December 2023.

Find out more about our organisation chart, our divisions and departments:
https://ansm.sante.fr/qui-sommes-nous/notre-organisation/nos-directions-et-nos-services

OUR GOVERNANCE BODIES

Management Board

The ANSM Management Board was renewed in November 2021 for a three-year period.

Its Chair is Valérie Delahaye-Guillocheau, a member of the French Council of State who was appointed by decree of the President of the French Republic in December 2021.

The Administrative Board has 27 members,[41] most of whom are Members of Parliament, healthcare professionals and patient representatives.
Votes are evenly distributed between government representatives (9 members, 18 votes) and the 18 other members, each of whom has one vote.

Apart from the representatives of ANSM's personnel, who are elected, the members of the Administrative Board are appointed by the Minister for Health. Except for the Members of Parliament, they are elected for a three-year term, renewable once.

The Administrative Board sets the broad policy guidelines for the Agency, deliberates on certain matters relating to its operations, particularly the Objectives and Performance Contract (COP) [prior to its conclusion with the Ministry of Solidarity and Health for the 2019-2023 period], and adopts the budget.

It met four times in 2023 (in March, June, September and November), in a hybrid format enabling the remote participation of Board members via videoconference, as permitted by its Rules of Procedure.

To find out more about the Administrative Board and consult the list of its members:
https://ansm.sante.fr/qui-sommes-nous/notre-organisation/nos-instances/p/le-conseil-dadministration#title

The Scientific Advisory Board

ANSM's Scientific Advisory Board was renewed in September 2023 for a three-year period.

Its president is Professor Joël Ankri, who was re-elected by the members of the Scientific Advisory Board in November 2023, and appointed Chair of the Scientific Advisory Board by order of the Ministry of Labour, Health and Solidarity on 26 January 2024.

"We would like to see the Scientific Advisory Board adopting a cross-disciplinary approach to public health issues, starting with everything to do with the evaluation and monitoring of medicines and health products, with the aim of anticipating problems and trying to provide solutions, or at least avenues to be explored by the Agency's senior management."
Joël Ankri, Chair of the Scientific Advisory Board

The Scientific Advisory Board comprises 16 members chosen for their fields of expertise and also includes foreign scientists. They are appointed by order of the Minister for Health.

The Scientific Advisory Board monitors the consistency of the ANSM's scientific strategy by taking account of advances in the knowledge of the efficacy and safety of health products.

It formulates opinions and recommendations for the Director General, in the context of referrals or self-referrals, relating to open and cross-cutting themes and public health issues. It contributes to the ANSM's forward-looking thinking on future issues and challenges.

Its 16 members are elected for a renewable three-year period:

- ten are appointed after a call for applications procedure run by the Agency;
- six renowned scientists, some from outside France, are appointed on the advice of the Minister for Higher Education and Research.

In 2023, the Scientific Advisory Board met four times in plenary session (February, April, September and November).

Review of the 2020 – 2023 term of office

The 2020-2023 term ended in September 2023. During its term of office, the Scientific Advisory Board covered a number of issues, including the following in the field of public health policy:

- actions taken to address the risks associated with taking medicines during pregnancy;
- preventing misuse or the inappropriate use of medicines;
- disruptions in the availability of healthcare products;
- the Agency's digital policy.

The Board also examined the Agency's themes and activities, such as pharmacovigilance, signal detection and the reform of early and compassionate access to medicines, the use of real-life data in scientific evaluation, and the renewal of the standing scientific committees.
The Board issued opinions and recommendations on studies and research projects funded by the Agency.

The Scientific Advisory Board also dealt with three self-referrals, with the aim of anticipating the impacts of current and future scientific developments on public health and ANSM:

- two led to the publication of articles in international scientific journals:
  - nanomaterials and health products: “Regulatory assessment of nano-enabled health products in public health interest. Position of the Scientific Advisory Board of the French National Agency for the Safety of Medicines and Health Products (ANSM)”, *Frontiers in Public Health* (March 2023);
  - the patient's role in the benefit-risk assessment. “Patient and public involvement in the benefit-risk assessment and decision concerning health products: position of the Scientific Advisory Board of the French National Agency for Medicines and Health Product Safety (ANSM)”, *BMJ Global Health* (April 2023);
- The Scientific Advisory Board's third self-referral on "Artificial intelligence: applications and prospects for ANSM and health products" was launched as part of discussions with the Agency's business divisions on the need to anticipate the impact of the development of AI and the integration of big data collected during the course of care on the Agency's missions, particularly in the assessment of benefit-risk throughout the life cycle of health products.

Find out more about the Scientific Advisory Board and consult the list of its members:
https://ansm.sante.fr/qui-sommes-nous/notre-organisation/nos-instances/p/le-conseil-scientifique#title

OUR OBJECTIVES

The Objectives and Performance Contract (Contrat d'Objectifs et de Performance – COP), entered into by the Ministry of Solidarity and Health and ANSM, defines the Agency's main strategic orientations for the 2019 to 2023 period. It is part of the implementation of the National Health Strategy (SNS), defined by the government for the 2018-2022 period and contributes to the first priority commitment of the "Ma Santé 2022" (My Health 2022) project: "Promoting quality and refocusing care on the patient".

The COP covers four strategic priorities divided into 21 major objectives, which are in turn composed of operational actions. Twenty-four monitoring indicators of a qualitative or quantitative nature are used to monitor implementation.
An assessment report on the implementation of the COP is presented to the ANSM Administrative Board and published on an annual basis.

Strategic Priority 1: Develop the Agency's openness to stakeholders and increase the transparency of its activities

The new framework of the National Health Strategy (2018-2022) and the "Ma Santé 2022" (My Health 2022) collective commitment project have reinforced ANSM's major policy of placing the patient at the heart of its safety measures. Within this framework and in consultation with the French Ministry of Health, the Agency must continue to build constructive, trusting and long-term relationships with its users: patients, health professionals and manufacturers.

Strategic Priority 2: Make risk management a common operating principle for all the Agency's missions

ANSM implements a risk management approach that permeates all its actions and decisions. This approach, applied to health security and based on paying particular attention to users, aims to prevent the occurrence of adverse events associated with treatments, and with health products in particular, or, failing that, to reduce their risks to an acceptable level.

Strategic Priority 3: Reinforce and stabilise the Agency's positioning to facilitate access to innovation in the European environment

ANSM is an essential link in supporting the development of innovative healthcare products and facilitating their availability under conditions that ensure patient safety. Today, innovation-support activities are very much in line with European procedures. In this context, the Agency is strengthening its European positioning to enable early and secure access to innovation.

Strategic Priority 4: Stabilise the institution's performance and efficiency

The Agency must meet the public service performance requirement of providing safer and more efficient services that meet the expectations of the audiences they serve. The aim is to guarantee the quality and safety of health products for all citizens, and fast access to the most recent products that improve patients' lives, thanks to ever more effective and efficient administration.

The 2024-2028 Objectives and Performance Contract was developed throughout 2023. ANSM teams worked in close collaboration with the government departments represented on the Administrative Board, under the guidance of the French Ministry of Health (DGS) and following the recommendations of the General Inspectorate for Social Affairs (IGAS). All employees were consulted on the strategic orientations, in order to optimise their engagement in the key issues facing the Agency over the next 5 years. This project will be submitted to the Administrative Board in 2024.

Read more about the Objectives and Performance Contract (COP):
https://ansm.sante.fr/qui-sommes-nous/publications-institutionnelles/contrat-dobjectifs-et-de-performance

2023 DATA

Indicators achieved: 21
Indicators not achieved: 7
Indicators not applicable to the measurement frequency: 4

The complete 2023 review of monitoring indicators can be found in Appendix 14, page 170 (results to 31 December 2023).

PRIORITY 1

The changes in the indicators for this priority over the 2019 to 2023 period demonstrate the agency's commitment to stepping up the stakeholders' involvement in its work and increasing its transparency. A survey conducted in 2022 confirms this trend. In 2023, stakeholders were involved in the handling of 97% of high-risk situations. In addition, the completion rate for the data publication work programme has increased since 2019, reaching 98% in 2023.

PRIORITY 2

The Agency's actions and decisions are based on a risk management approach. The development of the indicators for Priority 2 over the 2019-2023 period illustrates the extent to which this approach has become an integral part of the Agency's practices:

- the number of emergency actions to be rolled out has increased by 33% between 2022 and 2023. The completion rate of emergency action plans for high-risk situations (HRS) has improved since 2019 to reach 98% in 2023;
- the significant increase in the number of reports of risks of shortages or stockouts of medicines has had an impact on the time taken to deal with these situations. This is reflected in the results of the indicator measuring the rate of cases for which a risk-reduction measure was proposed within the deadline. However, the results for this indicator improved to 85% in 2023. Since 2022, the target of 100% has been achieved for the indicator relating to the application of financial penalties imposed by ANSM on manufacturers failing provide notification of a risk of stockout;
- the completion rate for the annual work programme on the coverage of misuse increased over the period as a whole, reaching 93% by the end of 2023.

PRIORITY 3

The indicators for Priority 3 indicators changed during the 2019-2023 COP in connection with the entry into force of the new European regulation on clinical trials and the reform of derogatory access to medicines in 2023. The strengthening of France's position in Europe in terms of access to innovation is reflected in the following indicators:

- in 2023, 85 scientific opinions were issued by France at European level;
- a 34% increase in the number of requests handled by the Innovation and Guidance Centre since it opened in 2021;
- a significant increase between 2022 and 2023 in the number of applications for clinical trials of medicinal products and advanced therapy medicinal products for which France was designated as the reference Member State.

PRIORITY 4

ANSM is continuing to develop its digital strategy, with the completion rate for its annual portfolio of IS projects reaching 90% in the last year of the COP.
The results of the indicators relating to the authorisation process for new MA applications and compliance with sub-regulatory deadlines need to be improved, with a result of 55% in 2023, up on 2022. Improvement initiatives are underway, the results of which will be assessed in 2024.

OPTIMISATION OF INTERNAL PROCESSES AND THE QUALITY MANAGEMENT SYSTEM

The Quality Policy ensures the operational implementation of the Objectives and Performance Contract (COP). It is aligned with its strategic orientations and is broken down into four priorities focusing on all the Quality Management System (QMS) processes:

- **continue the institution's policy of openness and public data access**, in order to strengthen our ties with healthcare professionals and patients and establish a constructive dialogue;
- **place the patient at the heart of risk management processes**, to reduce the risks associated with health products;
- **reinforce the Agency's European positioning**, in particular to facilitate and accelerate patient access to therapeutic innovations governed by European regulations;
- **stabilise the institution's performance and efficiency** by maintaining the quality of working life.

In 2023, the Agency not only renewed its ISO 9001 certification, but also achieved an excellent score in a European comparative study (BEMA V), making it one of the best-performing medicines agencies in Europe.

BEMA V: ANSM obtains an excellent rating

BEMA is a benchmarking exercise commissioned by the Heads of European Agencies (HMA). Its aim is to assess the European medicines system with a view to harmonising practices and achieving continuous improvement. It concerns all the European Union's medicines agencies – 38 in all (human and veterinary medicines) – and is carried out in three-year cycles.

Each agency is assessed individually on the basis of a questionnaire common to all agencies, comprising 40 indicators grouped into 12 themes. Three external evaluators from other EU agencies then assess the practices on the basis of a self-assessment report.

The last exercise – BEMA IV – was held in 2016, and the ANSM achieved a score of 3.9 out of 5, which already placed it among the leading agencies. Because of the pandemic, BEMA V had to be postponed. It finally took place in March 2023.

ANSM received an average score of 4.6 out of 5, up 0.7 points on the previous benchmark. This is the best score to date in the network of European agencies, making the ANSM one of the best-performing agencies in Europe.

Its strengths include:

- its transparency policy and the ANSM website;
- its know-how and organisational expertise in preventing and combating crises;
- its expertise in national and European scientific advice and the Innovation and Referral Service;
- its medical product monitoring system (pharmacovigilance and epidemiology) and the national pharmacovigilance database;
- the organisation of inspections and external recognition (COFRAC accreditation, JAP audit, etc.); ;
- and its information system.

"ANSM is a splendid operating Agency with excellent systems as competences. Above all, scientific and regulatory activities are performed in best in class manner"

Renewal of ANSM's ISO 9001 certification

ANSM's ISO 9001 certification was renewed in 2023 for processes falling within the scope of risk management, namely:

- monitoring healthcare products;
- managing high-risk situations;
- controlling healthcare products;

- inspecting;
- combating shortages of medicines;
- organising the quality control of medical devices and in vitro diagnostic medical devices;
- examining user requests.

Two new processes have also been integrated: “Authorising new MA applications and modifications” and “Managing establishments”.
During the certification audit, no discrepancies were identified, although a few areas for improvement were highlighted.

In 2024, two other new processes: “Authorising clinical trials” and “Supporting innovation” will be integrated.

IMPLEMENTATION OF THE INFORMATION SYSTEMS AND DATA MASTER PLAN (SDSID)

2023 saw the pursuit of the implementation of the Information Systems and Data Master Plan (SDSID), initiated in 2019 and revolving around five strategic objectives:

- **making data central to health and public health issues,** for the benefit of users, businesses and the ecosystem;
- **ensuring mastery of the information system (IS) and data** to address the needs of all users and stakeholders;
- **correlating the effectiveness and efficiency of the IS function** to meet ANSM's ambitions;
- **incorporating the IS and data within an innovation-oriented approach** in order to support the development of digital and societal practices;
- **promoting ANSM and its public health actions via the IS and data uses** as part of a collaborative approach that embraces external partners.

Roll-out of Wi-Fi as part of the drive to improve quality of working life

The opening of the Wi-Fi service throughout the Saint-Denis site in 2023 is part of the drive to improve the tools and technologies available to staff, and is totally consistent with the project to modernise the institution and its infrastructure.

Its implementation, in a context subject to time constraints and the strict security rules imposed by the Agency, required an efficient approach to several important areas:

- on a technical level: the definition and implementation by IT teams of a robust, secure architecture operating in an optimal manner;
- on an organisational level: project management requiring the involvement of multiple partners such as support departments as well as various service providers and experts in their specialities (cabling, network security, electromagnetic standards, etc.);
- In terms of support for this change: a coordinated three-week roll-out to monitor the ramp-up, while prioritising the provision of extensive support for staff on the new login methods.

