

Positive Drug Tests from Supplements

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There is a small but real risk that athletes will test positive to a banned substance as a result of ingesting supplements and sports foods. Lack of regulation of quality control and labeling of products in the supplement industry makes it impossible to identify supplements and sports foods that are risk free. Incentives or punishments for the supplement industry to improve manufacturing processes are therefore needed. Meanwhile sports authorities place the responsibility for a positive test with the athlete, necessitating better education of athletes, coaches and support staff.

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In many sports, athletes compete under a code of conduct that prohibits the use of specified drugs and related compounds. These sports use a system of drug testing to monitor compliance with the code. Recently, there has been speculation that some of the positive drug tests recorded by certain athletes have resulted from the use of supplements and special sports foods rather than deliberate use of banned products. This speculation has been particularly strong in the case of positive tests for the steroid, Nandrolone. Experts are divided over whether there has been a recent increase in the rate of Nandrolone positives among athletes, or whether there is simply more publicity about these tests. What is striking is that these positive tests appear to have occurred in clusters—for example, among British athletes—and they have often involved well-known athletes who should know better (or be smarter about being caught). Some athletes have claimed that these doping outcomes have occurred inadvertently, through the use of dietary supplements or sports foods. Is this claim true, or will supplement use become the "dog ate my homework" routine for drug users? The short answer is that supplement use is a possible cause of a doping positive, but the extent of the problem is not known.

One of the good things that may come out of the confusion surrounding this issue is the chance to warn athletes about the trust they put in supplements and sports foods. The regulation of these products varies between countries, and in this article I will compare the situation in two countries: Australia and the US. But first I will consider how an athlete might ingest a banned substance through the use of supplements, and what type of substances could be contained in supplements and sports foods.

Here is a list of some ingredients in supplements and sports drinks that are either directly banned by the International Olympic Committee's Medical Commission or that have been shown to cause a positive doping outcome in some people:

- Ephedrine
- Pseudoephedrine
- Strychnine
- Caffeine (if consumed in sufficiently high quantities to produce a urinary caffeine concentration of $>12 \mu\text{g/ml}$)
- Dehydroepiandrosterone (DHEA)
- Androstenedione, androstenediol

- 19-norandrostenedione, 19-norandrostenediol and related compounds

Now that these products are named on the IOC list of prohibited substances, an athlete who declares an intake of these substances will be deemed to have doped. An athlete who takes these products and gives a urine test carries a risk of testing positive. The newer pro-hormone products androstenedione, androstenediol, and DHEA may lead to an elevated testosterone/epitestosterone ratio (Bowers, 1999; Uralets and Gillette, 1999), and the 19-nor products may lead to a positive test for metabolites of the steroid Nandrolone.

An inadvertent doping outcome could arise from supplement use in a number of ways:

- The supplement contains a banned substance as a stated ingredient, but the athlete is not aware that the substance is banned or that it acts to cause a positive doping test
- The supplement contains a banned substance within stated ingredients, but the athlete is unaware of the relationship between the products. For example, athletes may not recognize that guarana has a high caffeine level, or that Ma Huang herbal products contain ephedrine
- The supplement contains banned substances that are not declared as a stated ingredient. These ingredients may be added deliberately and not declared, or added inadvertently as by-products of other ingredients or contaminants of the production process. Examples include herbal preparations that inadvertently contain ephedra or other herbal alkaloid stimulants found in a common plant source, or multi-ingredient "anabolic supplements" that have an undisclosed content of pro-hormones that convert into banned substances.

The risk of these problems lies with the level of education of athletes about possible sources of banned substances, and the accountability of the supplement industry to guarantee the content and correct labeling of product.

In Australia, the Australian Sports Drug Testing Agency (ASDA), an independent statutory authority established under a 1990 Federal Government Act, is responsible for maintaining awareness and understanding of anti-doping issues among athletes, coaches and sports medicine/science professionals. This role supports ASDA's primary function of conducting a comprehensive drug-testing program to deter elite athletes from taking prohibited substances. ASDA provides information about banned and permitted medications (both prescription and non-prescription) via its "Drugs in Sport Handbook" publication, pamphlets, a [website](#), and an information phone hotline. Although ASDA would appear to be the appropriate body to publicize information related to the sports safety of supplements, little information is currently available. The only advice provided to athletes is that they are responsible for their use of supplements and that it is not possible to guarantee the safety of these products.

