

MAKING THE WORLD ANTI-DOPING AGENCY PROHIBITED LIST: SHOW ME THE DATA

(Published in St. Louis Law J., Vol. 50, # 1, Fall 2005)

NAME: SRIKUMARAN MELETHIL*

BIO: * Ph.D., J.D., Professor Emeritus, Schools of Pharmacy and Medicine, University of Missouri-Kansas City, Patent Attorney, Findlay, OH, email: melethils@yahoo.com.

LEXISNEXIS SUMMARY:

... "So let the Games begin! I plan to adopt the English poet Samuel Taylor Coleridge's advice and follow the events having willfully suspended disbelief, confident that the playing field is level, that no one is on drugs and that no athlete has a concealed bionic assist. ... WADA's determination that the Use of the substance or method violates the spirit of sport A substance or method that meets two of the three criteria listed above "shall be considered for inclusion on the Prohibited List" The Code further states that all inclusion decisions "shall be final and shall not be subject to challenge by an Athlete or other Person based on an argument that the substance or method was not a masking agent or did not have the potential to enhance performance, represent a health risk, or violate the spirit of sport. ... Testing athletes for EPO use ignores another of the IOC's stated aims for drug-doping: prevention of health risks. ... The story of Olga Yegerova illustrates that complex drug tests can be in error, and that such errors in drug testing can unfairly affect an athlete's career and reputation. ... Therefore, even when caffeine was a prohibited substance, athletes and coaches knowledgeable of the principles of urinary drug excretion could have developed pharmacokinetic strategies to escape detection. ...

HIGHLIGHT: "Esteem Literacy and Despise Martiality" n1

"So let the Games begin! I plan to adopt the English poet Samuel Taylor Coleridge's advice and follow the events having willfully suspended disbelief, confident that the playing field is level, that no one is on drugs and that no athlete has a concealed bionic assist." n2

TEXT:

[*75] I. Introduction

Illegal drug use in sports has been a matter of much recent concern among lawmakers and organizations responsible for regulating sports, such as the International Olympics Committee (IOC), the National Football League, and Major League Baseball. The two widely stated reasons for such concerns are health risk to athletes and the unfair advantage gained (the so-called "performance enhancement") by such drug use. n3 The widely publicized United States Senate hearing on March 17, 2005, regarding steroid

use in professional baseball is one such example. n4 Sensational, tragic, and/or misleading issues, in addition to the lack of reliable information, obfuscate the truth about the extent of drug use in sports and the associated health risks. n5

This Review provides a scientific analysis of the efforts made by one major international organization, namely the IOC, to address these two issues [*76] of health risk to and unfair advantage for athletes who use drugs in competition to enhance their chances of winning. Suggestions for improvement of the currently used drug testing procedures are also presented. Part II provides a critical review of the inclusion criteria used by the World Anti-Doping Agency (WADA) to list a substance or a method in its Prohibited List. n6 WADA is the arm of the IOC responsible for prevention of drug abuse. Part III, using selected examples, focuses on the need for the IOC to make more science-based decisions relating to the addition or deletion of a given substance or method to the Prohibited List; such decisions can also enhance athlete safety, as in the case of erythropoietin. Specific suggestions for improving the drug testing programs are presented in Part IV.

II. The Prohibited List: Criteria for Inclusion

The Prohibited List is an exhaustive and extensive list of prohibited substances and methods provided by WADA. n7 Prohibited substances are classified in five groups: anabolic agents, hormones, beta-2 agonists, anti-estrogenic agents, and diuretics. n8 Prohibited methods include oxygen transfer enhancements, various methods used to tamper with samples, and gene doping. n9

WADA does not publicly disclose the scientific reasons or the literature (bibliography) used to include them in this list. In general, there is a paucity of competent data to support the conclusion that the majority of the listed substances in fact enhance performance, which is the main reason athletes use various drugs, methods, or dietary supplements.

WADA states that anti-doping programs are necessary to preserve "the spirit of sport," which consists of: "ethics, fair play and honesty[;] health[;] excellence in performance[;] character and education[;] fun and joy[;] teamwork[;] dedication and commitment[;] respect for rules and laws[;] respect for self and other participants[;] courage[;] [and] community and solidarity." n10 Doping is defined as using or attempting to use prohibited substances, having prohibited substances or its metabolites or markers in one's bodily fluids, refusing to provide a sample for testing without "compelling justification," refusing information about one's whereabouts or missed tests, tampering or attempting to tamper with one's samples, possessing or [*77] trafficking any of the prohibited substances and/or methods, and/or administering or encouraging the use of prohibited substances to other athletes. n11