NDS (National Drug Control System)

The NDS7 (National Drug System) is an application developed by the United Nations Drugs and Crimes branch (UNODC) for all States worldwide, to enable them to ensure the traceability required by the international conventions on narcotic drugs and psychotropic substances concerning the worldwide flows of these products. This application was first installed at ANSM in March 2004 with the following functions:

- registration of substances, medicines and establishments;
- issue of import/export permits;
- issue of authorisations for national trade ;
- recording of all data relating to production, manufacturing, stocks and consumption;
- preparation of INCB reports (Form A and AP, P, etc.).

All of the 12,000 applications received each year were sent to the Agency by email and entered into the application. Following the development by IOGM of "NDSWEB", a web module for the remote filing of authorisation applications, the project to roll out this new version was launched in 2021 with the DMM2 and DSI teams.

The main aim is to reduce the number of operations carried out by managers, but also to benefit from new functions such as the ability to extract and transmit annual reports previously sent by post.

Main projects in 2023 per strategic priority of the SDSID

Making data central to health and public health issues,

- Implementation of EDM for European projects
- Implementation of 3 new “Qlik” tables linked to material vigilance and the management of medical devices and in vitro diagnostic medical devices.
- Pursuit of the European Eudamed programme with the creation of the first European data warehouse.

Ensuring control over the IS and data

- Renewal of the IT servers at the Vendargues site, as part of the modernisation of the information system.
- Clustering of our storage bay, providing an additional level of security for our data storage.
- Implementation of an initial batch of IS supervision tools. The aim of this new supervision system is to improve incident detection time, and even to anticipate the occurrence of incidents by detecting certain warning signs.
- Implementation of an initial catalogue of services.
- Upgrading of several internal tools as part of the programme to reduce IS obsolescence.

Correlating the effectiveness and efficiency of the IS function

- Introduction of a new version of the compassionate access authorisation (AAC) management tool, including the option for prescribers and pharmacists in French hospitals to use their eCPS card.
- Pursuit of the development programme for the cross-functional data-monitoring application.
- Implementation of a new roll-out strategy for workstation updates, with an increase in the publication frequency of workstation-related security patches.
- Update of the stockout declaration tool.

Incorporating the IS and data within an innovation-oriented approach

- Implementation of a first version of the risk management tool, with the aim of harmonising and simplifying the risk assessment of applications between departments.
- Performance of a robotic data entry test as part of the Manufacturer Incident Report (MIR) management process.
- Automation of part of the data publication chain for the public medicines database.

Promoting the Agency and its public health actions via the IS and data uses

- Implementation of a new intranet with the addition of a connected mode enabling everyone to customise part of their interface.
- Implementation of the "lesmedicamentsetmoi.fr" domain as part of our information campaign on the proper use of medicines.

2023 DATA

- **> 168 production launches carried out** at ANSM, including production launches of business applications, technical tools and back office applications;
- **> 155 applications used** each day across **360** servers, including **240** virtual or physical internal servers and **124** external virtual servers.
- **> 1,500 user workstations maintained** (**1,400** in 2022, reduction due to rationalisation of the computer fleet and decommissioning of desktop computers);
- **> 5,808 incidents** (**-22%** vs 2022) and more than **4,088 user requests** (**+8%** vs 2022).

HUMAN RESOURCES

Within the framework of the 2019-2023 Objectives and Performance Contract (COP), ANSM's human resources policy is divided into five strategic priorities:

- **supporting transition** within the Agency;
- **consolidating practices and reinforcing the managerial collective;**
- **supporting individual and collective professional development**, by anticipating changes in careers;
- **fostering quality of working life and preventing psychosocial risks;**
- **ramping up modernisation and enhancing efficiency**, while meeting regulatory requirements.

In 2023, this strategy was put into practice with the introduction of a new social barometer survey designed to measure the social climate. This highly informative barometer survey will be used to identify the projects to be carried out in the coming months with a view to further improving the quality of working life and preventing psychosocial risks within the Agency.

Here are some key figures:

- at 31 December 2023, ANSM had a total workforce of almost 1,031 staff with different statuses, 90% of whom were employed under public law contracts;
- 857 staff on permanent contracts including civil servants and seconded civil servants, and 174 staff on fixed-term contracts and subsidised contracts);
- the mean age was 46 years of age;
- 72% female employment rate (64% of managers are women)

Renewal of employee representative bodies

Following the elections held in December 2022, ANSM's staff representative bodies were renewed for four years. This new term of office, which began in January 2023, is being marked by the renewal of employee representative bodies, driven by Law 2019-828 of 6 August 2019 on the transformation of the civil service, with, in particular, the introduction of two new bodies.

The Agency's Social Management Committee (SMC) and its specialist Health, Safety and Working Conditions Committee (HSWCC) were inaugurated on 1st January 2023.

The Human Resources Division has worked with elected employee representatives to define the operating framework for these bodies. The rules of procedure of the CSA and the FSSCT were adopted on 17 January 2023. This document governs the operation of the bodies and the organisation of exchanges. At the Agency, the frequency of meetings is set out in a social calendar drawn up jointly by the Human Resources Division and trade unions on a voluntary basis. It revolves around staff representative bodies, of course, in addition to thematic social dialogue meetings (recognition processes, annual appraisal interviews, GPEEC, etc.) and the Psychological and Social Risk Observatory.

Two years after its predecessor, the Agency has launched its new Social Barometer survey

The Agency has rolled out its new Social Barometer survey for the summer of 2023. The aim of the survey is to measure the social climate and understand employees' perceptions of the organisation. It has been drawn up using a questionnaire similar to the version used in 2021, to enable the observation of trends over time.

509 employees completed the 2023 edition of the Social Barometer survey, i.e. 50% of the establishment's workforce. The results were analysed by the Human Resources Division, while maintaining the anonymity of the contributions received.

The results of the 2023 Social Barometer survey were encouraging, with an improvement in the results. In general terms, respondents stated that they have a better understanding of the Agency's organisation

and of the internal allocation of responsibilities; mutual trust in managerial relations is also up by several points and has risen steadily since 2016, the date of the last major survey of this kind; the feeling of belonging and pride in working for the Agency is also overwhelmingly reaffirmed: 92% of respondents are proud to work for ANSM.

However, areas for improvement have been identified and further efforts are required in a number of areas, such as informing staff about strategic orientations, involving everyone in the Agency's transformation projects, and regulating workloads, which remains a priority.

DISCOVER THE PROFESSIONS OPERATING AT ANSM THROUGH STAFF TESTIMONIESS

https://ansm.sante.fr/qui-sommes-nous/rejoignez-nous/nos-metiers

. Regulatory scientific coordinator assessor
. Non-clinical assessor
. Stockout assessor
. Inspector
. Laboratory technician

BUDGET

In 2023, the Agency embarked on an ambitious approach designed to achieve energy sobriety. Measures such as temperature regulation and the installation of energy-efficient lighting have resulted in significant savings. At the same time, the project to renovate the main site at Saint-Denis - Pleyel has been launched, combining the refurbishment of premises with environmentally friendly adaptations, marking a step towards modernising infrastructures and promoting an environmental culture within the Agency.

Energy sobriety at ANSM

Starting in 2022, the Agency embarked on an ambitious energy efficiency programme, whose impact was fully felt in 2023. The main measures implemented are:

- setting of two temperature limits in offices at its main sites in Saint-Denis and part of its Vendargues site:
    - 19°C in winter and 26°C in summer,
    - by turning off the air conditioning and heating system every night between 8 p.m. and 7 a.m. and at weekends.
- renovation of the lighting systems in all of its buildings to install:
    - presence detectors in all corridors and public areas, as well as in all the offices at Saint-Denis – Pleyel,
    - low-energy light bulbs.

At the same time, all the radiators installed in the offices have been switched off or removed, as well as all the “high consumption” lamps (halogens in particular).

On the Saint-Denis – Pleyel site, the Agency's main site, savings of 16% in KWh have been recorded compared with electricity consumption in 2022, and 27% compared with that in 2021.

In addition, in-house information campaigns have been carried out to encourage environmentally friendly actions on a daily basis, both in the office and at home, and to develop more economical forms of transport, especially cycling, with the installation of bicycle shelters in the courtyard of the Saint-Denis agency.

Renovation and redevelopment of the Saint-Denis-Pleyel site

2023 saw the start of the project to refurbish and redevelop the premises at the Saint-Denis – Pleyel site, which was necessary both to free up the premises that the Agency rents alongside this site (Étoile), and to meet the obligations under the tertiary sector decree of the Elan Law.

After a phase dedicated to drawing up a programme of works and implementing the contractual materials (works contracts), the interior refurbishment works began at the end of 2023 and will continue throughout 2024. The work is being carried out in phases, and the teams are being relocated, department by department, as the finished premises are handed over.

During the preparation of the works programme, a number of smaller development projects were carried out on the Saint-Denis Pleyel site:

- replacement of the flooring and landscaping of the courtyard, with the installation of outdoor furniture and equipment;
- modification of the vehicle entrance, in connection with the work being carried out by the department in front of the Agency, in order to improve the access road to the new motorway interchange;
- creation of a “work café”, a space for social interaction and an “alternative workplace”.

2023 DATA

Revenue

Changes in ANSM revenue since 2019 (in thousands of €)

	2019	2020	2021	2022	2023
Health Insurance fund allocation	116,481	115,821	118,661	126,850	**137,430**
State subsidy	-	-	709	0	**507**
EMA	8,550	8,682	9,529	10,258	**10,796**
Other income from ongoing operations	1,237	1,430	1,300	1,504	**1,162**
Total operating income	126,268	125,934	130,199	138,612	**149,895**

The main source of revenue, accounting for almost 92% of the ANSM's total income, is the grant from the Assurance Maladie, which amounted to €137.43 M. It includes the additional portion allocated to the Agency in the summer of 2022 to take account of the increase in the value of the civil service index point, amounting to €1.51 M, which will actually be received in 2023.

The second main source of revenue comes from work carried out by the Agency for the EMA. This revenue, 5.2% higher than in 2022, is mainly due to work on new MA applications and variations, the annual tax relative to European marketing authorisations, and the scientific advice issued by the Agency.

Types of income in the 2023 financial account

	%
Health Insurance fund allocation	**91.7**
EMA	**7.2**
Other income from ongoing operations	**1.1**

	%
Scientific advice	11.4
New MA applications	11.0
Variations	31.4
Range extensions	2.0
Annual tax	31.5
Renewals	0.5
Inspections	4.6
Validation of translations	0.6
PSUR and PASS Pharmacovigilance	7.0

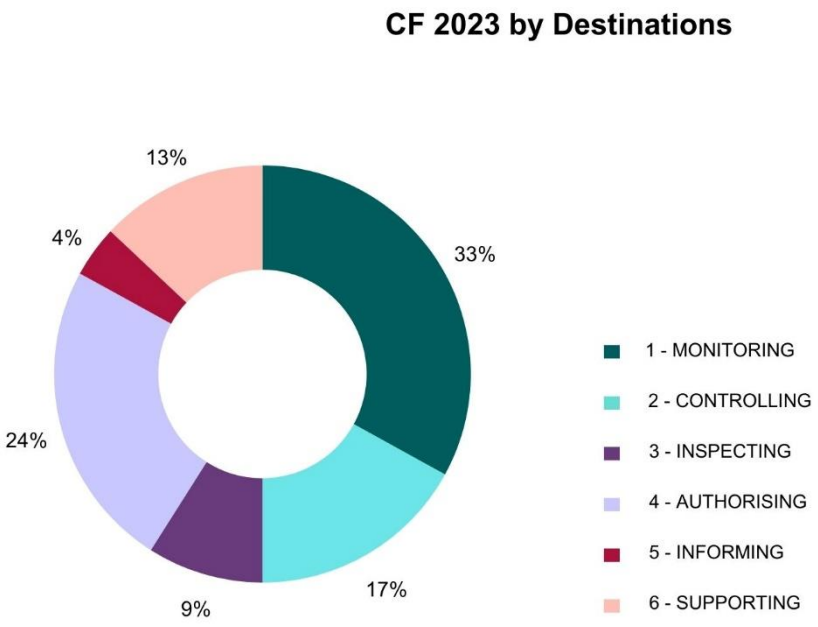
Expenditure

Expenditure by destination (calculated on the basis of actual time and activities)

Expenditure by destination was calculated on the basis of times and activities entered daily by ANSM employees, rather than on the basis of estimated figures as was the case in previous years. The time and activity management tool rolled out by the Agency means that it is now possible to carry out an increasingly precise analysis of the breakdown of the time dedicated to different missions. Cost-performance accounting has therefore been enhanced and the institution's management system reinforced.

The breakdown of expenditures by destination illustrates ANSM's major missions, namely five “business lines” comprising activities directly involved in carrying out the Agency’s missions, as well as the cross-cutting and steering activities directly associated with them, and a “support” destination.

Destinations	2023 Accounts (commitment authorisations – CA)	2023 Accounts (payment appropriations – PA)
1 – Monitoring	€48,540,719	€48,990,909
2 – Controlling	€21,518,452	€27,323,358
3 - Inspecting	€12,447,314	€12,655,067
4 - Authorising	€34,589,228	€35,388,081
5 – Informing	€6,091,455	€6,190,390
6- Supporting	€20,573,805	€18,982,393
Overall total	**€143,760,973**	**€149,530,199**



Expenditure by envelope

Changes in ANSM expenditure since 2019 (in millions of €)

	2019	2020	2021	2022	2023
Personnel	80	80.2	81.7	87.2	**89.4**
Operation	22.8	22.7	27.1	25.3	**24.9**
Intervention	9.6	9.3	13.6	23.9	**23.0**
Investment	8.1	4.5	7.5	6.1	**12.3**
Total payment appropriation expenditure	120.5	116.8	129.9	142.5	**149.5**

Staff: €89.4 million

The staff budget was implemented to the tune of €89,355,494 i.e. 97.72% of the second budget provision.

It includes:
- payroll: €88,169,930
- social actions: €557,927
- catering: €627,637

The execution of employment authorisations breaks down in the following manner:

Jobs	2023 authorisations	2023 execution	Execution rate
	FTE	**FTE**	**FTE**
Under ceiling	943	943	100%
Over ceiling	47.7	34.5	72.3%
Total	**990.7**	**977.5**	**98.7%**

Operation: €24.85 million

The operations envelope used €23,615,548 in CA and €24,853,603 in PA during the 2023 financial year, representing respective execution rates of 97.3% and 93.17% for CA and PA in relation to the available budget.

