

EVIDENCE REVIEW 08 • REGULATORY HISTORY

Why the FDA banned ephedrine alkaloids in supplements

The 2004 rule shows post-market evidence removing an entire class of supplement ingredients — and how long that took to assemble and enforce.

REVIEWED 9 SEPT 2026 3 SOURCES SOURCE-CHECKED

BOTTOM LINE

The FDA declared supplements containing ephedrine alkaloids adulterated because they present an unreasonable risk of illness or injury. The rule was published in February 2004 and took effect that April. It remains the clearest case of post-market evidence removing a whole ingredient class.

KEY POINTS

- The final rule was published on 11 February 2004 and took effect on 12 April 2004.
- A review of 140 reports to the FDA judged 31% definitely or probably related and 31% possibly related.
- Ten of those events ended in death and 13 in permanent disability.
- Spontaneous reports cannot establish how often harm occurs, because nobody knows how many people were exposed.

Regulators are often described as powerless over supplements. The ephedra rule is the counter-example — and also a lesson in what that power costs to use.

What ephedrine alkaloids do

Ephedrine alkaloids are stimulant compounds found in some *Ephedra* species. They were sold for weight loss and energy, frequently combined with caffeine.

Their adrenergic effects raise blood pressure and heart rate. In susceptible people they can contribute to arrhythmias, stroke and seizures. That is the difficulty at the centre of the case: the stimulant action was simultaneously the selling point and the hazard, so lowering the labelled dose did not separate one from the other.

What the adverse-event review found

Haller and Benowitz reviewed 140 reports submitted to the FDA between 1 June 1997 and 31 March 1999, published in the *New England Journal of Medicine* in December 2000.

They judged 31% of cases definitely or probably related to ephedra-containing supplements, and a further 31% possibly related. Among those definite, probable and possible cases, 47% involved the cardiovascular system and 18% the central nervous system. Hypertension was the single most frequent effect, followed by palpitations or tachycardia, then stroke, then seizures.

Ten events resulted in death and 13 in permanent disability — together about a quarter of the definite, probable and possible cases.

What those reports cannot prove

This is the part most often skipped, and it cuts both ways.

An adverse-event database has no denominator. Nobody knows how many people took these products, so no rate of harm can be calculated from the reports alone. Reports may be incomplete, duplicated, prompted by publicity, or never filed at all. What such a system produces is a signal — evidence that a hazard exists — not a measurement of how common it is.

The FDA did not rest on the count. The agency combined the reports with the established pharmacology of ephedrine alkaloids and the wider peer-reviewed literature. That combination, not the tally, is what supported the conclusion.

What the rule did, and how long it took

The final rule declared dietary supplements containing ephedrine alkaloids adulterated because they present an unreasonable risk of illness or injury under the conditions of use suggested in labelling, or under ordinary conditions of use where none are suggested. It was published on 11 February 2004, took effect on 12 April 2004, and is codified at 21 CFR Part 119.

The timeline is the uncomfortable part. The adverse-event review covering 1997 to 1999 was published in 2000. The rule took effect in 2004. Post-market authority can remove a dangerous category — but assembling evidence that survives legal challenge, and completing enforcement, takes years during which the products remain on sale.

In New Zealand, ephedrine is a controlled substance and is not permitted in dietary supplements; the framework governing what may be sold and claimed here is Medsafe's rather than the FDA's, and is described in [what supplement labels are allowed to claim in New Zealand \(/supplements/what-supplement-labels-can-claim-in-nz/\)](#). The general structure of that difference — approval before sale versus enforcement after it — is set out in [how supplements are regulated differently from medicines \(/evidence/supplement-regulation-vs-medicines/\)](#).

SOURCES

01. Final Rule Declaring Dietary Supplements Containing Ephedrine Alkaloids Adulterated Because They Present an Unreasonable Risk

Federal Register, US Food and Drug Administration

<https://www.federalregister.gov/documents/2004/02/11/04-2912/final-rule-declaring-dietary-supplements-containing-ephedrine-alkaloids-adulterated-because-they>

02. Adverse Cardiovascular and Central Nervous System Events Associated with Dietary Supplements Containing Ephedra Alkaloids

Haller CA, Benowitz NL, New England Journal of Medicine

<https://pubmed.ncbi.nlm.nih.gov/11117974/>

03. Small Entity Compliance Guide: Final Rule Declaring Dietary Supplements Containing Ephedrine Alkaloids Adulterated

US Food and Drug Administration

<https://www.fda.gov/regulatory-information/search-fda-guidance-documents/small-entity-compliance-guide-final-rule-declaring-dietary-supplements-containing-ephedrine>

Medical note. General information only. Not personalised nutrition or medical advice. This review explains published research and cannot diagnose or treat a condition. Ask a qualified clinician or pharmacist about your own health, medicines and supplement use.

Source of record. The current version of this review, with working links, is at

<https://www.proteinnotes.com/evidence/fda-ephedra-ban-evidence/>