The three major criteria for banning the use of a given substance or method are:

Medical or other scientific evidence, pharmacological effect or experience that the substance or method has the potential to enhance or enhances sports performance;

Medical or other scientific evidence, pharmacological effect, or experience that the Use of the substance or method represents an actual or potential risk to the Athlete;

WADA's determination that the Use of the substance or method violates the spirit of sport n12

In addition, a "substance or method shall also be included on the Prohibited List if WADA determines there is medical or other scientific evidence, pharmacological effect or experience that the substance or method has the potential to mask the Use of other Prohibited Substances and Prohibited Methods." n13

A substance or method that meets two of the three criteria listed above "shall be considered for inclusion on the Prohibited List" n14 The Code further states that all inclusion decisions "shall be final and shall not be subject to challenge by an Athlete or other Person based on an argument that the substance or method was not a masking agent or did not have the potential to enhance performance, represent a health risk, or violate the spirit of sport." n15 An argument does not necessarily include evidence in support of an argument. n16 The inability to challenge a scientific assertion by WADA with respect to performance enhancement or health risk undermines its claim that the Code is based on scientific principles. Coupled with this are the facts that the Code language is rather broad and vague, and others do not have access to [*78] WADA deliberations on inclusions and deletions to the Prohibited List. n17 Clearly, such inability to know the scientific basis of the inclusion criteria and/or to challenge it on scientific grounds poses the threat of a scientific monopoly by the IOC, and is a violation of the "spirit of science," which calls for peer review of biomedical literature. n18 Such IOC control can result in the banning of innocent athletes from competition, and resultant stories could decrease the enthusiasm among the young to pursue Olympic sports as a career. n19

III. The Prohibited List: Need for Greater Science-Based Inclusion Criteria

The following selected examples illustrate the need for WADA to incorporate policies consistent with its stated objectives of preventing drug abuse and associated health risk to athletes. n20

A. Erythropoietin

Erythropoietin (EPO) is a drug used in clinical medicine to increase the packed red blood cell volume, which is called a "hematocrit reading." n21 Increasing hematocrit can enhance an athlete's performance by increased availability of oxygen. n22 The health risks associated with EPO use were first suspected with the death of several Dutch cyclists who died in their sleep. n23 Normal (average) hematocrit values range between forty and fifty percent. n24 The risk of stroke increases significantly as hematocrit values increase over fifty percent and increased hematocrit coupled with hypertension increases nine-fold the risk of a stroke. n25 Dehydration during exercise, as in endurance [*79] sports, exacerbates this risk by increasing blood viscosity (reducing the ability to flow) and blood pressure. n26

EPO is a banned substance listed under prohibited methods for enhancement of oxygen transfer. n27 However, two other methods to increase hematocrit are not banned. One method involves the use of a hypoxic air tent, which costs about \$ 7000. n28 The second method, which can increase hematocrit to dangerous or fatal levels, involves training at high altitudes for extended periods of time; this method can be even more expensive than the first method. n29 It has been estimated that monthly EPO costs

about \$ 120 for 8600 international units; even a four-year use at this dose costs under \$ 6000. n30 Therefore, these rules favor the affluent athletes, which does not fit the "spirit of sport" criteria elaborated by the IOC.

Testing athletes for EPO use ignores another of the IOC's stated aims for drug-doping: prevention of health risks. Biological samples tested include urine or blood. Dr. Don Catlin, director of the only IOC approved laboratory in the United States, stated that the urine tests, which are more accurate, cost about \$ 400 per test, while the less accurate blood test costs about \$ 60. n31 Urine tests can detect EPO only when used within forty-eight hours prior to testing. n32 These tests provide no information about the risk associated with high hematocrit values. In addition to direct testing for EPO use, the International Cycling Union (ICU) has a hematocrit cut-off of fifty percent. n33 About five percent of the population has a natural level greater than fifty percent; n34 such athletes will require additional testing to show that their hematocrit value is natural. It is also technically difficult to measure EPO because it is an endogenous substance. Further, the cost of a hematocrit test is about \$ 10. n35 In view of these factors, it is recommended that the IOC abolish chemical testing for EPO. Instead, it should use the ICU hematocrit cut-off of fifty percent, with the provision that athletes with a hematocrit greater than fifty percent may be able to compete if they show evidence that their hematocrit level is natural. Though this might promote the use of EPO, it will be medically safe. It will definitely "level the playing field" since every athlete will have the option of [*80] achieving a safe maximum hematocrit level under supervised conditions. The cost savings on testing would also be substantial.