Intervention: €24.85 million

Intervention expenditure represented €23,241,675 in CA and €22,989,398 in PA, i.e. respectively 94.9% and 92.7%.

These intervention expenditures break down as follows:
- Vigilance networks: €21,444,668
- Epidemiology of health products): €1,313,097
- Other intervention expenditure: €231,634

Investment: €12.33 million

In 2023, investment expenditure represented €7,393,077 in CA (representing an execution rate of 59.7%), and €13,331,703 in PA (representing 81.1% of available appropriations).

The main areas of spending are generated by:

- IT: €2,562,672
- Real estate: €2,267,427
- Construction of laboratories in Lyon: €7,000,000
- Security: €16,118
- Laboratory equipment: €485,487

Expenditure	**2023 initial budget**	**2023 financial accounts**
Personnel	€91,440,131	€89,355,494
Operation	€26,675,060	€24,853,603
Intervention	€24,853,181	€22,989,398
Investment	€15,210,350	€12,331,703
Total expenditure	**€158,178,722**	**€149,530,199**
Budget surplus		**€365,783**

Income	**2023 initial budget**	**2023 financial accounts**
Health Insurance fund allocation	€135,920,000	€137,430,000
State subsidies	€266,277	€533,316
EMA income	€10,549,298	€10,796,504
Other resources	€1,249,999	€1,136,162
Total revenue	**€147,985,574**	**€149,895,982**
Budget deficit	**€10,193,148**	

Contracts

During the course of 2023, the Agency reported 82 new contracts (68 in 2022). The provisional total for these notified contracts is €28,485,758.65, up (by 60.2%) on 2022 (€17.78 M inclusive of tax). This increase is mainly due to the notification of works contracts, in particular for the refurbishment of the Saint-Denis – Pleyel premises, for a total of €11,880,000 including tax.

The total number of active contracts at ANSM is 376. The five main areas concerned are:

- the Controls Division with laboratory equipment and products, in particular;
- information systems, infrastructure and applications;
- real estate, general services and security;
- human resources management, with training and social actions;
- communication and information.

Breakdown by type of active contract

	%
Services (278 contracts)	74%
Supplies (86 contracts)	23%
Construction work (12 contracts)	3%

Breakdown by type of notified contract

	%
Services (61 contracts)	74%
Supplies (14 contracts)	17%
Construction work (7 contracts)	9%

Internal oversight of budgets and accounting

In 2023, the roll-out of ANSM's Internal Accounting and Budget Oversight mechanism (CICB) continued, revolving around three objectives:

- the objective of identifying the major accounting and budgetary risks in partnership with the risk management players (internal oversight - IO), the Quality Management System (QMS), performance steering) and the process managers represented by the authorising officer, the Finance and Administration Division (DAF), the Human Resources Division and the Accounting Office;
- analysis of the system and actions liable to have a significant financial impact and/or a high probability of occurrence of a risk;
- the implementation of control measures or actions for each risk, with the drafting of control sheets.

The risk mapping and action plan were presented to the Management Board on 09 March 2023. The risk analysis concerns the Finance Management process and the Human Resources Management process (authorising officer component):

- 45 risks and 45 actions to be monitored:

Risk summary table CICB 2023	**Net risk**	**Net risk**
Process	**Managing finances**	**Managing human resources**
Very high risks	0	0
High risks	0	0
Moderate risk	5	1
Low risk	31	8
Total RISKS	36	9
Number of risks in the Internal Accounting and Budget Oversight mechanism (CICB) map 2023	45	

The system and the actions rolled out by the actors involved in the CICB were deemed to be “relevant and satisfactory” by the Department of Finance, Procurement and Services (DFAS) for 2023.

With the new financial liability regime for public managers due to come into force on 1st January 2023, the CICB's activities were carried out against this backdrop of regulatory reform and the desire to consolidate an environment conducive to risk management.

This work was carried out in coordination with risk management, the quality management system and the public managers responsible for the management chain.

Glossary

3R	Reduce, Replace, Refine
AAC	Autorisation d'accès compassionnel [Compassionate access authorisation]
AAP	Autorisation d'accès précoce [Early access authorisation]
AE	Autorisation d'engagement [Commitment authorisation (CA)]
AIFA	Agenzia Italiana del Farmaco [Italian Medicines Agency]
AIMD	Active implantable medical devices
AIP	AIP Autorisation d'importation parallèle [Parallel import authorisation]
ALCL	Anaplastic large-cell lymphoma
AMA	African Medicines Agency
ANMV	Agence nationale du médicament vétérinaire [French National Veterinary Medicines Agency]
ANSES	Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail [French Agency for Food, Environmental and Occupational Health Safety]
ANSM	Agence Nationale de Sécurité du Médicament et des Produits de Santé [French National Agency for Medical and Health Product Safety]
AP-HP	Assistance Publique – Hôpitaux de Paris [Public Assistance – Hospitals of Paris]
ARS	Agence régionale de santé [Regional health agency]
ASCO	American Society of Clinical Oncology
ASR	Annual Safety Reports
ATMP	Advanced therapy medicinal product
ATU	Autorisation temporaire d'utilisation [Temporary Authorisation for Use, a French early access programme]
ATUc	Autorisation temporaire d'utilisation de cohorte [Cohort Temporary Authorisation for Use, a French early access programme]
ATUn	Autorisation temporaire d'utilisation nominative [Named-Patient Temporary Authorisation for Use, a French early access programme]
AV	Addiction vigilance
AVFIN	Aide aux victimes du finastéride [French Association to help finasteride victims]
BCG	Bacillus Calmette–Guérin vaccine (tuberculosis vaccine)
BD	Blood donor
BDM	Blood-derived medicinal products
BEMA V	European benchmarking
BIA-ALCL	Breast-implant-associated anaplastic large-cell lymphoma
BMRFin	Bureau de la maîtrise des risques financiers [Financial Risk Management Office]
BNPV	Base Nationale de Pharmacovigilance [French national pharmacovigilance database]
BRAF	B-raf proto-oncogene
BRAFi	B-raf proto-oncogene inhibitors
CAARUD	Centres d'accueil et d'accompagnement à la réduction des risques pour usagers de drogues [French support centres for the reduction of risks to drug users]
CADA	Commission d'accès aux documents administratifs [Commission for access to administrative documents]
CAMD	Competent Authorities for Medical Devices
CAP	Centrally Authorised Products
CAT	Committee for Advanced Therapies (committee attached to the EMA)
CEIP	Centre d'Evaluation et d'Information sur la Pharmacodépendance [French Centre for Evaluation and Information on Pharmaceutical Drug Dependence]

CEIP-A	Centres d'évaluation et d'information sur la pharmacodépendance-addictovigilance [Drug dependence-addiction evaluation and information centres]
CFP	Comités français de la Pharmacopée [French Pharmacopoeia committees]
CFTR	Cystic fibrosis transmembrane conductance regulator
CHMP	Committee for Medicinal Products for Human Use (committee attached to the EMA)
CHSCT	Comité d'hygiène, de sécurité et des conditions de travail [Health and Safety committee]
CI	Clinical investigations
CIANE	Collectif inter-associatif autour de la naissance [French group of childbirth associations]
CICB	Contrôle interne comptable et budgétaire [Internal accounting and budget control]
CLL	Chronic lymphocytic leukaemia
CMDH	Coordination group for mutual recognition and decentralised procedures - Human (committee attached to the HMA)
CMG	Collège de la médecine générale [French College of General Medicine]
CNAM	Caisse nationale d'assurance maladie [French National Health Insurance Fund]
CNGOP	Collège national des gynécologues et obstétriciens français [National College of French Gynaecologists and Obstetricians]
CNIL	Commission nationale de l'informatique et des libertés [French Data Protection Authority]
CNPCV	Conseil national professionnel cardiovasculaire [French national council for cardiovascular professionals]
CNR	Centre national de référence [French National Reference Centre]
CNRS	Centre national de la recherche scientifique [National Scientific Research Centre]
CNS	Central nervous system
COFRAC	Comité français d'accréditation [French Accreditation Committee]
COMP	Committee for orphan medicinal products (committee attached to the EMA)
COP	Contrat d'objectifs et de performance [Objectives and Performance Contract]
CP	Convalescent plasma
CPAP	Continuous Positive Airway Pressure
CPC	Cadre de prescription compassionnelle [Compassionate prescription framework]
CPD	Conditions de prescription et de délivrance [Prescribing and dispensing conditions]
CPP	Comité de protection des personnes [Ethics Committees]
CRH-ST	Coordonnateurs régionaux d'hémovigilance et de sécurité transfusionnelle [regional haemovigilance and transfusion safety coordinators]
CRM	Customer Relationship Management
CRPV	Centre régional de pharmacovigilance [Regional pharmacovigilance centre]
CSAPA	Centres de soin d'accompagnement et de prévention en addictologie [Addiction prevention, support and treatment centres]
CSP	Code de la Santé Publique [French Public Health Code]
CSP	Comité scientifique permanent [Permanent scientific committee]
CST	Comité scientifique temporaire [Temporary scientific committee]
CT	Clinical Trials
CT	Clinical trial
CTA	Clinical trial authorisation
CTA	Coordination territoriale d'appui [local coordination support mechanism]
CTCG	Clinical Trials Coordination Group
CTFG	Clinical Trials Facilitation Group
CTIS	Clinical Trials Information system
CTP	Cell therapy preparation
CTR	Clinical Trials Regulation

CTROL	Direction des contrôles [ANSM Controls Division]
CVA	Cerebrovascular accident (stroke)
D	Direct Healthcare Professional Communications
DAF	Direction de l'administration et des finances [Finance and Administration Division (ANSM)]
DCP	Decentralised procedure
DFAS	Direction des finances, achats et services [Department of Finance, Procurement and Services of the General Secretariat of the Social Ministries]
DG	Directorate General
DG SANTE	Direction générale de la santé et des consommateurs [French Ministry of Health and Consumers]
DGCCRF	Direction générale de la consommation, de la concurrence et de la répression des fraudes [French Directorate General for Fair Trade, Consumer Affairs, and Fraud Control]
DGDDI	Direction générale des douanes et des droits indirects [Directorate General of Customs and Excise Duties]
DGS	Direction générale de la Santé [French Ministry of Health]
DIVAS	Miscellaneous other signals
DMCDIV	Direction médicale des dispositifs médicaux et dispositifs de diagnostic in vitro [Division for Medical Devices, Cosmetics and in vitro Diagnostic Devices
DMFR	Direction de la maîtrise des flux & référentiels [Division for Data Flows & Repositories (ANSM)]
DNA	DeoxyriboNucleic Acid
DNS	Délégation ministérielle au Numérique en Santé [French Ministerial delegation for digital health]
DPI	Déclaration publique d'intérêts [Public conflict-of-interest statement]
DRH	Direction des ressources humaines [Human Resources Division]
DROM	Départements et régions d'outremer [French overseas regions]
DSI	Direction des systèmes d'information [Information Systems Division]
DSS	Direction de la Sécurité sociale [French Social Security Department]
DTaP – IPV – HiB – HepB	Diphtheria, tetanus, pertussis, polio, haemophilus influenzae type B, hepatitis B
EC	European Commission
ECDC	European Centre for Disease prevention and Control
EDM	Electronic document management
EDQM	European Directorate for the Quality of Medicines & HealthCare
EEA	European Economic Area
EFS	Etablissement français du sang [French National Blood Service]
EMA	European Medicines Agency
EMACOLEX	European Medicines Agencies Co-operation of Legal and Legislative Issues (committee attached to the HMA)
EMRN	European Medicines Regulatory Network
ENT	Ear-nose-throat
ESAT	Etablissement ou services d'aide par le travail [Protected work facility for disabled people]
ESMP	European Shortages Monitoring Platform
EU	European Union
EU IN/EU Innovation	European innovation network
EUDAMED	European database on medical devices
EUROPOL	European Union Agency for Law Enforcement Cooperation
EZH2:	Enhancer of zeste homolog 2
FAMHP	Federal Agency for Medicines and Health Products
FAS	France Assos santé
FDA	Food and Drug Administration (US FDA)
FEV1	Forced expiratory volume per second
FSPF	Fédération des syndicats pharmaceutiques de France [Federation of French pharmaceutical unions]

G-CSF	Granulocyte – Colony Stimulating Factor
GERS	Groupement pour l'élaboration et la réalisation de statistiques (French group for the development and production of statistics)
GHS	Groupe homogène de séjours [diagnosis-related group]
GIO	Guichet innovation et orientation [Innovation and referral service]
GLP	Good Laboratory Practice
GLP-1	Glucagon-like reptide-1
GMED	Groupement pour l'évaluation des dispositifs médicaux [Medical device evaluation group]
GP	General public
GPP	Good Preparation Practice
GRIO	Groupe de recherche et d'informations sur les ostéoporoses [Osteoporosis research and information group]
GVP	Good Pharmacovigilance Practice
HAS	Haute autorité de santé [French National Health Authority]
HATVP	Haute autorité pour la transparence de la vie publique [French High Authority for the Transparency of Public Life]
HCSP	Haut Conseil de la santé publique [French High Council for Public Health]
HIV	Human Immunodeficiency Virus
HMA	Heads of Medicines Agencies
HMPC	Committee on Herbal Medicinal Products (committee attached to the EMA)
HMPWG	Homeopathic Medicinal Products Working Group (committee attached to the HMA committee)
HPS	Hors produits de santé [Non-health products]
HRS	High-risk situation
HSP	Home healthcare service provider
IA	Import authorisation
ICMRA	International Coalition of Medicines Regulatory Authorities
ICSR	Individual case safety report
IEG	Identification par empreintes génériques [DNA profiling]
IGAS	Inspection générale des affaires sociales [Inspectorate General of Social Affairs]
IgG1	Immunoglobulin G1
IGR	Institut Gustave Roussy
INCA	Institut national du cancer [French National Cancer Institute]
INN	International Non-proprietary Name
IO	Internal oversight
IS	Information system
ISO	International Organisation for Standardisation
IT Directors	Information Technology Directors
ITCC	Innovative Therapies for Children with Cancer
IU	International Unit
IVD	In vitro diagnosis
IVDMD	In vitro diagnostic medical device
IVG	Interruption volontaire de grossesse [Voluntary termination of pregnancy, abortion]
JAK	Janus Kinases
JAMA	Journal of the American Medical Association
LBP	Labile blood product
Leem	Les entreprises du médicament [French pharmaceutical industry organisation]
LFSS	Loi de financement de la sécurité sociale [French Social Security Financing Act]
LYSARC	Lymphoma Academia Research Organisation
MA	Marketing authorisation
MARR	Mesures additionnelles de réduction du risque [additional risk reduction measures]
MD	Medical device
MDCG	Medical devices coordination group

