Exposure to titanium dioxide via drugs

● Mean daily intake via medication of this carcinogen, which is banned in food in the European Union, has been estimated at 1.7 mg per person in the French population.

Titanium dioxide has been banned from use as an additive in food products since 2020 in France, and since 2022 in the European Union, on the grounds that it is genotoxic, carcinogenic, and mutagenic in vitro and in animal studies. However, it continues to be used as an excipient in many drugs, in particular as a colouring and opacifying agent (1). The International Agency for Research on Cancer (IARC) and the European Chemicals Agency (ECHA) consider this substance to be possibly carcinogenic in humans (2).

A recent study cross-referenced data on the composition of all pharmaceutical products marketed in France between 2001 and 2020 with data on the drugs dispensed by community pharmacies and reimbursed by the French national health insurance system over the same period. The objective was to quantify the presence of titanium dioxide in these drugs, and to estimate population exposure to this excipient via reimbursement data (3).

In 2020, 36% of the 2.2 billion boxes of drugs that were dispensed and reimbursed contained titanium dioxide, primarily in forms for oral use. This excipient was present in 79% of coated tablets, 94% of film-coated tablets and 82% of hard and soft capsules (3).

Between 2001 and 2020, half of these forms contained more than 1.4 mg of titanium dioxide per dosage unit. Over this period, mean daily intake per person was 1.7 mg, with differences depending on age group and sex. In the 20- to 59-year-old age group, women had the highest daily intake, at 1.34 mg. In the 60 years or older age group, it was men who had the highest daily intake, at 4 mg (3).

These intake estimates are approximate, however. They may be overestimated, since they do not account for drugs that were reimbursed but not used; they may also be underestimated by about 30%, since they do not include drugs that were dispensed but not reimbursed by the national health insurance system, in particular in the context of self-medication (3). Nor do they include the titanium dioxide present in hospital-administered drugs or dietary supplements.

Unfortunately, in August 2025, based on a new evaluation by the European Medicines Agency, a European Commission working group took the view that the use of titanium dioxide in medicinal products should be maintained (4,5).

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European drug regulatory agencies: strategy through to 2028

● The proposed priorities focus too much on new technologies, and not enough on seeking therapeutic advances for patients.

The European Medicines Agencies Network, which consists of the European Medicines Agency (EMA) and the national drug regulatory agencies, recently ran a public consultation on a reflection paper setting out its proposed priorities through to 2028: the accessibility of new drugs; digitalisation, artificial intelligence and health data; "regulatory science", innovation and competitiveness; antimicrobial resistance and other health threats; the availability and supply of drugs; and the sustainability of the network (1).

In its response to this consultation, submitted in November 2024, Prescrire particularly stressed the need to foster the generation of robust scientific evidence as part of the decision-making process. For several years, the bar for marketing authorisation has been set too low. As a general rule, the European drug regulatory agencies should require randomised comparative trials versus the standard treatment (where one exists).

Prescrire also emphasised that scientific committee experts should be free from competing interests, in order to ensure the independence of the regulatory process.

In addition, Prescrire proposed other priorities that were not mentioned in the consultation document:

– Improving the safety of drugs, medical devices and in vitro diagnostic tests. The agencies should pursue their efforts to prevent medication errors. Preventing drug-related iatrogenesis and medication errors should be a major objective over the coming years;

– Improving the quality and safety of packaging, patient leaflets and medicine "overviews" (online plain-language summaries of public assessment reports). The EMA should systematically require user testing by patients and/or health professionals. It should also provide clear information about the benefits of treatments demonstrated in clinical studies and the remaining uncertainties, as well as about the gaps and weaknesses in the evidence for the drug's efficacy.

Overall, Prescrire considers that the network's proposed priorities focus too much on new technologies and interactions between institutions and partners, and not enough on the key role of drug regulatory agencies, which is to ensure that new drugs provide documented benefits while also protecting patients from adverse effects (2).

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References 1- EMA and HMA "Seizing opportunities in a changing medicines landscape" 2025: 20 pages. www.ema.europa.eu accessed 24 March 2025: 15 pages. **2-** "Prescrire's response to Public consultation on European Medicines Agencies Network Strategy to 2028" 3 December 2024: 21 pages.

EMA: handling the competing interests of its experts

● Prescrire has contributed to a public consultation organised by the European Medicines Agency on its new policy for handling the competing interests of scientific committee members and experts.

The European Medicines Agency (EMA) recently proposed changes to its policy for handling competing interests, after two pharmaceutical companies succeeded in getting EMA decisions annulled by a European court on the grounds of competing interests that called into question the impartiality of the experts (1,2).

In November 2024, in its response to the public consultation on this policy, Prescrire emphasised the need for the EMA to follow the principles set out in Article 63 (2) of Regulation (EC) No 726/2004, which stipulates that scientific committee members and experts shall not have financial interests in the health products industry that could affect their impartiality.

Prescrire noted that it was puzzled by the fact that the EMA presents the requirements for its experts to be impartial and independent as being in conflict with its responsibility to provide the best possible scientific advice concerning the evaluation of drugs. This indicates that the EMA remains in denial about the influence of competing interests on the decision-making process. In Prescrire's view, these requirements in fact go hand in hand and complement one another: consulting independent, impartial experts is essential for robust evaluation of the safety and efficacy of drugs.

Prescrire called for the EMA policy to refrain from spreading the fallacious message that the best experts necessarily have interests in pharmaceutical companies. It recommended that the EMA build up a network of independent experts instead.

Prescrire suggested that the EMA improve its system for assessing declarations of competing interests by appointing an independent ethics expert responsible for checking the accuracy of the declarations submitted by experts.

To ensure the transparency of this work, Prescrire recommended that this ethics expert should send an annual report of their findings to the European Court of Auditors, the European Parliament and the European Ombudsman, with a particular focus on any cases of non-compliance that they identify. This report should also be made publicly available (3).

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