The story of Olga Yegerova illustrates that complex drug tests can be in error, and that such errors in drug testing can unfairly affect an athlete's career and reputation. n36 Her urine tested positive for EPO in 2001 at the Paris Grand Prix 5000m event; while the French accepted this as conclusive proof of EPO use, the International Association of Athletics Federations disagreed, insisting that a blood test was needed for exclusive proof. n37 When Yegerova was tested for EPO a few weeks later at the World Championships, "her blood test came back as suspicious, but the urine test did not show EPO usage." n38 As stated, urine tests do not detect EPO if ingested more than forty-eight hours prior to testing. n39 These events caused one opponent to state that she would not participate if Yegerova did; two other athletes held up a sign in the stadium that read, "EPO drug cheats out." n40 "Collateral damage" caused by such erroneous drug testing may turn promising athletes to other careers.

B. Steroids

Success stories, such as that of Arnold Schwarzenegger, who used steroids in the past, would make it difficult to dissuade the public, especially athletes, from believing in the dangers of steroid use. n41 Even with the highly publicized steroids, "the secrecy that surrounds the use of androgens to enhance performance makes it difficult to investigate their effects on strength and performance in an objective and controlled manner." n42 One controlled study has shown performance enhancement in "normal" men on "supraphysiologic" doses of testosterone. n43 However, a close analysis of the data shows that exercise and weight training alone can result in significant performance enhancement; the data also suggests that such improvement might be less [*81] pronounced in individuals with naturally higher abilities. n44 Confirmative clinical studies in athletes to test this hypothesis may be difficult, if not

impossible, due to ethical or risk considerations. Similarly, dose-response studies, which might also inform us about those dose levels that are beneficial and those that pose a health risk, would also be difficult to conduct. Therefore, as a first step, the IOC should encourage and support the development of animal models to study the effects of steroids on performance and health.

C. Caffeine

The rationale behind the decision to drop caffeine from the Prohibited List in 2004 is unknown; questions from this Author to WADA officials (phone calls) were unanswered. It has been speculated, perhaps in jest, that this decision might have been due, at least in part, to pressure from the soft drink industry. n45 However, the following discussion comparing two stimulants, namely amphetamine and caffeine, illustrates the complex pharmacological issues that need to be considered when making decisions of either inclusion or exclusion of a stimulant to the Prohibited List. n46

The use of many (about forty) stimulants, identified by name, are banned with the added proviso that "other substances with a similar chemical structure or similar biological effect(s)" are also included. n47 Such a proviso can be a pharmacological nightmare for any athlete or coaching staff. Caffeine, a stimulant, was removed from the Prohibited List in 2004; amphetamine continues to be on the List. n48 The pharmacology of both is similar, though amphetamine is a more potent stimulant than caffeine. n49 Improved performance with amphetamine was observed in "highly" trained athletes such [*82] as swimmers, runners, and weight throwers; improved performance was attributed to the masking of the fatigue and/or pain. n50 While performance enhancement results with caffeine were less definitive, it was reported that while "major effects of caffeine on exercise capacity have not been found, ... some small (but, in competitive sports, important) effects may be present." n51 Further, caffeine increases the use of free fatty acids in the blood, which can serve as an additional fuel source to glycogen and thus promote performance. n52 From a pharmacological point of view, it is important for the IOC to justify the retention of amphetamine, and other less potent stimulants, but not caffeine, on the Prohibited List.

In general, tests based on urine concentrations of drugs, though convenient, are fraught with problems that are widely recognized in pharmacological circles; for example, water consumption or urine acidity can influence such concentrations. n53 When caffeine was banned, its use was established if the urine concentration was twelve micrograms per milliliter or greater. n54 Therefore, even when caffeine was a prohibited substance, athletes and coaches knowledgeable of the principles of urinary drug excretion could have developed pharmacokinetic strategies to escape detection. n55 Obviously, it would be almost impossible to document such cases. The case of Ms. Terri Edwards, a sprinter for the United States Olympic Team, illustrates the reverse situation, where the coaching staff appeared to be unfamiliar with drugs and supplements; this lack of expertise had a major negative impact on her career. n56 A urine sample obtained from Edwards on April 24, 2004, tested positive for nikethamide, a prohibited stimulant; she had ingested two "Coramine Glucose" tablets, given to her by her physical therapist (chiropractor). n57 On June 21, 2004, the United States Anti-Doping Agency (USADA) charged her with [*83] doping and recommended a 2-year suspension. n58 The product label clearly indicated that it contained 125 milligrams of nikethamide. n59 On appeal, the Court of Arbitration for Sport (CAS) upheld the suspension, though it noted that "the Panel is satisfied that she has conducted herself with

honesty, integrity and character and that she has not sought to gain any improper advantage or to "cheat' in any way." n60

Another issue that further questions the pharmacological rationale of dropping caffeine from the Prohibited List is that, in rat studies, caffeine potentiates the effects of cathinone, a prohibited substance. n61 While these effects do not appear to be performance-related, it further questions the deletion of caffeine from the Prohibited List.