MDITF	Medical Devices Inspectors Task Force
MEK	Methylethylketone
MEKi	Methylethylketone inhibitors
MG	Milligram
MI	Myocardial infarction
MIA	Multiplex Immunoassay
MIG	Mission d'intérêt général [General interest mission]
MITM	Médicament d'intérêt thérapeutique majeur [Medicine of major therapeutic interest]
ML	Millilitre
MOT	Pathogenic microorganisms and toxins
MP	Publicité médicale [medical advertising]
mpox	Monkeypox
MRI	Magnetic Resonance Imaging
mRNA/messenger RNA	Messenger ribonucleic acid
MRP	Mutual Recognition Procedure
MS	Market Surveillance
MS	Multiple sclerosis
MSA	Modification substantielle d'essais cliniques pour autorisation [Application to authorise substantial amendments to clinical trials]
MSC	Member state concerned
MSM	Men who have sex with men
MSSG	Medicines Shortages Steering Group
MTI-PP	Médicament de thérapie innovante préparé ponctuellement [Advanced therapy medicinal product prepared on an ad hoc basis]
MVF	Multiple vertebral fractures
NAAT	Nucleic acid amplification tests
NB	Notified body
NBO	Notified Bodies Oversight
NCWP	Non-clinical Working Party
NFP	National Focal Point
NotS	Notifications
OCABR	Official Control Authority Batch Release
OECD	Organisation for Economic Cooperation and Development
OMCL	Official Medicines Control Laboratories
ONDAM	Objectif National des Dépenses de l'Assurance Maladie [French National health insurance spending target]
OSIAP	Ordonnances suspectes, indicateur d'abus possible [Suspect prescriptions, an indicator of possible abuse]
OTC	Organs tissues cells
PA	Payment appropriations
PASS	Post-authorisation safety studies
PDCO	Paediatric Committee (committee attached to the EMA)
PEG G-SC	Polyethylene glycol granulocyte-colony stimulating factor
PFUE	French Presidency of the Council of the European Union
PHEIC	Public health emergency of international concern
PHP	Public health policy
PIA	PIC/s Inspection Academia
PIC/S	Pharmaceutical inspection Co-operation Scheme
PIP	Paediatric Investigation Plan
PRAC	Pharmacovigilance Risk Assessment Committee (committee attached to the EMA)
PrEP	Pre-exposure prophylaxis
PS	Performance study
PSR	Psycho-social risks
PSUR	Periodic Safety Update Report
PUT	Protocole d'utilisation temporaire [temporary use protocol]

PUT	Protocole d'utilisation thérapeutique [therapeutic use protocol]
PV	Pharmacovigilance
Q	Association des lactariums de France [French Association of Breast Milk Banks]
QIG	Quality Innovation Group
QMS	Quality Management System
RDT	Rapid diagnostic test
RETEX	Retour d'expérience [Feedback]
RGP	Responsabilité financière des gestionnaires publics [financial liability of public managers]
RICAI	Réunion Interdisciplinaire de chimiothérapie Anti-Infectieuse [Interdisciplinary meeting on anti-infectious chemotherapy]
RIPH1	Recherche impliquant la personne humaine [Human research 1]
RMP	Risk Management Plan
RMS	Reporting Member State
RSU	Rapport social unique [Single social report]
RTU	Recommendation Temporaire d'Utilisation [Temporary recommendation for use, a French early access programme]
RWE	Real world evidence
saMs	safety Member state
SAMU	Service d'aide médicale urgente [French emergency medical services]
SARS-COV-2	Severe acute respiratory syndrome coronavirus 2
SAWP	Scientific Advice Working Party (working group attached to the EMA)
SDSID	Schéma directeur des systèmes d'information et de la donnée [Information and Data Systems Master Plan]
SER	Social and environmental responsibility
SFC	Société française de cardiologie [French Cardiology Society]
SFCE	Société française de lutte contre les Cancers et les leucémies de l'Enfant et de l'adolescent [French society for childhood and teenage cancers and leukaemias]
SFN	Société française de néonatologie [French Neonatology Society]
SFO	Société française d'ophtalmologie [French Ophthalmology Society]
SFP	Société française de pédiatrie [French Paediatric Society]
SFR	Société française de rhumatologie [French Rheumatology Society]
SGA	Streptococcus group A
SI-DEP	Système d'information de dépistage [Screening information system]
SIRHIUS	Système d'information de réception, de hiérarchisation et de pilotage des urgences sanitaires [Information system for receiving, ranking, and managing emergencies]
SmPC	Summary of Product Characteristics
SNDS	Système national des données de santé [French National Health Database] (formerly SNIIRAM)
SNPHPU	Syndicat national des pharmaciens hospitaliers [French national union of hospital pharmacists]
SNS	Stratégie nationale de la santé [French National Health Strategy]
SNSA	Simultaneous national scientific advice
SpF	Santé publique France
SPOC	Medicines Shortages Single Point of Contact
SSE	Situation sanitaire exceptionnelle [Exceptional health situation]
SUSAR	Suspected unexpected serious adverse reaction
T21	Trisomy 21
TNFα	Tumor Necrosis Factor
TPE	Très petite entreprise [micro-company]
TTC	Toutes taxes comprises [inclusive of tax]
UGT1A1	UDP-glycosyltransferase 1 polypeptide A1
UMR	Unité mixte de recherche [Mixed research unit]
UNC	Usage non-conforme [non-compliant use]

USPO	Union des Syndicats de Pharmaciens d'Officine [Retail Pharmacists' Trade Union]
VAC-SI	COVID-19 vaccine information system
VES	Vigilance expert subgroup
VOC	Volatile organic compounds
VPN	Virtual private network
WFTE	Worked full-time equivalent
WG	Working group
WG	Working group
WGCP	Working Group of Communication Professionals (committee attached to the HMA)
WGEO	Working Group of Enforcement Officers (committee attached to the HMA)
WHO	World Health Organisation

Appendices

Acting in complete transparency through dialogue and openness

Ensuring the safety of patients exposed to medicines and health products

Facilitating patient access to innovative treatments

Moving forward, drawing on our resources

Acting in complete transparency through dialogue and openness

APPENDIX 1: CONSULTATION AND MULTIDISCIPLINARITY - THE WORK OF OUR ADVISORY BODIES

Standing Scientific Committees (January to August 2023)	Date of creation and appointment of members	Number of meetings in 2023
Labile blood products and blood donors	29/07/2019	1
Therapy and cardiovascular risk	12/07/2019	2
Dermatology medicines	29/07/2019	2
Diagnostic and nuclear medicine medicinal products	29/07/2019	2
Oncology and haematology	29/07/2019	3
Safety and quality of medicines	12/07/2019	1
Promotion of safe use of medicines	12/07/2019	3
Reproduction, pregnancy and lactation	12/07/2019	3
Paediatrics	29/07/2019	2
Psychotropics, narcotics and addictions	12/07/2019	3
Monitoring and pharmacovigilance	12/07/2019	11
Haemovigilance	29 July 2019	2
Medical device vigilance and reagent vigilance	12/07/2019	3
Interface with the toxicovigilance network	12/07/2019	2
Quality control of medical devices	29/07/2019	22

Standing scientific committees (September to December 2023)	Date of creation and appointment of members	Number of meetings in 2023
QUality control of medical devices	27/07/2023	7
Haemovigilance	27/07/2023	2
Interface with the toxicovigilance network	27/07/2023	1
Infectious and emerging diseases	27/07/2023	1
Dermatology medicines	27/07/2023	2
Diagnostic and nuclear medicine medicinal products	27/07/2023	1
Oncology and haematology	27/07/2023	1
Paediatrics	27/07/2023	1
Pharmaco-surveillance and proper use	27/07/2023	8
Labile blood products and blood donors	27/07/2023	1
Psychotropics, narcotics and addictions	27/07/2023	5
Quality and safety of medicines	27/07/2023	2
Reproduction, pregnancy and lactation	27/07/2023	5
Surveillance of medical devices and in vitro diagnostic medical devices	27/07/2023	2
Therapy and cardiovascular risk	27/07/2023	1

Temporary scientific committees	Date of creation and appointment of members	Number of meetings in 2023
Analysis of the Use of GLP-1 Analogues	14/12/2023	1
Initial analysis of MetaPreg studies	07/10/2022	1
Changes in the dispensing circuit for medicines indicated for the treatment of haemophilia and other rare bleeding disorders – finalisation of work	16/05/2023	1
Progestins and the Risk of Meningioma	13/01/2023	3
Reassessment of the pictogram on the outer packaging of teratogenic or foetotoxic medicinal products	24/01/2023	16
Monitoring of French trials on medicinal cannabis use	08/06/2021	8
Virology and emerging viruses	21/02/2023	2

Standing French Pharmacopoeia Committees (January to December 2023)	Date created and appointment of members	Number of meetings in 2023
Biological Products and Advanced Therapy Medicinal Products	09/07/2021	1
Chemical, Pharmaceutical and Radiopharmaceutical Substances and Preparations - Galenical	09/07/2021	4
Medicinal Plants, Essential Oils and Homeopathy	09/07/2021	5

APPENDIX 2: DIALOGUE AND INFORMATION SHARING WITH OUR STAKEHOLDERS

Changes in the number of different visitors to the ANSM website

Number of different visitors[42]	2019	2020	2021	2022	2023
January	339,968	390,881	480,341	637,185	417,502
February	291,605	359,406	445,591	371,319	357,004
March	288,563	459,741	218,867	297,619	417,219
April	315,315	431,090	338,698	307,464	462,814
May	302,681	377,966	357,502	269,560	320,863
June	304,458	316,969	312,843	273,808	320,170
July	287,225	282,922	531,491	300,323	253,673
August	257,573	267,409	640,879	252,229	254,502
September	305,968	324,631	397,853	333,312	395,509
October	330,257	346,630	362,185	360,727	422,453
November	366,798	369,017	467,899	402,950	402,730
December	320,397	361,533	561,140	396,215	380,187
Total for the year	3,710,808	4,209,711	5,115,289	4,209,711	4,404,626

[42] One visitor = one IP address

ANSM SCIENTIFIC PUBLICATIONS IN 2023

Interventions carried out and posters produced in 2023

Scientific posters

- S. Fosset, Comparison of measurements of “contact force” in multi-dose eyedrops used to treat glaucoma: are there any differences?, SFO Congress, Paris (France), 6-8 May 2023.
- E. Parpaillon, A. Jeanjean, D.Chauvey, Numerical study of the deployment of a femoral artery self-expanding nitinol stent, Annual Congress of the Biomechnics Society, Grenoble (France), 25-27 October 2023.
- National map of erythrocyte alloimmunisations reported between 2010 and 2020, R Boukhari, K Boudjedir. 21st SFTS Congress, Toulouse, November 2023.
- *Post Donation Information in Haemovigilance: the French experience*, S Drougard, I Sandid, K Boudjedir, C Freyche, M Fromage, AM Lenzotti, C Matko, I Sainte-Marie, I Yoldjian. 33rd ISBT Congress (International Society of Blood Tranfusion), Gothenburg, June 2023.
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- Botton, J., Bertrand, M., Jabagi, M.-J., Bouillon, K., Drouin, J., Baricault, B., Semenzato, L., Le Vu, S., Weill, A., Zureik, M., & Dray-Spira, R. (2023). COVID-19 vaccination and hospitalization for heavy menstrual bleeding in 15-50 year-old women: A case-control study using the French nationwide SNDS database. 39th International Conference on Pharmacoepidemiology & Therapeutic Risk Management, ICPE, Halifax (Canada), August 23-27, 2023.
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Presentations at conferences

- D. Chauvey, E. Parpaillon, New European Regulation on MDs and E .Parpaillon's thesis, Annual Meeting of OMCLs, Madrid (Spain), 06/06/2023.
- J.C. Ourlin, P. Guinot, Use of a biological approach to search for prohibited plants. Annual meeting of OMCLs, Madrid (Spain), 06/06/2023.
- Y. Grange, Optimisation of microbiological controls, Annual meeting of OMCLs, Madrid (Spain), 06/06/2023.
- F. Cano, Implementation of the 3Rs over the years – an OMCL perspective, Annual Meeting of OMCLs, Madrid (Spain), 07/06/2023
- F. Duperray, OCABR of IV and SC immunoglobulins; strategy review for anti-D testing, annual meeting of OMCLs, Madrid (Spain), 08/06/2023.
- Y. Grange, Common guidance for interaction with manufacturers, Annual Meeting of OMCLs, Madrid (Spain), 09/06/2023.
- C. Civade, Implementation of a risk analysis during the assessment of applications. Training course on HMA Risk Assessment Tool of Human and Veterinary Medicinal Products, Tallin (Estonia). 02-03/10/2023.
- S. Cauchard, AdG-CAP activities since last CAP Annual Meeting, CAP annual meeting, Strasbourg (France). 15/11/2023.
- Y. Grange, Optimisation of surveillance programmes for generics CAP. CAP annual meeting, Strasbourg (France), 16/11/2023.
- Y. Grange, Collaborative Study Project for the Testing of Inhaler Products: Status report. CAP annual meeting, Strasbourg (France). 16/11/2023.
- V. Ridoux, AAV infectious titre determination, Networks of OMCLs in GT, Copenhague (Denmark), 30/11-01/12/2023.
- Regional event on “MD and IVDMD Security and Vigilance”, 6 April 2023, in Lyon (69). ANSM presentation: Medical device vigilance incidents: how does ANSM assess them?
- IVDMD Forum on 9 November 2023, organised by the GMED: issues relating to the implementation of Regulation (EU) 2017/746. Two ANSM presentations:
    a. Activities of the competent authority in the implementation of Regulation (EU) 2017/746
    b. EUDAMED database: status of functionalities and modules, work in progress and calendar to date