The production and sale of sports supplements in Australia falls under the jurisdiction of two government bodies: the Australian and New Zealand Food Authority (ANZFA), which controls sports food products, and the Therapeutic Goods Administration (TGA), which controls pills and other formulations marketed as therapeutic goods. Sports foods and energy formulations such as sports drinks, sports bars, sports gels and liquid meal supplements generally fall within Standards R9 and R10 of the ANZFA Foods Standards code. These standards make provision for a range of acceptable formulations and permitted additives, as well as a list of permitted or compulsory education messages for presentation on product packaging. It is up to individual states and territories to adopt these standards within their Food Laws, and to check and regulate that these laws are upheld. There is no requirement to take sport safety issues into account within the relevant standards for sports food products. A positive drug test is not likely to be an outcome from using most of the

mainstream products (sports drinks and bars) produced by major food companies. However, a small number of sports foods, usually produced by smaller manufacturers targeting a niche market of athletes, contain added ingredients such as herbals and botanicals.

The availability and marketing of dietary supplements fitting the pill, powder or other non-food form fall within the jurisdiction of the TGA, under the Australian Therapeutic Goods Act 1989. This act distinguished two classes of products: drugs and therapeutic devices. Although dietary supplements may be packaged in a way suggesting medical or scientific rigor, as therapeutic devices they are regulated at an entirely different level to prescription pharmaceutical products. Therapeutic devices are further classified into categories of "registrable" and "listable" products, with almost all dietary supplements falling within the "listable" or less regulated category. Although they need to comply with relevant statutory standards, for example to exclude ingredients banned by Australian Customs laws, they are considered low-risk self-medications and are not subjected to a comprehensive review of quality, safety and efficacy. They are expected to comply with a recognized code of good manufacturing practice and with advertising regulations that permit only limited therapeutic claims. In practice these products receive little investigation of quality and claims unless they are the subjects of serious complaints regarding health and safety issues. There is no requirement of manufacturers to provide information or safeguards related to sports safety issues for athletes, even for products that are manufactured specifically for sports performance. However, the risk of a doping outcome from Australian products is greatly reduced by the fact that pro-hormones (e.g., DHEA, androstenedione, 19-norandrostenedione, 19-norandrostenediol and related compounds) are banned as ingredients in over-the-counter preparations and supplements in Australia.

Since athletes now have ready access to supplements from overseas via mail order, Internet sales and personal importation, it is important that they have a global understanding of the regulation of supplements. In countries such as the US, there is less regulation of the production and marketing of supplements than under the Australian system. For example, pro-hormones are permitted ingredients in over-the-counter preparations, supplements and sports foods. All forms of food and non-food supplements fall under the jurisdiction of the Food and Drug Administration (FDA). The Dietary Supplement Health and Education Act (DSHEA), passed in 1994, reduced the regulation of dietary supplements and broadened the category to include new ingredients, such as herbal and botanical products. The DSHEA shifted responsibility from the manufacturer to the FDA to enforce guidelines for safety and claims, but the FDA is allowed to investigate a supplement only after a safety problem has been reported. Requirements for good manufacturing practice and accurate labeling are included in the DSHEA, but there has been little enforcement.

In the absence of rigorous government evaluation, quality control of supplement manufacturing is trusted to supplement companies. Large companies that produce conventional supplements such as vitamins and minerals, particularly to manufacturing standards used in the preparation of pharmaceutical products, are likely to achieve good quality control. This control includes precision with ingredient levels and labeling, and avoidance of undeclared ingredients or contaminants. However, there is evidence that such control does not occur with all supplement types or manufacturers:

- Analysis of 16 commercial DHEA products revealed that only half the products contained the amount of DHEA stated on the product label; content varied from 0 to 150% of the stated content (Parasrampur et al., 1998).
- Over-the-counter androstenedione is contaminated with 19-norandrostenedione, which produces a positive urine test for Nandrolone;

furthermore, some brands of androstenedione are grossly mislabeled (Catlin, et al., 2000).