D. Marijuana

Cannabinoids are prohibited, n62 though nobody really believes that marijuana is a performance-enhancing drug. In fact, marijuana most probably impairs performance. n63 One widely reported controversial case related to marijuana use in competitive sports illustrates the ineffectiveness and confusion regarding implementation of IOC rules to prevent drug use in sports. n64 Ross Rebagliati, a Canadian, won the gold medal for snow boarding at the 1998 Winter Olympics in Nagano, Japan. n65 A urine sample obtained from Rebagliati "immediately after he won" had a concentration of 17.8 nanograms per milliliter (ng/ml) of cannabis metabolites. n66 Based on this finding, the IOC stripped him of his medal. n67 On appeal, the CAS reversed the IOC decision stating the IOC "had disqualified Rebagliati even though the IOC has no prohibitions or sanctions for the use of cannabis (marijuana)." n68 While the IOC had no doping rules relating to marijuana, the International Ski [*84] Federation (FIS), n69 the governing body for skiing and snowboarding, sets a limit of 15 ng/ml for cannabis metabolites. n70 Since there was no official agreement between the IOC and the FIS regarding marijuana, the IOC did not have the authority to enforce the latter's prohibitions. n71 Since only athletes who possess the financial resources to bring such appeals can contest such decisions, as with the EPO regulations, less affluent athletes are at a disadvantage.

Later events related to this story also demonstrate that, by using selective facts advantageous to their cause, those who benefit from and advocate drug testing exaggerate the significance of their efforts. More than a year later, in 1999, Barry McCaffrey, director of the Office of National Drug Control Policy (ONDCP), testified before Congress:

Today, the Office of National Drug Control Policy is releasing a national strategy to help address the threat of drug use and doping in sport This Strategy builds upon a series of important successes. ONDCP pushed the International Olympic Committee (IOC) to make marijuana a banned substance after an athlete who tested positive for marijuana was awarded the Olympic gold and hoisted up on the medal platform as a hero to all the world's youth. The IOC responded and marijuana is now prohibited. n72

The failure of McCaffrey to include the reversal by the CAS in his testimony ignores the ineffectiveness of the IOC in enforcing its anti-doping rules. Apparently, he considers this a major victory against drug doping because he refers to this incident a second time in his testimony, where he states, "since the infamous Nagano snowboarding incident described above." n73 Clearly, marijuana use is not one of the

serious problems in drug doping. In fact, Rebagliati had argued in his defense that his exposure this time was due to "second hand" smoke; n74 while not so indicated, it is likely to have been another reason for the CAS to reinstate his gold medal.[*85]

E. Growth Hormone

Human growth hormone (hGH) is another prohibited substance. n75 However, there is little evidence that this hormone is a performance-enhancement substance. n76 "In any case most elite athletes have low body fat, so it is doubtful whether any small increase in power to weight ratio as the result of loss of more fat could be significant in terms of increased performance." n77 The belief that hGH has an anabolic effect is based on results in hGH-deficient adults. n78 In fact, hGH can decrease performance in healthy adults; in studies conducted at the Danish Institute of Sports Medicine, athletes were unable to complete cycling tasks after being treated with hGH. n79 Ironically, use of this hormone in sports has been inadvertently promoted by anti-doping authorities by merely listing it as a prohibited substance. Educational efforts to inform athletes that hGH "does not "work"" in normal healthy subjects and that its use has "immediate and long term hazards - everything from decreased performance to cancer" is likely to be more effective in combating its use among athletes. n80

F. Diuretics and Other Masking Agents

The use of diuretics and other masking agents is prohibited. n81 Diuretics are agents that increase urine output. n82 The major "masking" effect is the decrease in concentrations of other prohibited substances due to this increased urine volume, making the detection of other prohibited substances in the urine difficult. It is beyond the scope of this Review to discuss the wide availability of sensitive and specific methods for detecting many prohibited substances in the urine. n83 These methods are capable of detecting parts per billion (nanogram quantities) or parts per trillion (picogram quantities). The IOC should expand the use of these methods to anti-doping efforts, which should simplify the Prohibited List by removing many currently prohibited diuretics from the list. Such simplification would be very helpful to an honest athlete, for whom the fear of accidental ingestion of a prohibited substance is real.