- Scientific days of the French Society of Medical Physics from 7 to 9 June 2023. ANSM presentation: review of quality control decisions in radiotherapy.
- “Journées francophones” (French-Language Days) for users of the clinical pharmacy decision-support system in Lille on 7 June 2023. ANSM presentation: Medical device vigilance circuit relating to pharmacy decision-support systems.
- SNITEM conference on 26 September 2023: New MD Regulation: initial assessment of the new transitional period and outlook. Participation in the “Extending the transition period” session, 1st assessment.
- Meeting with ANSM organised in Paris by IFIS on 15 December 2023. Participation in the workshop on the attractiveness of clinical research in France and European regulations.
- 5th meeting in 2003 on “Early Phases in Oncology” in Issy-les-Moulineaux on 30 November 2023. Participation in the round-table discussion: “2023 review and views on France's attractiveness for early stages in oncology.
- Biomedical Engineering Days organised by AFIB in Bordeaux from 27 to 29 September 2023. ANSM presentation: “Preventing stockouts and shortages of medical devices: A new mission for professionals.”
- Team_PCCR Annual Summit held in Strasbourg from 16 to 17 November 2023. ANSM presentation: Legal interpretation of Article 15 by the competent authorities.
- Overview of haemovigilance in France, with a focus on TACO.
- K Boudgedir, I Sandid, S Drougard, C Freyche, M Fromage, AM Lenzotti, C Matko, I Sainte-Marie. 21st Congress of the French Blood Transfusion Society (SFTS), Toulouse, November 2023
- Analysis of adverse transfusion events following platelet concentrate transfusion from 2007 to 2021.
- K Boudgedir, G Andreu, M Carlier, C Drouet, P-M Mertes, J-Y Py, C-A Tacquard. 21st Congress of the SFTS, Toulouse, November 2023
- Microbiota and Health Day, Laure de Ligniville, National and European Regulatory Prospects for Medicinal Products Derived from Faecal Microbiota, https://journee-microbiotes-et-sante-2023.b2match.io/page-2261
- Académie nationale de pharmacie, Pharma 4.0 Day: Dream and Reality. Valérie Salomon and Dr. Leticia Martinez-Peyrat, ANSM's Innovation and Referral Service: an Organisation Dedicated to the Development of Innovative Products – Focus on Innovative Manufacturing Processes, https://www.acadpharm.org/seances/page.php?id_doc=6549
- Bamouni, S., Billioti de Gage, S., Desplas, D., Valbousquet, J., Lamant, J., Joseph, J.-P., Dabis, F., Viot, A., Fakir, S., Dray-Spira, R., & Carles, M. (2023). Implementation of the first prescription of PrEP in the non-hospital sector in France between June 2021 and December 2022. 24th SFLS Congress, Tours (France), 6-8 December 2023.
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- Jourdain, H., Hoisnard, L., Sbidian, E., & Zureik, M. (2023a). Persistence on treatment with anti-TNF alpha, biosimilar or originator: An equivalence study based on SNDS data. 36th French Rheumatology Congress, Paris (France), 10-12 December 2023.
- Jourdain, H., Hoisnard, L., Sbidian, E., & Zureik, M. (2023b). Persistence on treatment and safety of TNF-alpha inhibitors biosimilars compared to originators: An observational study on the French National Health Data System. 39th International Conference on Pharmacoepidemiology & Therapeutic Risk Management, ICPE, Halifax (Canada), August 23-27, 2023.
- Jourdain, H., Hoisnard, L., Sbidian, E., & Zureik, M. (2023c). Use of anti-TNF alpha biosimilars in France A study based on SNDS data. EMOIS Congress, Nancy (France), 16-17 March 2023. https://www.snfge.org/content/les-jfhod
- Jourdain, H., Hoisnard, L., Sbidian, E., & Zureik, M. (2023d). Use of Rituximab and hypersensitivity reactions: A study on the National Health Data System. EMOIS Congress, Nancy (France), 16-17 March 2023.
- Le Vu, S., Bertrand, M., Botton, J., Jabagi, M.-J., Drouin, J., Semenzato, L., Weill, A., Dray-Spira, R., & Zureik, M. (2023). Risk of Guillain-Barré syndrome following Covid-19 vaccines : A nationwide self-controlled case series study. 39th International Conference on

Pharmacoepidemiology & Therapeutic Risk Management, ICPE, Halifax (Canada), August 23-27, 2023.

- Meyer, A. (2023a). Benefits and risks associated with continuing anti-TNF therapy after 24 weeks of pregnancy in women with inflammatory bowel disease. “Journées francophones” (French-Language Days) for Hepatogastroenterology and digestive oncology, JFHOD, Paris (France), 16-19 March 2023.
- Meyer, A. (2023b). Risk of cancer in children exposed to thiopurines and anti-TNF alpha during pregnancy. Journée francophones d'hépato-gastroentérologie et d'oncologie digestive, JFHOD, Paris (France), 16-19 March 2023.
- Neumann, A. (2023). PMSI data on outpatient activity in the field of psychiatry: Did chaining with inter-scheme healthcare utilisation data (DCIR) become possible in 2021? REDSIAM Group, 16-17 March 2023.
- Neumann, A., Dayani, P., Duranteau, L., Yoldjian, I., Zureik, M., Froelich, S., & Weill, A. (2023). Highly effective measures to reduce the risk of intracranial meningioma associated with prolonged high-dose use of the progestogen cyproterone acetate in France. EMOIS Congress, Nancy (France), 16-17 March 2023.
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- V.Ridoux, S. Laurens, S. Venturini, D.Le Tallec, A. Costanzo, Validation of a qPCR method for determination of viral genome titres of AAV2-based vector preparations, *Pharmeuropa Bio.* September 2023.

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  Michel Guerbet, Joel Guillemain, Isabelle Fabre, Gaelle Louin, Valérie Salomon, National reflection on organs-on-chip for drug development: New regulatory challenges, Toxicology Letters. September 2023
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- Book: Regulatory Aspects of Gene Therapy and Cell Therapy Products - A Global Perspective. Marie-Thérèse Duffour is one of the authors of the chapter entitled "European Pharmacopoeia's Approach to Cell and Gene Therapy": Focus on How Gene Therapy Texts Are Evolving". https://link.springer.com/book/10.1007/978-3-031-34567-8
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APPENDIX 3: ROBUST LEGAL AND REGULATORY ACTIVITY

Change in the number of financial sanctions imposed by ANSM

Sector	Field of activity	2019	2020	2021	2022	2023
Medical device	Advertising	0	1	0	**0**	**0**
	Marketing	0	0	3	**0**	**0**
	Medical device vigilance	0	0	0	**0**	**0**
Pharmaceutical site	Good Distribution Practice	0	2	1	**0**	**0**
	Public service obligations	0	0	2	**1**	**0**
	Good Manufacturing Practice	-	1	0	**0**	**0**
Medicines	Advertising	1	0	0	**0**	**0**
	Stockouts	2	2	0	**2**	**6** **3**-information failure/delay, **3**-safety stock not built up
Raw material for pharmaceutical use	Good Manufacturing Practice	0	1	0	**2**	**0**
Total		3	7	6	**5**	**6**
Total (euros)		264,175	1,269,325	508,048	445,360	**559,809.62**

OVERVIEW OF MAJOR FRENCH AND EUROPEAN TEXTS PUBLISHED (EXCLUDING COVID-19 TEXTS), HEALTH DECISIONS, INDIVIDUAL DECISIONS, PARALLEL IMPORT AUTHORISATIONS, MAS, PLANTS, HOMEOPATHY AND OUTSIDE THE ORGANISATIONAL STRUCTURE OF THE AGENCY AND ITS BODIES

MEDICINES

COMMUNITY TEXTS

Council Decision (EU) 2023/567 of 9 March 2023 on the position to be taken, on behalf of the European Union, in the 66th session of the Commission on Narcotic Drugs on the scheduling of substances under the Single Convention on Narcotic Drugs of 1961, as amended by the 1972 Protocol, and the Convention on Psychotropic Substances of 1971

NATIONAL TEXTS

Decree No. 2023-202 of 25 March 2023 regarding the extension of the trial of the medical use of cannabis
Decree 2023-303 of 21 April 2023 setting the time frame mentioned in 1° of VIII of Article L. 5121-12-1 of the French Public Health Code (early access)
Decree 2023-1113 of 28 November 2023 on the authorities responsible for the supervision and vigilance of cosmetic and tattoo products
Decree 2023-1224 of 20 December 2023 on the labelling of each unit of packaging for products exclusively containing nitrous oxide
Order of 25 March 2023 amending the order of 16 October 2020 laying down the specifications for cannabis-based medicinal products used during the trial provided for in Article 43 of the 2020 Social Security Funding Act No. 2019-1446 of 24 December 2019, the terms of their supply, as well as the therapeutic indications or clinical circumstances in which they will be used
Order of 25 March 2023 amending the Order of 29 October 2020 laying down the technical terms and conditions of the national electronic register provided for in Article 4 of Decree No. 2020-1230 of 7 October 2020 on the trial of the medical use of cannabis
Order of 25 March 2023 amending the Order of 29 December 2020 laying down the terms of the voluntary participation of doctors and pharmacists in the trial, provided for in Article 43 of Law No. 2019-1446 of 24 December 2019 on the financing of the French social security system for 2020, as well as the conditions for compulsory prior training and remuneration of healthcare professionals taking part in this trial
Order of 18 December 2023 supplementing the Order of 12 April 2022 defining the list of biosimilar groups that can substituted by retail pharmacists and the conditions for this substitution, and for informing the prescriber and patient as provided for in 2° of Article L. 5125-23-2 of the French Public Health Code.

BIOLOGICAL PRODUCTS

NATIONAL TEXTS

Decree 2023-453 of 9 June 2023 on the development of screening for anti-A and anti-B immune antibodies at the time of each donation of blood or blood components
Decree 2023-672 of 27 July 2023 on the authorisation of the collection of faeces and the importation of faeces or faecal microbiota preparations
Decree 2023-673 of 27 July 2023 on the regulation of the collection of faeces and the importation of faeces or faecal microbiota preparations

Decree 2023-711 of 31 July 2023 relating to the automated national register for refusing organ removal and to the conservation and distribution of tissues and their derivatives authorised in accordance with Article L. 1243-2 of the Public Health Code

MEDICAL DEVICES AND IN VITRO DIAGNOSTIC MEDICAL DEVICES

COMMUNITY TEXTS

Commission Delegated Regulation (EU) 2023/503 of 1st December 2022, amending Regulation (EU) 2017/746 of the European Parliament and of the Council as regards the frequency of complete re-assessments of notified bodies (published in March 2023)
Commission Delegated Regulation (EU) 2023/502 of 1st December 2022, amending Regulation (EU) 2017/745 of the European Parliament and of the Council as regards the frequency of complete re-assessments of notified bodies (published in March 2023)
Regulation (EU) 2023/607 of the European Parliament and of the Council of 15 March 2023, amending Regulations (EU) 2017/745 and (EU) 2017/746 as regards the transitional provisions for certain medical devices and in vitro diagnostic medical devices
Commission Delegated Directive (EU) 2023/1526 of 16 May 2023, amending Directive 2011/65/EU of the European Parliament and of the Council as regards an exemption for lead as a thermal stabiliser in polyvinyl chloride used as base material in sensors used in in vitro diagnostic medical devices
Regulation (EU) 2023/1542 of the European Parliament and of the Council of 12 July 2023 concerning batteries and waste batteries, amending Directive 2008/98/EC and Regulation (EU) 2019/1020, and repealing Directive 2006/66/EC
Commission Delegated Regulation (EU) 2023/2197 of 10 July 2023, amending Regulation (EU) 2017/745 of the European Parliament and of the Council as regards the assignment of Unique Device Identifiers for contact lenses
Commission Implementing Regulation (EU) 2023/2713 of 5 December 2023 designating European Union reference laboratories in the field of in vitro diagnostic medical devices

NATIONAL TEXTS

Order of 5 September 2023 amending the Order of 5 March 2020 on restrictions on the use of certain hazardous substances in electrical and electronic equipment

OTHER PRODUCTS FALLING WITHIN THE SCOPE OF ANSM

NATIONAL TEXTS

Order of 26 April 2023 establishing the list of micro-organisms and toxins provided for in Article L. 5139- 1 of the French Public Health Code
Order of 26 April 2023 setting maximum doses and concentrations of micro-organisms and toxins appearing in the list provided for in Article L. 5139-1 and adopted pursuant to Article R. 5139-20 of the Public Health Code

APPENDIX 4: SURVEILLANCE OF MEDICINES

SIGNAL IDENTIFICATION AND PROCESSING

French pharmacovigilance

Changes to the number of adverse effect reports submitted to the national pharmacovigilance system	2019	2020	2021		2022		2023	
			Total	Excluding COVID-19 vaccines	Total	Excluding COVID-19 vaccines	Total	Excluding COVID-19 vaccines
Total number of cases received and recorded by Regional Pharmacovigilance Centres(1)	59,177	49,758	169,336	34,822	102,221	46,829	58,996	52831
• number of cases of serious adverse effects	34,237	27,920	50,545	18,654	42,339	25,451	31288	28,940
•number of cases of adverse effects reported by patients	7,802	6,492	64,957	6,081	42,565	8,117	12,045	8,618
Number of cases of serious adverse effect reports from pharmaceutical companies(2)	51,807	40,258	40,999	38,343	41,467	38,223	39,695	39,124
• number of cases of serious adverse effects	17,192	13,486	13,689	12,974	13,385	12,494	13,505	13,172

(1) The number of adverse effect reports includes initial and follow-up cases
(2) The number of cases of adverse effects includes initial cases

Profile of reporters reporting recorded adverse effects in BNPV	Number of cases	%
Patients	12,045	20.4
Physicians*	29,294	49.6
Pharmacists	14,321	24.3
Other health professionals**	3,329	5.6
Others:	7	0.1

* Including general practitioners and specialists
** Including nurses and dentists

Number of new national pharmacovigilance surveys

2019	2020	2021	2022	2023
6	11	5	5	**9**

70 ongoing national pharmacovigilance surveys in 2023

European pharmacovigilance

Number of cases recorded in PRAC agendas	2019	2020	2021	2022	2023
Number of cases recorded in PRAC agendas	2,391	2,295	2,557	2,870	**2,368**
• for which France is Rapporteur	184	188	186	146	**127**

Breakdown by type of procedure (France as Rapporteur)

Referrals	Signals	PGR Plan de gestion des risques (Risk management plan)	Periodic Safety Update Report (PSUR)	Post-Authorisation Safety Study (PASS)	Other (including renewals and changes)	2023 total
3	2	26	47	35	14	**127**

France's contribution to international pharmacovigilance

Contributor countries in VigiBase	ICSR[43] cumulative data on 31/12/2023	%
United States	1,188 900	37.75
South Korea	328,571	10.43
China	217,411	6.90
India	120,352	3.82
Germany	109,934	3.49
Mexico	104,338	3.31
France	**88,588**	**2.81**
United Kingdom and Northern Ireland	65,474	2.08
Egypt	60,388	1.92
Others	865,612	27.48
Total		**100**

France has been involved in the programme since 1986. It is the seventh-largest contributor to Vigibase, providing approximately 3% of the total number of adverse effect reports received.

