WORLD ANTI-DOPING AGENCY

PROHIBITED LIST

REFERENCED REVIEW OF SPECIFIC SUBSTANCES

In preparing the Draft Prohibited List the WADA List Committee has adhered to the requirements of the WADA Code.

The List has been constructed carefully and with due regard for the performance-enhancing properties of a substance, and the degree to which the use of certain substances may represent a hazard to the health of the athlete, or contravenes the 'Spirit of Sport'.

A synopsis of information available about many of the substances that are listed appears below. Relevant scientific references follow. An examination of this material will be helpful in permitting a thoughtful review of the Draft List.

In preparing comments or criticisms about the Draft it is hoped that all submissions will be supported, where possible, with references to the scientific or clinical literature.

The committee has adopted a comprehensive approach to its review of the 2003 IOC prohibited list.

As a consequence of this work, some changes have been recommended to the list.
Some substances have been removed from the list, some have been added and a number of changes have been made in the wording, classification or other elements of the list's organization.

Specific Areas of Interest and Review:

The committee has spent considerable effort examining a number of particular issues. The conclusions of the committee following such examinations have been instrumental in permitting the above recommended changes to the List for 2004.

Caffeine:

There has been extensive scientific study of the effects of caffeine on exercise performance.[1,2,3,4,5,6]

Caffeine was first prohibited in 1984 with a urinary level >15ug/ml. In 1985, this was reduced to >12ug/ml. Caffeine was listed as a doping agent in class I A "Stimulants" of the IOC list of Prohibited Substances and Prohibited Methods as a consequence of the reported misuse of high doses of pure caffeine in some sports. Urinary caffeine levels are determined by many factors including the size and time of the ingested dose, the metabolic clearance (fast or slow acetylators), body mass, hydration, exercise, gender, habitual use, oral contraceptives and smoking.

Urinary caffeine concentrations are notoriously inaccurate reflections of caffeine intake partly because only ~1% of ingested caffeine is excreted unchanged.[7] Some sports do not accept a urinary caffeine >12ug/ml as positive without undertaking a dose response study in that athlete.

Performance enhancement following ingestion of caffeine varies greatly and recent studies confirm that in some subjects, extremely modest levels of 1-3 mg/kg body mass or ~ 70-150 mg caffeine can enhance performance.[8] It is clear that performance enhancement can occur with the ingestion of caffeine at levels well below those likely to produce urinary levels > 12 ug/ml – the current threshold for determining a doping infraction.

To reduce the urinary threshold to a level compatible that at which performance enhancement commences would likely produce the situation that very large numbers of athletes would be reported as having incurred a doping violation. There is no evidence of a dose-response relationship and in fact, the side-effects of excessive caffeine ingestion may impair performance at or close to the existing prohibited urinary level of >12ug/ml.

Caffeine is a constituent of many foods and beverages (chocolate, tea, coffee, colas, sports gels, "energy" drinks etc) and total prohibition of all caffeine containing foods and beverages at or around the time of competition would be impractical. Translating the above, in a female marathoner weighing 50kg or less, a can and a half of cola, or two cups of tea or one cup of coffee would each provide 1-2mg of caffeine per kg body mass.
It is impractical to prohibit such quantities of food and beverage. The performance enhancement from caffeine could be analogous to that from carbohydrate loading but less than the beneficial effects of consuming adequate fluid to combat dehydration.[9]
Caffeine, when used in combination with *ephedrine* has been noted to improve athletic performance;[10] this reality is best addressed by continuing to test for, and sanction the presence of *ephedrine*.

In summary, caffeine is a ubiquitous and widely consumed constituent of a worldwide array of foodstuffs and beverages.

It is capable of enhancing performance at low levels of ingestion, urinary levels of caffeine concentration are an unreliable indicator of caffeine dose, it is not possible to distinguish casual, normal use of caffeine from doping attempts, and the ergogenic benefits of caffeine are small and realized by the vast majority of competitors most of whom are caffeine users.

Action: ***Caffeine has been removed from the "Prohibited List".***

Sympathomimetics:

The sympathomimetics, substances that emulate the activity of the sympathetic nervous system by stimulating a variety of physiological processes central to the "fight or flight" response, were among the first to be banned in sport. Closely related structurally to the amphetamines they include *ephedrine, pseudoephedrine, phenylpropanolamine, phenylephrine and synephrine.* They have been used in a variety of medications and over-the-counter products and are a common ingredient of products whose use is intended to relieve the symptoms of colds, flu and other upper respiratory infections. Several authorities have noted that that the ergogenic or performance-enhancing properties of the sympathomimetics are unclear.[11,12,13]

Investigations designed to assess the ergogenic properties of ephedrine on physical work capacity have generally failed to show an effect.[14] Recent evidence supports the view that *ephedrine*, when used in combination with caffeine is capable of accentuating endurance and anaerobic performance.[15,16,17,18,19]

This effect is consistently noted and provides support for the position that the use of *ephedrine* should be prohibited in sport, particularly given the many problematic issues surrounding any consideration of maintaining a ban on caffeine (discussed elsewhere).

The sympathomimetics are found worldwide in a broad array of over-the-counter medications that enjoy widespread use. This is particularly true of *pseudoephedrine, phenylephrine, phenylpropanolamine and synephrine.*

A number of investigators have sought to assess the ergogenic properties of *pseudoephedrine*. Almost universally, little evidence has been found to support the contention that *pseudoephedrine* is capable of enhancing performance.[20,21,22,23] The lack of ergogenic effect is noted even when urinary concentrations of *pseudoephedrine* dramatically exceed the threshold at which current sport regulations mandate that a doping infraction be determined.[xxii] (Under current Olympic Movement Anti-Doping Rules urine concentrations of *pseudoephedrine* > 25ug/ml result in a positive test.)

As with any consideration of urinary levels there is no correlation with the actual dose of a compound that has been ingested – which seriously undermines the use of urinary thresholds for the determination of doping violations.

Only one group of researchers has reported that *pseudoephedrine* use was associated with increases in peak torque produced in knee extension, and improved peak power during maximal cycle performance was noted in their study.[24]

The limitations of the studies conducted in this area must be acknowledged; they include small numbers of subjects, athletes of varying skill levels and varying doses of sympathomimetics. Nonetheless, it is noteworthy that with the exception of the use of *ephedrine* in association with caffeine, there is very little evidence to justify the ban on sympathomimetics.

Action: *The sympathomimetics phenylephrine, phenlypropanolamine, pseudoephedrine and synephrine have been removed from the "Prohibited List".*

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Caffeine:

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Sympathomimetics:

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