Ephedra failures

Q&A with Steven Shapiro, Rivkin Radler LLP

Last year marked 20 years since ephedra was banned from use in dietary supplements, and though the decades since have not lacked for scandalous headlines, it remains the only legal supplement ingredient removed from the market. We asked lawyer Steven Shapiro what the supplement industry got wrong 20 years ago and what the industry of today can still learn from those mistakes.

NBJ: Ephedra marks the only time an ingredient legally on the market was prohibited by the FDA. Is that a sign that the industry is being careful or that the FDA is being careless?

Shapiro: Ephedra presented a rather unique situation, and that may be why dietary supplements containing ephedrine alkaloids were, and have been, the only "legal" dietary ingredients to be prohibited based on their posing an unreasonable risk of illness or injury. The investigation into ephedra began in October 1995, a time when DSHEA was still in its infancy, as was the industry, and many of the companies selling ephedra products generally focused on that ingredient almost solely. There were dietary supplement companies marketing herbal ephedra for its traditional Chinese medicinal value, as part of a line of herbal supplements, and had that alone continued, ephedra would probably never have become an issue.

Unfortunately, the problem was in the way that many ephedra products were being marketed. There were stimulants (e.g., "Ripped Force," "Ripped Fuel" and "Up your Gas"); weight-loss products (e.g., "Metabolife 356," "Xenadrine" and "Stacker 2") and, most concerning, products claiming to provide a natural "high" (e.g., "Herbal Ecstasy," "Cloud 9" and "Ultimate Xphoria").

The FDA initially offered what seemed a rational compromise that would have likely kept ephedra legally available for sale, but industry could not agree.

Such messaging seemed designed to encourage misuse and abuse, with consumers far exceeding recommended serving sizes and looking for the claimed results, and companies willing to combine ephedra with increasing amounts of other synergistic ingredients, primarily caffeine and yohimbe, looking to satisfy and "capture" the marketplace. Having reviewed most of the adverse events reports at the time, I recall that many linked ephedra to unsafe behavior and alcohol and other substance abuse.

It did not help the overall situation that, at the same time there was the FDA focus on ephedra, the Drug Enforcement Administration and Congress were separately focused on the problem of synthetic ephedrine, which was not only being abused but also being used by illicit "meth labs" to create methamphetamine, ultimately resulting in the Comprehensive Methamphetamine Act of 1996, greatly restricting its sale.

NBJ: Was the FDA right to ban ephedra in 2004?

Shapiro: Looking back, I believe that it was an incorrect decision on the part of the FDA to totally remove ephedra from the market. The herb had a long history of safe use and provided many benefits to its users. The FDA initially offered what seemed a rational compromise that would have likely kept ephedra legally available for sale, but industry could not agree.

On June 4, 1997, FDA proposed a regulation, 21 CFR Section 111.100, that would have limited ephedra serving size to 8 mg ephedrine alkaloids per 6-hour period (24 mg per day). At that point, the most common serving size was 25 mg of ephedrine alkaloids multiple times per day. FDA also proposed a ban on combining ephedra with other stimulants, a rather strongly worded warning, and prohibiting claims for weight loss or body building that would require long-term intake to achieve the purported effect.

Had industry agreed to these restrictions, it is conceivable that ephedra would have remained on the market.

Ultimately, with numerous media reports of adverse events (despite the lack of causation, in many of them, or extenuating factors, such as abuse of other substances), and with state after state enacting legislation, the FDA made the decision to entirely ban ephedrine alkaloids.

NBJ: What do you think the key takeaways and lessons were at the time, and has the current state of the market changed your view?

Shapiro: There was not a willingness for the major marketers of ephedra to work with the FDA to agree to the limitations mentioned. Again, many of the "major players" at the time were solely focused on the ephedra market and what seemed to be the race to create the most "potent" products possible.

In the past 20 years, the industry has become fully developed, with many diverse companies offering a wide array of products. Except for perhaps CBD and caffeine energy drinks, in today's market there is not really any single ingredient "dominating" the market or raising concern the way ephedra did 25 years ago. I also believe that the industry trade associations, including the American Herbal Products Association, Council for Responsible Nutrition and Natural Products Association, have much more influence and are able to affect the industry and marketplace far more than they could have 20 years ago. The trade associations have played instrumental roles in helping the industry navigate and avoid issues like what happened with ephedra.

I am not aware of another "legal" ingredient raising issues like ephedra, except for caffeine in energy drinks. There was, for example, a congressional hearing on energy drinks a few years back. While energy drinks remain extremely popular, it seems that the marketers are taking care to manage caffeine levels, and it seems that many of the past concerns over that category of products have died down.

NBJ: Has the industry lived up to the lessons from the ephedra ban?

Shapiro: Yes. The exponential growth of the industry, the increasing diversity of safe and beneficial dietary supplements, and the public trust in the industry demonstrate that lessons have been learned. To maintain this growth, it is crucial that the industry continue to make certain that the public and the government regulators understand that individuals and companies that market products spiked with drug ingredients or products containing ingredients such as tianeptine, which is often referred to as "gas station heroin," are criminals marketing illegal products that are not part of the dietary supplement industry and should be dealt with by government authorities accordingly.

NBJ: How much of the blame goes to irresponsible players on the fringe, and how much goes to the basic risks of the ingredient itself?

Shapiro: In the case of ephedra, the blame would seem to rest on the marketing of products with names and claims that invited excess consumption and formulations that included synergistic ingredients, such as caffeine and yohimbe, that greatly added to potential adverse consequences. It is reported that the herb was traditionally used in China and India for centuries without serious consequences. Had that type of use alone continued, we might still have ephedra on the market today.

NBJ: Do you think there are ingredients on the market or on the horizon that could risk the same fate as ephedra?

Shapiro: There are no currently legal dietary ingredients that come to mind that seem to risk the same fate as ephedra. Moreover, when issues do arise, industry and the trade associations are much better prepared to address them. I am concerned with the perception that the FDA is not exercising its enforcement authority over entities marketing clearly illegal products as dietary supplements. I am also concerned that there remains a perception that the FDA does not have adequate resources or authority to address perceived issues with the legitimate dietary supplement industry.

I am concerned about future state restrictions on specific ingredients and the passage of New York's law restricting the sale of certain dietary supplements to minors, that went into effect in April 2024, and similar legislation that is pending in several states. Whether or not these age restriction laws are justified, their vagueness in setting forth the parameters for which products are restricted and the added cost and difficulty in delivering age restricted products directly to consumers may become increasingly problematic as more states pass similar restrictions. I appreciate the trade association efforts to have these laws overturned on constitutional grounds, but if they ultimately pass muster, industry needs to come up with a plan to address them on a national level because numerous different and potentially conflicting state laws will make it nearly impossible to continue in business.