[43] ICSR: individual case safety report (reporting of cases of adverse effects).

Changes in stockout-risk and stockout reports by therapeutic class

Therapeutic class	Market share of the therapeutic class	Proportion		Number of reports		
		2021	2022	2021	2022	2023
Cardiovascular system	8%	28%	29%	603	1,088	**1,430**
Nervous system	33%	21%	19%	446	721	**1,086**
Anti-infective agents (systemic use)	5%	14%	15%	295	554	**679**
Digestive system and metabolism	16%	9%	9%	204	336	**465**
Antineoplastic and immunomodulating agents	0.8%	7%	7%	147	260	**354**
Systemic hormones, excluding sex hormones and insulins	2%	2%	3%	48	125	**171**
Respiratory system	6%	3%	3%	63	117	**138**
Blood and haematopoietic organs	7%	7%	4%	142	166	**134**
Sensory organs	3%	2%	2%	33	63	**125**
Miscellaneous	6%	3%	3%	63	124	**108**
Musculoskeletal system	3%	2%	2%	42	84	**100**
Genitourinary system and sex hormones	2%	2%	2%	34	62	**68**
Dermatology	7%	1%	0.8%	24	29	**40**
Parasiticides, insecticides and repellents	0.3%	0.6%	0.9%	14	32	**27**

APPENDIX 5: SURVEILLANCE OF BLOOD PRODUCTS

Haemovigilance reports of serious adverse effects among donors (2023 cumulative data)	Number of serious adverse effects among donors	Severe adverse effects (>2)
January	651	132 (20.3%)
February	516	114 (22.1%)
March	709	162 (22.8%)
April	561	125 (22.3%)
May	606	146 (24.1%)
June	848	247 (29.1%)
July	638	172 (27%)
August	751	186 (24.8%)
September	632	169 (26.7%)
October	716	157 (21.9%)
November	683	141 (20.6%)
December	682	165 (24.2%)
TOTAL	**7,993**	**1,916 (24%)**

Haemovigilance reports of serious adverse effects among receivers (2023 cumulative data)	Number of adverse effects among receivers	Severe adverse effects (grade>1)
January	735	68 (9.3%)
February	781	96 (12.3%)
March	840	86 (10.2%)
April	735	73 (9.9%)
May	737	84 (11.4%)
June	807	72 (8.9%)
July	795	78 (9.8%)
August	800	81 (10.1%)
September	804	57 (7.1%)
October	816	80 (9.8%)
November	770	64 (8.3%)
December	1,030	98 (9.5%)
TOTAL	**9,650**	**937 (9.7%)**

Reporting of serious transfusion chain incidents (2023 cumulative data)	
January	87
February	101
March	127
April	77
May	69
June	112
July	102
August	76
September	97
October	94
November	85
December	122
TOTAL	**1,149**

Post-donation haemovigilance reporting (2023 cumulative data)	
January	190
February	184
March	186
April	117
May	136
June	164
July	148
August	141
September	146
October	180
November	147
December	194
TOTAL	**1,933**

APPENDIX 6: SURVEILLANCE OF MEDICAL DEVICES AND IN VITRO DIAGNOSTIC MEDICAL DEVICES

MONITORING OF INCIDENTS AND RISKS OF INCIDENTS

Change in the number of medical device vigilance reports between 2019 and 2023

Medical device vigilance reports	2019	2020	2021	2022	2023
Number of reports	18,994	19,871	20,492	29,203	**26,722**
• **Number of severe events**	1,206	1,086	1,183	1,073	**923**
• **Number received from patients and patient associations**	553	794	776	1,451	**658**

Proportion of actors responsible for medical device vigilance reports

Origin of medical device vigilance reports	%
Manufacturers	60
Healthcare institutions	30
Other actors (home healthcare providers, patients, non-hospital healthcare professionals, French and European institutions)	10

Change in the number of reagent vigilance reports between 2019 and 2023

Reagent vigilance reports	2019	2020	2021	2022	2023
Number of reports	1,628	1,554	2,012	1,754	**1,642**

Proportion of actors responsible for reagent vigilance reports

Origin of reagent vigilance reports	%
Manufacturers	78
Healthcare institutions	12
Others	10

MARKET CONTROL

Change in the number of registrations of medical devices between 2019 and 2023

Registration of medical devices	2019	2020	2021	2022	2023
Class I medical devices	4,316	4,515	6,027	2,322	**2,204**
Class IIa, IIb, III medical devices and AIMDs	9,734	10,518	6311	2,878	**2,618**
Custom-made medical devices	371	404	65	321	**450**
In vitro diagnostic medical devices	609	272	258	419	**208**

Number of quality controls carried out on radiation-emitting medical devices between 2019 and 2023

Quality control of radiation-emitting medical devices	2019	2020	2021	2022	2023
Number of new standards	1	0	0	0	**1**
Number of non-conformities declared	923	846	1,074	977	**998**

National quality control of medical laboratory tests

Discipline	Operation	Month	Tests controlled	Maximum number of laboratories / experts controlled per operation
DNA profiling	23IEG1	June 2023	IEGAY1, IEGAY2, IEGAY3, IEGAY4: genetic profile	107
Screening for trisomy 21	23T211	March 2023	23TC-2T: MSM2T (AFP, hCG, hCGß, free estriol) 23TD-1T: MSM1T Combined screening (PAPP-A, hCGß) + CN	74
DNA profiling	23IEG2	November 2023	IEGAZ1, IEGAZ2, IEGAZ3, IEGAZ4: genetic profile	106

APPENDIX 7: INSPECTION TO ENSURE QUALITY COMPLIANCE

Inspection of medicines and their raw materials

Chemical and biological medicines

Domain operators[44]	2019	2020	2021	2022	2023
Number of operators: total	ND[45]	ND	ND	ND	**995**
• manufacturers and/or importers	ND	ND	ND	ND	**423**
• operators	ND	ND	ND	ND	**295**
• wholesale distributors	ND	ND	ND	ND	**449**

Contrary to the activity reports for previous years, pharmaceutical sites and establishments authorised to prepare, store, distribute, transfer, import and export advanced therapy medicinal products in the context of the research defined in Article L. 1121-1 have been added to the sites manufacturing chemical medicinal products.

Administrative management	2019	2020	2021	2022	2023
Opening authorisations	59	51	54	50	**63**
Closure rulings	44	47	69	43	**38**
Modification authorisations	133	149	127	141	**149**

Inspection of medicines	2019	2020	2021	2022	2023
Inspections	227	154	227	194	**197**
• carried out in France	213	150	216	179	**179**
• conducted abroad	14	4	11	15	**18**
GMP compliance certificates	228	121	279	179	**199**
Injunctions	19	14	8	10	**10**
Health policy rulings	2	1	0	1	**0**
Cases passed on to the judicial authorities	1	1	1	0	**0**

[44] Manufacturers, distributors, importers of active substances (for human and veterinary use) and/or excipients (for human use)
[45] ND: Not determined

Raw materials for pharmaceutical use

Operators in the field	2019	2020	2021	2022	2023
Number of operators: total	740	760	800	800	**820**

Raw material inspection	2019	2020	2021	2022	2023
Inspections	105	67	92	89	**79**
• carried out in France	84	62	92	82	**63**
• conducted abroad	21	5	0	7	**14**
GMP compliance certificates	65	41	80	58	**70**
Injunctions	7	3	4	2	**1**
Health policy rulings	1	0	0	1	**1**
Cases passed on to the judicial authorities	0	0	0	0	**0**

Pharmacovigilance systems

PV inspections	2019	2020	2021	2022	2023
Inspections	32	16	17	19	**25**
• carried out in France	31	16	17	19	**25**
• conducted abroad	1	0	0	0	**0**
Injunctions	3	1	2	0	**1**
Health policy rulings	0	0	0	0	**0**
Cases passed on to the judicial authorities	0	0	0	0	**0**

Inspection of clinical trials

Clinical trials

Inspection of pre-clinical trials	2019	2020	2021	2022	2023
Inspections	30	27	30	22	**29**
GLP compliance certificates	26	25	30	21	**26**
Injunctions	1	0	0	0	**0**
Health policy rulings	0	0	0	0	**0**
Cases passed on to the judicial authorities	1	0	0	0	**0**

Clinical trials

Inspection of clinical trials	2019	2020	2021	2022	2023
Inspections	33	18	25	20	**29**
• carried out in France	27	18	25	19	**26**
• conducted abroad	6	0	0	1	**3**
Injunctions	0	1	0	2	**1**
Health policy rulings	2	0	0	1	**0**
Cases passed on to the judicial authorities	5	1	1	1	**0**

Inspection of blood products and other biological products

Labile blood products

Production and distribution sites	2019	2020	2021	2022	2023
Number of sites	14	14	14	14	**14**
Number of transfusion sites	ND	ND	ND	ND	**190**
Administrative management	**2019**	**2020**	**2021**	**2022**	**2023**
Modification of operators subject to declaration	21	22	26	21	**14**
Changes to operators subject to authorisation	21	15	15	13	**8**
Inspections	**2019**	**2020**	**2021**	**2022**	**2023**
Total	32	35	45	35	**25**
Injunctions	2	0	0	0	**0**
Health policy rulings	0	0	0	0	**0**
Cases passed on to the judicial authorities	0	0	0	0	**0**

Tissues and cells

Domain operators	2019	2020	2021	2022	2023
Number of operators: total	67	68	70	68	**68**
• tissue banks	33	32	33	32	**32**
• cell therapy units	34	36	37	36	**36**
Administrative management	**2019**	**2020**	**2021**	**2022**	**2023**
Opening authorisations	2	1	4	3	**1**
Closure rulings	3	3	2	3	**1**
Modification authorisations	125	136	105	120	**155**
Inspections	**2019**	**2020**	**2021**	**2022**	**2023**
Total	24	20	27	23	**28**
Injunctions	1	0	1	0	**0**
Health policy rulings	0	0	0	0	**0**
Cases passed on to the judicial authorities	0	0	0	0	**0**

Contrary to previous years' activity reports, pharmaceutical establishments and establishments authorised to prepare, store, distribute, transfer, import and export advanced therapy medicinal products in the context of the research defined in Article L. 1121-1 have been added to the list of sites manufacturing chemical medicinal products.

Breast milk

Domain operators[46]	2019	2020	2021	2022	2023
Total	34	34	34	34	**33**

Evaluation of breast milk banks[47]	2019	2020	2021	2022	2023
Number of applications examined	2	4	21	4	**3**

Inspections	2019	2020	2021	2022	2023
Inspections	14	7	11	13	**10**
Injunctions	0	0	0	0	**0**
Health policy rulings	0	0	0	0	**0**
Cases passed on to the judicial authorities	0	0	0	0	**0**

[46] Breast milk bank
[47] ANSM evaluates applications for autorisation and the renewal of autorisation for breast milk banks and issues an opinion on regulatory compliance to the Regional Health Agencies (ARS), which issue the autorisation.

Micro-organisms and toxins

Domain operators	2019	2020	2021	2022	2023
Numbers of sites	103	102	95	95	**90**
Administrative management	**2018**	**2019**	**2021**	**2022**	**2023**
Total number of microorganism and toxin (MOT) authorisations issued	983	810	1,229	1,636	**1,626**
Number of applications received to store MOTs (excluding temporary storage for inter-laboratory operations)	50	41	31	65	**53**
Number of holders of authorisations to store MOTs (excluding temporary storage for inter-laboratory operations)	120	120	111	117	**102**
Inspections	**2019**	**2020**	**2021**	**2022**	**2023**
Inspections	30	15	23	24	**29**
Injunctions	0	0	0	0	**0**
Health policy rulings	0	2	1	0	**1**
Cases passed on to the judicial authorities	1	0	0	0	**0**

Inspection of medical devices and in vitro diagnostic medical devices

Medical devices

Medical device inspections	2019	2020	2021	2022	2023
Inspections	78	53	80	84	**65**
• carried out in France	76	53	78	84	**65**
• conducted abroad	2	0	2	0	**0**
Injunctions	6	17	11	9	**4**
Health policy rulings	4	0	1	1	**0**
Cases passed on to the judicial authorities	4	0	0	0	**0**

In vitro diagnostic medical devices

IVDMD inspections	2019	2020	2021	2022	2023
Inspections	26	16	25	19	**20**
• carried out in France	26	16	25	19	**20**
• conducted abroad	0	0	0	0	**0**
Injunctions	5	3	5	4	**2**
Health policy rulings	0	0	0	0	**0**
Cases passed on to the judicial authorities	0	0	0	0	**0**

Medical device vigilance systems

Medical device vigilance inspections	2019	2020	2021	2022	2023
Inspections	7	7	11	10	**14**
• carried out in France	7	7	11	10	**14**
• conducted abroad	0	0	0	0	**0**
Injunctions	1	1	0	1	**2**
Health policy rulings	0	0	0	0	**0**
Cases passed on to the judicial authorities	0	0	0	0	**0**

Inspection of cosmetic products

Inspection of sites manufacturing cosmetic products	2019	2020	2021	2022	2023
Inspections	22	6	10	10	**3**
Injunctions	5	0	1	1	**0**
Health policy rulings	1	0	0	1	**0**
Cases passed on to the judicial authorities	0	0	0	0	**1**

APPENDIX 8: LABORATORY-BASED QUALITY CONTROL OF HEALTHCARE PRODUCTS

Laboratory-based controls	Raw materials and chemical medicinal products	Raw materials, medicines and biological products	Other health products	Total
January	23	233	7	**263**
February	9	283	2	**294**
March	68	292	3	**363**
April	36	206	23	**265**
May	29	273	8	**310**
June	11	244	2	**257**
July	43	283	39	**365**
August	43	231	16	**290**
September	40	317	13	**370**
October	36	303	10	**349**
November	41	307	10	**358**
December	25	214	58	**297**
TOTAL	**404**	**3,186**	**191**	**3,781**

Test reports Change from 2019 to 2023	2019	2020	2021	2022	2023
All reports combined	4,387	4,395	4,249	3,879	**3,781**

Quality control of medicines and biological products

Laboratory controls in a European context	Medicines under the centralised European procedure,	Number of controls conducted for the EDQM	Medicines under the decentralised European or mutual recognition procedure	Urgent controls conducted	Total
Chemical medicinal products	14	8	94	4	**112**
Biological medicines	9	9	/	/	**9**

Detection of non-conformities	Number of controls carried out	Number of non-conformities detected
Controls carried out in a scheduled context		
Chemical medicines	348	23
Chemical raw materials	22	0
Urgent controls conducted		
Chemical medicines	9	0
Chemical raw materials	0	0

Laboratory control campaigns for medical devices

Laboratory controls[48] on medical (and related) devices	2019	2020	2021	2022	2023
Medical devices controlled	40	199	104	120	**122**
Non-conformities detected	2	6	2	2	**0**

[48] Including in urgent contexts.