[*86] The inclusion in 2003 of the oral contraceptive Yasmin to the Prohibited List, and its subsequent quick removal in 2005, clearly shows the need for the IOC to exercise scientific restraint in preparing this List. The Athlete Advisory in 2003 stated: "Yasmin, a popular birth control pill, contains a prohibited substance - the diuretic DROSPIRENONE. The purpose of the diuretic is to prevent the retention of water. The use of Yasmin could, therefore, result in an adverse laboratory finding and a doping violation." n84 In 2005, the IOC removed Yasmin from the prohibited list without comment. n85 Attempts by this Author to get additional information from WADA (phone calls) about these deletions from the Prohibited List were unsuccessful. By its own admission, WADA recognized the wide use of this contraceptive, and therefore, certainly should have recognized the unnecessary disruption to the daily lives of female athletes brought about by prohibiting its use.

IV. Suggestions for Improving the Chemical Drug Testing Paradigm

The major intent of these recommendations is to ask WADA to simplify the Prohibited List and provide explanatory notes for the inclusion of each substance or method in the List. Such an "athlete-friendly" list is likely to improve compliance and minimize inadvertent violations which have devastating effects on the careers and lives of athletes. In this context, anti-doping agencies should revisit the issue of strict liability.

This standard makes enforcement easier. However, there are other issues that must also be considered. First, many athletes use dietary supplements that are not prohibited to enhance performance, though the claimed beneficial effects of many of these products remain clinically unproven. Second, many in the sports world appear to be unaware that many of these products are contaminated because they are not manufactured under the high standards used for drugs and do not require pre-market approval by the Food and Drug Administration (FDA).ⁿ⁸⁶ In 2003, the FDA proposed a rule that would require [*87] that these supplements be manufactured under standards of current good manufacturing practices; a final rule is expected in 2005.ⁿ⁸⁷ Third, sophisticated chemical analytical methods can detect minuteⁿ⁸⁸ amounts of prohibited substances; more sensitive and specific methods are expected in the future. Therefore, the detection limits are well below pharmacological thresholds for performance enhancement, the main reason athletes ingest these supplements. Besides, there is an acute lack of data to support the conclusion that many of the substances or methods listed in the current Prohibited List do enhance performance. The standard of strict liability as applied to drug testing, though highly pragmatic, is based on a ritualistic "gotcha" policy, which neither enhances the stature of competitive Olympic sports, nor the IOC. In contrast, the stated standard of proof for doping is the "balance of probability" standard; this standard is greater than "a mere balance of probability but less than proof beyond a reasonable doubt."ⁿ⁸⁹ It is recommended that, when an athlete tests positive for a prohibited substance, anti-doping agencies allow, on a case by case basis, expert pharmacological testimony to the issue of performance enhancement. While such a change would clearly make the current proceedings more confrontational and prolonged, it will be fairer to athletes. In one example, an athlete inhaled a prohibited substance when he used the American brand of Vicks, a decongestant inhaler, instead of the British brand.ⁿ⁹⁰ However, even some athletes are in support of the strict liability standard.ⁿ⁹¹ It would appear that the examples stated above provide the "blinding reason and cause" needed to reconsider this standard of liability.ⁿ⁹²

It appears that the mission of anti-doping agencies today is to make sports "squeaky clean" of drugs, whether they enhance an athlete's performance abilities or not. They have become de facto drug enforcement agencies for athletes. Hence, the Prohibited List includes everything "under the sun" that is perceived to offer an advantage. The unanticipated negative consequence of such a draconian approach is that it promotes drug doping. The mere listing of a substance or method in such a list is misinterpreted by most athletes that the substance or method offers an advantage. The logic simply is: If a substance or method does not offer an advantage, why would WADA put it on the list? [*88] So, it is recommended that WADA convene a panel consisting primarily of clinical and basic pharmacologists, exercise physiologists and sports medicine researchers, and bioanalytical chemists to reconsider the following central and related questions:

(1) Does competent science support the belief that a listed substance enhances performance? This is the key question because athletes "take drugs" to enhance performance. Further, making public the rationale for inclusion of a substance or method, along with supporting data such as specific publications or bibliography used to make inclusion or deletion decisions, will enable anti-doping agencies to educate athletes and to receive constructive comments from the scientific community at large.

(2) How can chemical analytical tools available today be better used to detect drugs of abuse in biological fluids such as urine, blood, and other body fluids and tissues? Such knowledge, for example, could eliminate or drastically minimize the number of prohibited substances, such as diuretics.