- A study of nutritional supplements containing *Ephedra sinica* (Ma Huang) reported considerable variability in alkaloid content between various brands of supplements, failure to report the *Ephedra* content on product labels, and batch-to-batch variability of nearly 140% within the same product (Gurley et al., 1998).
- Melatonin supplements have failed to meet quality claims or delivery profiles stated on their labels (Hahm et al., 1999).
- A herbal supplement used by a Dutch cyclist who tested positive for ephedrine contained *Ephedra* as a stated ingredient but also contained significant amounts of another alkaloid stimulant that was not declared as an ingredient (Ros et al., 1999).
- An expert committee reported to the UK Sports Council in January 2000 that some dietary supplements contain pro-hormone compounds without obvious signs on the label that such substances are present and are banned (UK Sports Council, 2000). They concluded that users of inadequately or incorrectly labeled products are at risk of unknowingly ingesting a banned substance.

So where do we go from here? Here are some ideas that might help to reduce the rate of positive doping outcomes:

- *Educate coaches, athletes, trainers and other sports science/medicine staff.* The message: there will always be a risk that dietary supplements will cause a positive doping outcome, and that the responsibility lies with the athlete. The risk is small, but real, and the price is a substantial loss of earnings and respect.
- *Develop programs that help athletes to distinguish levels of risk with various supplements.* For example, in Australia we are discussing the idea that an accredited assessment/testing program could allow Australian manufacturers to have their products assigned by brand name into categories of "low risk", "unknown risk", "restricted" and "banned". This information could be circulated like lists of permitted and banned medications. Athletes who wish to use supplements could be directed to use only those products designated as low risk.
- *Stop trying to excuse or exonerate athletes who claim that their positive tests are the result of supplement use.* This claim is almost impossible to prove, after the fact. Even if you could show that a supplement contained banned substances, how could you prove that it was taken inadvertently by the athlete, or that the athlete was not also taking other proscribed agents at the same time. The [International Court of Arbitration for Sport](#) has held that athletes are liable for drug offences, in that they have a duty to be aware of banned substances and to know what they are ingesting. Although it is sad to think that innocent athletes may be punished (e.g., the Romanian gymnast at the Sydney Olympics), drug education messages are quite clear that athletes are responsible for their own actions.
- *Apply pressure to supplement companies to produce only high-quality well-labeled products.* Changing government regulations to set up surveillance of the supplement industry is a desirable but almost impossibly huge task. Self-regulation might improve if customers demanded higher standards, or if there were real penalties for providing contaminated, mislabeled products that failed to deliver the promised ingredients. The sports supplement industry flourishes because athletes are prepared to buy anything that claims to improve performance. What would happen if a few celebrity athletes who have had their careers ruined because of a positive drug test sued the company that made the supplement containing an undeclared banned substance? We all might be better off if athletes undertake complicated legal battles with supplement companies

rather than sporting organizations or drug testing agencies.

References

Bowers, LD (1999). Oral dehydroepiandrosterone supplementation can increase the testosterone/epitestosterone ratio. *Clinical Chemistry* 45, 295-297

Catlin DH, Leder BZ, Ahrens B, Starcevic B, Hatton, CK, Green GA, Finkelstein JS (2000). Trace contamination of over-the-counter androstenedione and positive urine test results for a nandrolone metabolite. *JAMA* 284, 2618-2621

Gurley BJ, Wang P, Gardner SF (1998). Ephedrine-type alkaloid content of nutritional supplements containing *Ephedra sinica* (Ma Huang) as determined by high performance liquid chromatography. *Journal of Pharmaceutical Science* 87, 1547-1553

Hahm H, Kujawa J, Ausberger L (1999). Comparison of melatonin products against USP's nutritional supplements standards and other criteria. *Journal of the American Pharmaceutical Association* 39, 27-31

Parasrampur, J, Schwartz K, Petesch R (1998). Quality control of dehydroepiandrosterone dietary supplement products. *JAMA* 280,1565

Ros JJ, Pelders MG, de Smet PA (1999). A case of positive doping associated with a botanical food supplement. *Pharmaceutical World Science* 21, 44-46

UK Sports Council (2000). Nandrolone review: report to the UK Sport Council from the expert committee. London: UK Sport Council

Uralets VP, Gillette PA (1999). Over-the-counter anabolic steroids 4-androsten-3,17-dione; 4-androsten-3beta,17beta-diol; and 19-nor-4-androsten-3,17-dione: excretion studies in men. *Journal of Analytical Toxicology* 23, 357-366

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