Facilitating patient access to innovative treatments

APPENDIX 9: EARLY ACCESS TO HEALTH PRODUCTS

Derogatory access decisions

Summary of named-patient temporary authorisations for use (ATUns) and compassionate access authorisations (AACs)	2019 (ATUn)	2020 (ATUn)	2021		2022 (AAC)	2023 (AAC)
			H1 (ATUn)	H2 (AAC)		
Granting of ATUn and AAC	26,528	40,437	25,575	25,521	63340	**57,176**
Medicines (or active substances) made available per year	227	266	284		293	**24,346**
Patients included	NA[49]	23,347	28,876		27,427	**373 (277)**

Summary of cohort temporary authorisations for use (ATUcs) and early access authorisations (AAPs)	2019 (ATUc)	2020 (ATUc)	2021		2022 (AAP)	2023 (AAP)
			H1 ATUc	H2 AAP		
New ATUcs/ ANSM AAP opinions	20	37	27	7	30	**25 (+ 3 renewals and 6 modifications)**
Medicinal products under ATUc/AAPs having obtained an MA	14	20	22		21	**10**
Patients included	3,766	7,300	Not available		Not available	Not available[50]

[49] Year in which the ATUn unit was created, data not available.
[50] This indicator is no longer managed by the ANSM, but by the HAS

Summary of temporary recommendations for use (RTUs) / compassionate prescription frameworks (CPCs)	2022	2023
New CPCs	4	1
Renewed CPCs	3	4

APPENDIX 10: CLINICAL TRIALS

CLINICAL TRIAL APPLICATION AUTHORISATIONS

Clinical trials of medicines/ATMPs under Jardé Law	2019	2020	2021	2022	2023
Number of applications submitted	938	1,011	1,056	824	**108**
Number of authorisations	813	809	855	738	**241**
Number of refusals	12	18	28	25	**1**
Early-phase clinical trials					
Number of applications submitted	145	152	156	162	**20**
Number of authorisations	124	127	145	153	**47**
Number of refusals	8	7	7	10	**0**
Clinical trials of advanced therapy medicinal products (ATMPs)					
Number of applications submitted	40	41	34	36	**3**
Number of authorisations	26	36	20	40	**18**
Number of refusals	0	0	1	0	**0**

- Average time for all medicinal product trials: **60 days under Jardé Law**
  - Trials authorised in one round: **36 days** (out of 55 applications)
  - Trials subject to an interim letter: **66 days** (out of 219 applications)

Since 1st February 2023, all initial submissions for clinical trials of medicinal products/ATMPs must be filed on the European CTIS portal under European Regulation 536/2014.

Clinical trials of Regulation medicines/ATMPs	2022[51]	2022[52]	2023[53]
Number of applications submitted	214	178	780
Number of authorisations	64	51	446
Number of refusals	2	2	25
Early-phase clinical trials			
Number of applications submitted	38	27	182
Number of authorisations	14	10	90
Number of refusals	0	0	3
Clinical trials of advanced therapy medicinal products (ATMPs)			
Number of applications submitted	6	9	36
Number of authorisations	6	0	10
Number of refusals	0	0	0

[51] Data from the 2022 Annual Report included the number of transitional trials (clinical trials previously authorised under the Jardé Law)
[52] Data for 2022 and 2023 without the number of transitional trials
[53] Data for 2022 and 2023 without the number of transitional trials

Under the regulation on clinical trials, authorisations and refusals (single decision) include the opinions of the personal protection committees (CPP).

Overall, there has been an increase in the number of early clinical trials in recent years, reflecting the interest shown by sponsors in conducting these trials in France.

"Organ Tissue Cell" clinical trials and "Preparation of cellular therapies" (OTC/PTC)	2022	2023
Number of applications submitted	8	**11**
Number of authorisations	4	**9**
Number of refusals	0	**0**
Clinical trials of "Labile blood products" (LBPs)		
Number of applications submitted	1	**0**
Number of authorisations	1	**0**
Number of refusals	0	**0**

Clinical trials of "Non-health products"	2019	2020	2021	2022	2023
Number of applications submitted	203	172	209	167	**172**
Number of authorisations	168	156	183	163	**152**
Number of refusals	1	6	5	0	**2**

Average examination time: **21 days**

- Trials authorised in one round: **15.4 days** (for 121 applications).
- Trials subject to an interim letter: **34.5 days** (for 54 applications)

Clinical investigations (CI) on medical devices (MDs) since 26 May 2021

Clinical investigations	2021	2022	2023
Number of CIs submitted	214	403	**290**
Number of CIs approved	160	281	**240**
Number of CIs refused	6	8	**8**
Number of CIs in the process of approval withdrawn by the sponsor	26	65	**26**
Number of CIs authorised	23	69	**54**[54]
Number of refusals	0	2	**0**
Number of CIs in the process of evaluation withdrawn by the sponsor	0	10	**15**

Average CI validation times: **18 days**[55]
Average CI evaluation times: **46 days**[56]

54 clinical investigation authorisations for medical devices granted.

- 68% are industrial sponsors
- 32% are institutional sponsors

Breakdown of clinical investigations by therapeutic area	%[57]
Cardiology	19
Neurology	12
Orthopaedics	12
Anaesthesia/Resuscitation	10
Ophthalmology	8
Imaging/Diagnostics	7
Oncology	5
Dermatology	4
Endocrinology / Diabetology	4
Urology/Nephrology	4
Gastroenterology	3
Gynaecology	2
ENT	2
Others	7

Scientific opinions issued in medicinal product clinical trials (CT)	2022	2023
Favourable opinions on MD	25	**5**
Negative opinions on MD	0	**0**

[54] CI subject to a scientific evaluation.
[55] These times take account of the 10-day sponsor response time, but do not include additional days requested by sponsors for certain applications
[56] These times are the average of the times in which applications are evaluated with and without the intervention of an expert
[57] Percentage in relation to the total number of CIs received.

Performance studies (PS) on in vitro diagnostic medical devices (IVDMDs) since 26 May 2022

Performance Studies (PS)	2022	2023
Number of PS submitted	9	**55**
Number of PS approved	3	**40**
Number of PS refused	0	**3**
Number of PS in the process of approval withdrawn by the sponsor	2	**9**
Number of PS authorised	0	**29**[58]
Number of refusals	0	**0**
Number of PS in the process of evaluation withdrawn by the sponsor	0	**5**

Average PS validation times: **24 days**[59]
Average PS evaluation times: **46 days**[60]

29 performance study authorisations for medical devices granted
- 100% are industrial sponsors
- 0% are institutional sponsors

Breakdown of performance studies by therapeutic area	%[61]
Oncology	78
Imaging/Diagnostics	7
Neurology	7
Cardiology	2
ENT	2
Orthopaedics	0
Anaesthesia/Resuscitation	0
Ophthalmology	0
Gastroenterology/ Hepatology	0
Dermatology	0
Gynaecology	0
Urology/Nephrology	0
Endocrinology / Diabetology	0
Others	4

[58] CIs subject to scientific evaluation.
[59] These times take account of the 10-day sponsor response time, but do not include the additional 20 days requested by sponsors for certain applications.
[60] These times are the average of the times taken to evaluate cases with and without the intervention of an expert.
[61] Percentage in relation to the total number of CIs received.

Scientific opinions issued in medicinal product clinical trials (CT)	2022	2023
Favourable opinions on IVDMD	12	**9**
Unfavourable opinions on IVDMDs	5	**10**

Combined trials of medicines and medical devices or in vitro diagnostic medical devices (IVDMD) since 26 May 2021

Mixed tests	2022	2023
Number of CI/MEDs submitted	6	**3**
Number of PS/MEDs submitted	1	**4**
Number of CI/MEDs approved	6	**3**
Number of PS/MEDs approved	1	**4**
Number of CI/MEDs refused	0	**0**
Number of PS/MEDs refused	0	**0**
Number of CI/MED authorised	4	**4**
Number of PS/MED authorised	0	**3**
Number of CI/MED refusals	1	**0**
Number of PS/MED refusals	0	**0**

The validation or authorisation times are those described in CTIS for the medicine.

AMENDMENTS TO CLINICAL TRIALS

Substantial amendments to clinical trials for authorisation (MSA)

Substantial amendments to trials for all medicines / ATMP	2019	2020	2021	2022	2023
Number of applications submitted	3863	4,085	3,941[62]	3,953	**3,509**
Number of applications granted	3,700	4,017	3,778	3,837	**3,449**
Number of applications refused	13	13	9	14	**7**
Number of early-phase MSA CT	-	-	-	-	**750** 711 authorised 1 refusal

Average processing time:

- Applications authorised in one round : **16 days** (for 2,842 applications)
- Applications authorised subject to an interim letter: **49 days** (for 711 applications)

Substantial amendments to trials of Regulation Medicinal products/ATMPs	2022	2023
Number of applications submitted	20	**421**
Number of authorisations	4	**200**
Number of refusals	0	**1**

In addition, for 2023, the number of MSAs submitted for early-phase trials was 750, with 711 authorised over the year and 1 refused.

Substantial amendments to trials on "Organs, tissues, cells" and "Cell-therapy preparations" (OTC/CTP)	2022	2023
Number of applications submitted	**15**	**6**
Number of authorisations	**14**	**6**
Number of refusals	**0**	**0**
Substantial amendments to trials of "Labile blood products" (LBP)		
Number of applications submitted	**1**	**3**
Number of authorisations	**1**	**3**
Number of refusals	**0**	**0**

Substantial amendments to trials of non-health products (HPS)	2019	2020	2021	2022	2023
Number of applications submitted	384	317	306	292	**311**
Number of applications granted	371	307	300	291	**312**
Number of applications refused	2	2	2	0	**0**

[62] 172 of which concerned ATMPs.

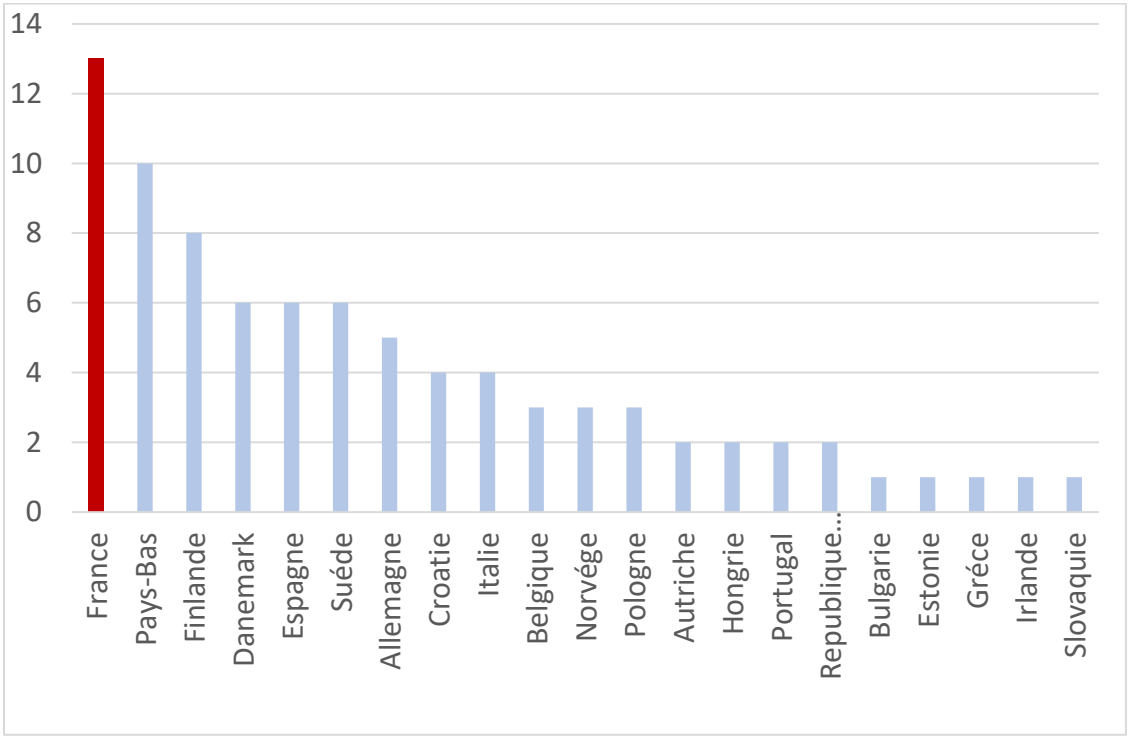
Average processing time: **3 days**

- Trials authorised in one round: **3 days** (for 312 applications)
- Trials subject to an interim letter: **NA**

Substantial amendments to clinical investigations (CI) of MDs since 26 May 2021	2021	2022	2023
Number of MSAs for CIs submitted	4	**44**	**74**
Number of MSAs for CIs approved	1	**38**	**68**
Number of MSAs for CIs refused	0	**2**	**0**
Number of MSAs for CIs authorised	1	**35**	**62**
Number of MSA refusals for CIs	0	**0**	**0**

Average time for approval of substantial amendments to CIs: **13 days**[63]
Average time for authorisation of substantial amendments to CIs: **21 days**[64]

Number of designated saMS per MSC[65]



Since the first saMS designation of France in June 2022, ANSM has received a total of **4,405** reports of serious unexpected adverse reactions, including **315** initial reports and **8** FR recipient ASRs.[66]

[63] These times take account of the 10-day sponsor response time, but do not include the additional 20 days requested by sponsors for certain applications.
[64] These times are the average of the times taken to assess applications with and without the intervention of an expert.
[65] Member State concerned
[66] Annual Safety Report

APPENDIX 11: MARKETING OF MEDICINES

MARKETING AUTHORISATION AND REGISTRATION APPLICATIONS FOR MEDICINES

496 marketing authorisations and registrations granted by ANSM in 2023 (national procedure and European decentralised and mutual recognition procedures) versus 588 in 2022.