(3) What are the "information" gaps in knowledge regarding drug use and performance? This would help in designing appropriate clinical studies; when such studies are not possible for ethical or health risk reasons, there should be development of animal models to study drug-induced performance enhancement.

As new understanding of the physiology of athletic performance becomes available, efforts by anti-doping agencies to curb doping and cheating by athletes (the "cat and mouse game") could become irrelevant. For example, it was recently reported that lactic acid, whose accumulation is believed to cause muscle fatigue, may have beneficial effects on muscle performance. ⁿ⁹³ Athletes now use many approaches, such as creatine supplementation, carbohydrate loading, and high-altitude training to combat muscle fatigue. ⁿ⁹⁴ Athletes and trainers, especially in developed countries, who have the resources to understand and apply such information are likely to benefit from such new developments.

[*89] Drug abuse in sports in America has become an over-sensitized, emotional issue; the recent Senate hearing on steroid use in baseball is one such example. ⁿ⁹⁵ On the other hand, there is hardly any discussion on the use of drugs by musicians to suppress stage fright, and thus improve performance. ⁿ⁹⁶ Historically, efforts to curb recreational drug use have not fared well. Prohibition was repealed; the success of drug enforcement agencies in combating drug abuse in the general public has been limited at best. It is therefore reasonable to believe that efforts to combat drug use in sports through drug testing are unlikely to be a big success. It has been argued that drugs should be made legal, because "by allowing everyone to take performance enhancing drugs, we level the playing field." ⁿ⁹⁷ The relatively small number of athletes who are "caught" suggest that either drug abuse is not a rampant problem or, if it is rampant, that most of the "cheaters" escape detection. In conclusion, the IOC, by exposing myths of drug-induced performance enhancement, and educating athletes regarding the risks and lack of effectiveness of many popular drugs and dietary supplements, combined with limited drug testing, is likely to be more successful in combating the problem of drug doping in sports.

FOOTNOTES

n1. Ancient Chinese Proverb

n2. Donald Kennedy, Editorial: Here Come the Olympics, 305 Science 573, 573 (2004) (note to readers from Editor in Chief).

n3. See Restoring Faith in America's Pastime: Evaluating Major League Baseball's Efforts to Eradicate Steroid Use: Hearing Before the H. Comm. on Gov't Reform, 109th Cong. 8 (2005), available at http://frwebgate.access.gpo.gov.ezproxy.mnl.umkc.edu/cgi-bin/useftp.cgi?IPaddress=162.140.64.21&filename=20323.pdf&directory=/diskb/wais/data/109_house_hearings [hereinafter Restoring Faith in America's Pastime] (statement of Chairman Tom Davis).

n4. See id.

n5. See Duff Wilson, After Young Athlete's Suicide, Steroids Are Called the Culprit, N.Y. Times, Mar. 10, 2005, at A1 (reporting teenager's suicide resulting from an abrupt withdrawal of steroid use and the failure of the treating physician to recognize the consequences of such abrupt withdrawal).

n6. To view the substances and methods listed on the current Prohibited List, see World Anti-Doping Agency, World Anti-Doping Code: The 2005 Prohibited List: International Standard (2005), available at http://www.wada-ama.org/rtecontent/document/list_2005.pdf [hereinafter Prohibited List].

n7. World Anti-Doping Agency, World Anti-Doping Code, 4.2 cmt. (2003), http://www.wada-ama.org/rtecontent/document/code_v3.pdf [hereinafter WADA Code].

n8. Prohibited List, *supra* note 6, S1-S5.

n9. Id. M1-M3.

n10. WADA Code, *supra* note 7, at 3 (introduction).

n11. International Olympic Committee, Anti-Doping Rules Applicable to the Games of the XXVIII Olympiad in Athens in 2004, arts. 1-2 (2004), available at http://www.baseball.com.au/site/baseball/abf/downloads/olympics/IOC%20Anti-Doping%20Rules%20-%20Athens%202004.pdf?MenuID=National_Teams%2F86%2F0%2CNational_Senior_Men%2F365%2F6264%2CCURRENT_NEWS%2F1762%2F0&MenuID=National_Teams%2F86%2F0%2CNational_Senior_Men%2F365%2F6264%2CLIBRARY%2F1761%2F0%2CAthens_Library<abval1>News%2F1763%2F0 [hereinafter IOC Rules].

n12. WADA Code, *supra* note 7, 4.3.1.1-4.3.1.3 (first emphasis added).

n13. Id. 4.3.2.