Centralised procedures	2019	2020	2021	2022	2023
Number of MA applications submitted	117	115	116	100	**99**
Number of MAs granted[67]	66	97	92	89	**77**
Number of MA applications denied	4	2	5	3	**3**
Number of applications assigned to France (rapporteur, co-rapporteur)	19	19	18	19	**19**

Mutual recognition procedures (MRP)	2019	2020	2021	2022	2023
Number of MA applications submitted	78	99	80	45	**48**
Number of MAs granted	77	79	100	38	**43**
Number of MA applications denied	0	0	0	0	**2**
Number of MAs for which France is the reference Member State[68]	0	2	3	6	**9**

Decentralised procedures (DCP)	2019	2020	2021	2022	2023
Number of MA applications submitted	546	448	464	447	**515**
Number of MAs granted	404	375	314	395	**297**
Number of MA applications denied	0	0	0	0	**14**
Number of MAs for which France is the reference Member State[69]	21	4	4	4	**5**

In 2023, the average time for notification of national decisions for MAs resulting from European procedures (MRP/DCP) was **67 days.**[70]

National procedures	2019	2020	2021	2022	2023
Number of MA applications submitted	154	127	157	143	**146**
Number of MAs granted	265	168	117	154	**141**
Number of MA applications denied	20	1	5	0	**0**

[67] Data expressed in number of proprietary medicinal products.

[68] Number of applications submitted

[69] Number of applications submitted

[70] This time is calculated on the basis of 12 applications.

National procedures	2019	2020	2021	2022	2023
Number of registration applications for herbal proprietary medicinal products submitted	1	0	3	1	**1**
Number of registrations of herbal proprietary medicinal products granted	16	26	7	1	**1**
Number of registrations of herbal proprietary medicinal products denied	0	0	0	0	**0**
Number of registration applications for homeopathic proprietary medicinal products submitted	16	42	26	0	**2**
Number of registrations of homeopathic proprietary medicinal products granted	254	291	96	12	**10**
Number of registrations of homeopathic proprietary medicinal products denied	1	0	0	2	**0**

AMENDMENTS TO MARKETING AUTHORISATIONS

MA amendments[71]

The different categories of amendments are:

- "Minor variation of type IA" : a variation which has only a minimal impact, or no impact at all, on the quality, safety or efficacy of the medicinal product concerned.
- "Minor variation of type IB": a variation which is neither a minor variation of type IA nor a major variation of type II nor an extension.
- "Major variation of type II": a variation which is not an extension and which may have a significant impact on the quality, safety or efficacy of the medicinal product concerned.
- MA extensions.
- Urgent safety restrictions for safety reasons: any interim change to the terms of a marketing authorisation due to new information having a bearing on the safe use of the medicinal product.

Average times for notification of national decisions for MA variations resulting from European procedures

Mutual recognition procedures (France as Reference Member State)	2019	2020	2021	2022	2023
Number of type IA applications submitted	278	256	279	269	**275**
Number of type IA applications granted	248	238	252	256	**247**
Number of type IA applications denied	3	12	5	5	**11**
Number of type IB applications submitted	200	245	263	251	**224**
Number of type IB applications granted	131	217	203	241	**228**
Number of type IB applications denied	2	4	1	1	**4**
Number of type II applications submitted	97	93	118	102	**104**
Number of type II applications granted	41	82	91	99	**88**
Number of type II applications denied	0	2	1	1	**2**

(MRP/RMS): **3 days.**

Average processing times:

- For national type IA applications: **5 days**
- For national type IB applications: **9 days**
- For national type II applications: **100 days**

Average processing times:

- For national type IA applications: **5 days**
- For national type IB applications: **9 days**

[71] The number of applications and time frames should be interpreted with caution due to the change of IT tools for monitoring applications in 2021.

National procedures	2019	2020	2021	2022	2023
Number of type IA applications submitted	3427	2,950	2,901	2,489	**2,528**
Number of type IA applications granted	3,232	2,863	2,781	2,399	**2,420**
Number of type IA applications denied	121	54	30	65	**112**
Number of type IB applications submitted	2,305	2,998	2,591	2,544	**2,312**
Number of type IB applications granted	2,165	2,924	2,306	2,381	**2,107**
Number of type IB applications denied	38	22	27	29	**30**
Number of type II applications submitted	739	681	583	610	**493**
Number of type II applications granted	465	640	512	530	**480**
Number of type II applications denied	39	45	34	33	**36**

GENERIC MEDICINE AUTHORISATIONS

325 of the marketing authorisations issued by the ANSM in 2023 concerned generic medicines.

Summary of generic medicine authorisations	2019	2020	2021	2022	2023
MAs granted for generic medicines	539	442	439	402	**325**
Number of generic groups included in the directory	1,432	1,459	1,510	1,525	**1,561**

Scheduled controls	2023 summary	
	Batches controlled	% non-conformities detected
Non-generic proprietary medicines	173	6%
Generic proprietary medicines	175	7%
Generic raw materials	16	0

Main generic groups controlled in 2023
Acebutolol
Amlodipine
Amlodipine/Valsartan
Baclofen
Glimepiride
Pregabalin
Ropivacaine
Silodosin
Tramadol

For more information about generic medicines:
https://ansm.sante.fr/qui-sommes-nous/notre-perimetre/les-medicaments/p/medicaments-generiques#title

APPENDIX 12: RELEASE OF BATCHES OF VACCINES AND BLOOD-DERIVED MEDICINES

Release of batches of vaccines and blood-derived medicines

Indicators	2019 aggregate	2020 aggregate	2021 aggregate	2022 aggregate	2023 aggregate
Certified batches	2,934	3,205	3,353	2,851	**2,770**
• **number of vaccines**	1,589	1,668	1,745	1,442	**1,165**
• **number of blood-derived medicinal products and plasma pools**	1,345	1,537	1,608	1,409	**1,605**

Involvement of Member States in vaccine batch release in Europe

	%
France	**27.2**
Belgium	**26.7**
Germany	**19.6**
Netherlands	**15.6**
Austria	**5**
Italy	**2.1**
Norway	**2.1**
Switzerland, Poland, Bulgaria, Czech Republic	**1.7**

Involvement of Member States in vaccine batch release in France

	%
Germany	**27**
Belgium	**25**
France	**18**
Netherlands	**16**
Austria	**7.2**
Italy	**2.9**
Norway	**3.2**
Czech Republic, Switzerland	**0.5**

APPENDIX 13: AUTHORISATION OF BLOOD PRODUCTS AND OTHER BIOLOGICAL PRODUCTS

Opinions issued for labile blood products	2019	2020	2021	2022	2023
New applications	6	8	1	0	0
Amendments	14	14	16	16	21
Updating of the list and characteristics of LBPs	1	3	1	1	0

Opinions issued for cell product processes (CPPs) and tissue product processes (TPPs)	2022	2023
New applications	0	0
Substantial amendments to the process		
Applications received	51	64
Final release notification	25	53
Declarative changes to the process		
Applications received	19	20
Opinions issued	19	17

APPENDIX 14: INDICATORS FOR MONITORING CONTRACTS OF OBJECTIVES

2019/2023 Objectives and Performance Contract – 2023 Results

Priority 1: Develop the Agency's openness to stakeholders and reinforce the transparency of its work

Objective: Reinforce the public nature of decision-making processes

Indicator	Indicator title	Baseline	Target	Attained
1	Number of public hearings per year	≥ 5	8	8

Objective: Diversify partnership-based working methods in order to adapt to the variety of situations and stakeholders' expectations

Indicator	Indicator title	Baseline	Target	Attained
2	Rate of high-risk situations (HRS) involving stakeholders in application management processes	80%	100%	97%
3	Overall stakeholder satisfaction rate	-	Continuous improvement plan	A continuous improvement plan has been put in place for 2023 based on the results obtained.

Objective: Reinforce stakeholder involvement in decision development processes

Indicator	Indicator title	Baseline	Target	Attained
4	Rate of increase in satisfaction of stakeholders in standing and temporary committees	-	+30% / reference year	No survey launched in 2023 on the satisfaction of stakeholders in SSCs and TSCs because this was a year of renewal for SSCs

Objective: Guarantee an improvement in public access to our data

Indicator	Indicator title	Baseline	Target	Attained
5	Implementation rate of the data publication work programme	75%	100%	98%

Priority 2: Make risk management a common operating principle for all the Agency's missions

Objective: Ensure reinforced management of high-risk situations throughout the life cycle of health products

Indicator	Indicator title	Baseline	Target	Attained
6	Implementation rate of emergency action plans for high-risk situations (HRS)	80%	100%	98%

Objective: Secure the coverage of patients' health needs for health products of major therapeutic interest

Indicator	Indicator title	Baseline	Target	Attained
7	Percentage of cases in which a measure to reduce the risk of stockout was proposed on time	95%	100%	85%

8[72]	% of financial penalties applied to a detected breach of regulations relating to shortages	90%	100%	100%

Objective: Secure and optimise access to health products for patients

Indicator	Indicator title	Baseline	Target	Attained
9	Consumption rates of intervention credits allocated to pharmacoepidemiology	80%	100%	56%
10	Completion rate of the annual work programme on the coverage of misuse identified in the framework of an inter-operator approach	-	≥ 80%	93%
11	Proportion of sensitive inspection follow-ups controlled	85%	100%	91%
12	Proportion of batches analysed in the context of the scheduled annual control programme	85%	100%	97%

Priority 3: Reinforce and stabilise the Agency's positioning to facilitate access to innovation in the European environment

Objective: Reinforce ANSM's position in Europe in order to facilitate early access to innovative health products for patients

[72] In 2022, Indicator 8 changed to take account of the new regulations. Previously, this was the "Increase in the proportion of stockouts in cases leading to financial sanctions implemented at the Agency", which no longer seemed relevant since the entry into force of Decree No. 2021-349 on 1st September 2021. This introduced the obligation for manufacturers to build up a safety stock of medicines intended for the national market, and enables ANSM to penalise manufacturers who fail to provide it with advance notification of any risk of stockouts.

Indicator	Indicator title	End 2023	2023 target	Attained
13	Number of European scientific opinions attributed to France	60 opinions	80 opinions	85 opinions
14a	Clinical trials of medicinal products and non-health products (excluding ATMPs) in accordance with the Jardé Law: average time between the date of complete submission of the application for a clinical trial authorisation and the decision, including the sponsor response time(s)	≤ 55 days	≤ 45 days	57
14b	Clinical trials of advanced therapy medicinal products in accordance with the Jardé law: average time between the date of complete submission of the application for a clinical trial authorisation and the decision, including the sponsor response time(s)	≤ 140 days (≤ 180 days in the regulation)	≤ 110 days	125
14c	Clinical trials of medicinal products governed by regulation EU 2014/536 (CTR) – Mononational excluding ATMPs: average time between validation of the application for a clinical trial authorisation in the CTIS and submission of the opinion on part 1 by ANSM in the CTIS, including the sponsor response time(s)	≤ 60 days	≤ 50 days	59
14d	Multinational clinical trials of medicinal products governed by the CTR: proportion of trials in which France is the Reporting Member State, compared with the previous year (reference year: 2022)	1% increase	3% increase	121 applications

Objective: Reinforce mechanisms for early access to innovations

Indicator	Indicator title	Baseline	Target	Attained
15a	Applications for early access authorisation: rate of compliance with processing times	≥ 90%	100%	32%
15b	Applications for compassionate access authorisation: rate of compliance with processing times	≥ 90%	100%	-
15c	Compassionate prescription frameworks: rate of compliance with management times	≥ 90%	100%	-

Objective: Help ensure active early support for sponsors in the field of health innovation

Indicator	Indicator title	Baseline	Target	Attained
16	Growth rate in the number of applications processed by the Innovation and Referral Service	-	Increase in the number of applications processed	+34%[73]

Objective: Guarantee the European activity sustainability strategy

Indicator	Indicator title	Baseline	Target	Attained
17	Ratio of revenue and expenditure on European activity	-	≥1.5	2.47

Objective: Reinforce ANSM's European standing in the field of MDs and IVDMDs

Indicator	Indicator title	Baseline	Target	Attained
18a	Rate of compliance with regulatory timeframes for applications subject to validation only	90%	100%	96%
18b	Rate of compliance with regulatory evaluation timeframes for applications subject to an ANSM evaluation	≥ 90%	100%	98%
18c	Proportion of applications validated in a single round	≥ 25%	50%	18%

[73] Indicator 16 shows the increase in the number of cases "processed" by the Innovation and Referral Service, unlike the data presented on page 81, which shows the number of cases received.

Priority 4: Stabilise the institution's performance and efficiency

Objective: Adapt the organisation to improve performance

Indicator	Indicator title	Baseline	Target	Attained
19	Implementation rate for the annual portfolio of IS projects	≥ 90%	100%	90%

Objective: Ensure compliance of authorisation processes with regulatory timeframes and implement target infra-regulatory timeframes for priority products

Indicator	Indicator title	Baseline	Target	Attained
20a	Rate of national and European procedures examined for all MA submissions, new applications within regulatory timeframes	90%	100%	55%
20b	Rate of national and European procedures examined for all MA submissions, variations and translation within infra-regulatory timeframes	90%	100%	85%

Objective: Secure the expertise resources required to perform the Agency's missions

Indicator	Indicator title	Baseline	Target	Attained
21	Rate of reduction in use of external individual expertise	-	≤-5%/ previous year	- 16%

Objective: Maintain high risk-management standards in terms of ethics and anti-corruption

Indicator	Indicator title	Baseline	Target	Attained
22	Compliance rate derived from internal oversight (staff / collegial expertise/ individual expertise)	95%	100%	-99%

Objective: Improve quality of working life to reinforce internal performance

Indicator	Indicator title	Baseline	Target
23	PSR action plan implementation rate	75% implementation rate of the new PSR working programme over 2 years	89%
24	Teleworking employee percentage	45%	94%

Qualitative explanations:

Indicator 23: the Action Plan is measured from June to June.
Consequently, the 63% rate of actions in progress or completed only concerns the period from June to December 2022. The result is positive and instils confidence in the overall achievement of the action plan by June 2023.
Indicator 24: all of the Agency's personnel telework, with the exception of a few posts in which it is impossible or very difficult to work remotely (laboratories and some general services posts), as well as personnel who do not wish to do so..

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