n14. Id. 4.3.1 (second emphasis added).

n15. Id. 4.3.3 (third emphasis added).

n16. "Argument" is defined as "[a] statement that attempts to persuade[.]" Black's Law Dictionary 114 (8th ed. 2004).

n17. My efforts in calling WADA to get information about its reasons for dropping caffeine and the contraceptive agent Yasmin from the Prohibited List were unsuccessful.

n18. See Lois Ann Colaianni, Peer Review in Journals Indexed in Index Medicus, 272 JAMA 156, 156 (1994).

n19. See J. Savulescu et al., Why We Should Allow Performance Enhancing Drugs in Sport, 38 Brit. J. Sports Med. 666, 669 (2004) ("Linford Christie, who served a two year drug ban from athletics competition, said that athletics "is so corrupt now I wouldn't want my child doing it.").

n20. An exhaustive analysis of such an example is beyond the scope of this effort.

n21. Savulescu et al., supra note 19, at 667. A hematocrit reading is "the percentage of the whole blood volume occupied by the red blood cells after centrifugation." Blakiston's Gould Medical Dictionary 597 (4th ed. 1972).

n22. See Savulescu et al., supra note 19, at 667.

n23. See id.

n24. Id.

n25. Id.; see also G. Wannamethee et al., Haematocrit, Hypertension, and Risk of Stroke, 235 J. Internal Med. 163, 165 (1994).

n26. Savulescu et al., supra note 19, at 667.

n27. Prohibited List, supra note 6, M1.

n28. Savulescu et al., supra note 19, at 668.

n29. Id.

n30. Id.

n31. EPO Drug Testing Q&A (Sept. 11, 2003), <http://letsrun.com/2003/epoqa.php> (last visited Nov. 20, 2005) [hereinafter EPO Q&A].

n32. Id.

n33. Savulescu et al., *supra* note 19, at 667.

n34. *Id.*

n35. This was the cost of the procedure at the Clinical Reference Laboratory, in Lenexa, Kansas.

n36. See EPO Q&A, *supra* note 31; Andrew Morton, *Yegerova the Top: Athletics Tainted - by Institutional Racism*, <http://freespace.virgin.net/bobbing.cardiffcity/yeg.html> (last visited Nov. 20, 2005).

n37. See EPO Q&A, *supra* note 31.

n38. *Id.*

n39. See *supra* text accompanying note 32.

n40. Morton, *supra* note 36.

n41. See Anne E. Kornblut, *The Steroids Hearings: The Politicians: Two Parties in Congress Are at Odds Only Against Witnesses*, *N.Y. Times*, Mar. 18, 2005, at D6.

n42. Carrie J. Bagatell & William J. Bremner, *Androgens in Men-Uses and Abuses*, 334 *New Eng. J. Med.*, 707, 712 (1996).

n43. See Shalender Bhasin et al., *The Effects of Supraphysiologic Doses of Testosterone on Muscle Size and Strength in Normal Men*, 335 *New Eng. J. Med.* 1 (1996) (finding that high doses of testosterone along with weight training increased performance due to increased fat-free muscle mass and size).

n44. See *id.* at 5 (placing results in a table). The participants in this study were "normal" men, ages 19 to 40 years, and had experience with weightlifting. *Id.* at 2. In a ten-week span, men who began only able to lift 126 kilograms squatting increased performance to 151 kilograms through weight training alone (a 20% increase). *Id.* at 5. The testosterone group (those ingesting 600 mg of testosterone for the ten weeks) increased squatting from a baseline (average) of 102 kg to 140 kg (a 37% increase). *Id.*

n45. Comments made at the 17th Annual Health Law Symposium: Sports Medicine: Doping, Disability and Health Quality, Saint Louis University School of Law, March 18, 2005.

n46. This discussion is by no means a complete discussion of the pharmacology of amphetamine and caffeine; such discussion is beyond the scope of this Review.

n47. Prohibited List, *supra* note 6, S6.

n48. Canadian Centre for Ethics in Sport, *Advisory Note: The 2004 WADA Prohibited List: Summary of Revisions*, <http://www.cces.ca/pdfs/CCES-ADV-2004WADA ProhibitedList-E.pdf>; see Prohibited List, *supra* note 6, at S6.

n49. See P. N. R. Dekhuijzen et al., *Athletes and Doping: Effects of Drugs on the Respiratory System*, 54 *Thorax* 1041, 1042 (1999), available at http://thorax.bmjournals.com/cgi/reprint/54/11/1041?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&andorexactfulltext=and&searchid=1126823303800_2949&stored_search=&FIRSTINDEX=0&sortspec=relevance&volume=54&firstpage=1041&resourcetype=1&journalcode=thoraxjnl.

n50. See id.; Joe V. Chandler & Steven N. Blair, *The Effect of Amphetamines on Selected Physiological Components Related to Athletic Success*, 12 *Med. & Sci. Sports & Exercise* 65, 66, 68 (1980).

n51. Dekhuijzen et al., *supra* note 49, at 1043.

n52. Endurance Research Board, *Caffeine and Endurance*, Trifuel (Feb. 2, 2004), <http://www.trifuel.com/triathlon/nutrition/caffeine-and-endurance-000402.php> (last visited Nov. 20, 2005).

n53. See Milo Gibaldi & Donald Perrier, *Pharmacokinetics* 253-54 (1975), reprinted in 1 *Drugs and The Pharmaceutical Sciences* (James Swarbrick ed., Marcel Dekker, Inc. 1975).

n54. Endurance Research Board, *supra* note 52.

n55. "Pharmacokinetics" is the study of the rates of absorption, distribution, metabolism, and excretion of drugs and the effects of these rates on their actions. Gibaldi & Perrier, *supra* note 53, at v.

n56. See *Edwards v. Int'l Ass'n of Athletics Fed'ns*, CAS Arb. OG 04/003 (Ct. of Arb. for Sport 2004).

n57. *Id.* at 14-16.

n58. *Id.* at 2.

n59. *Id.* at 16.

n60. *Id.* at 15, 16.

n61. Martin D. Schechter, *Potentiation of Cathinone by Caffeine and Nikethamide*, 33 *Pharmacol. Biochem. & Behav.* 299, 300 (1989); see *Prohibited List*, *supra* note 6, S6.

n62. *Prohibited List*, *supra* note 6, S8.

n63. See Kari Egan & Brandon Arnold, *History of Snowboarding in the Olympics*, About, http://snowboarding.about.com/od/snowboardingbackground/a/Olympic_history.htm (last visited Nov. 20, 2005).

n64. See *id.*

n65. *Id.*

n66. Sports Court Overturns IOC Marijuana Ruling, Shinano Mainichi (Japan), Feb. 11, 1998, <http://www.shinmai.co.jp/oly-eng/19980212/0009.htm> (last visited September 9, 2005) [hereinafter Sports Court].

n67. Egan & Arnold, *supra* note 63.

n68. Sports Court, *supra* note 66.

n69. The International Ski Federation is commonly known as the FIS, which stands for Fédération Internationale de Ski.

n70. Rebagliati Wins Back His Gold, Mountain Zone, Feb. 12, 1998, <http://classic.mountainzone.com/olympics/nagano/up2-12a.html> (last visited September 9, 2005).

n71. *Id.*

n72. Effects of Performance Enhancing Drugs on the Health of Athletes and Athletic Competition: Hearing Before the S. Comm. on Commerce, Sci., & Transp., 106th Cong. 13 (1999), available at http://frwebgate.access.gpo.gov.ezproxy.mnl.umkc.edu/cgi-bin/getdoc.cgi?dbname=106_senate_hearings&docid=f:75594.pdf (statement of General Barry R. McCaffrey, Director, Office of National Drug Control Policy).

n73. *Id.* at 19.

n74. Rebagliati Wins Back His Gold, *supra* note 70.

n75. Prohibited List, *supra* note 6, S2.

n76. M. J. Rennie, Claims for the Anabolic Effects of Growth Hormone: A Case for the Emperor's New Clothes, 37 *Brit. J. Sports Med.* 100, 103 (2003); see Dekhuijzen et al., *supra* note 49, at 1044, 1046 nn. 82-84.

n77. Rennie, *supra* note 76, at 103.

n78. *Id.* at 102.

n79. *Id.* at 103 (discussing study of Dr. Kai Lange of the Danish Institute of Sports Medicine).

n80. *Id.*

n81. Prohibited List, *supra* note 6, S5. The list names about twenty compounds. *Id.*

n82. Blakiston's Gould Medical Dictionary 402 (4th ed. 1935).

n83. See generally M. Thevis & W. Schanzer, Mass Spectrometry in Doping Control Analysis, 9 *Current Organic Chem.* 825, 825-44 (2005).

n84. United States Anti-Doping Agency, Athlete Advisory - Update on Prohibited Substance List/Yasmin (July 2, 2003), [http://www.usantidoping.org/files/active/athletes/athlete%20advisory-yasmin\[1\].pdf](http://www.usantidoping.org/files/active/athletes/athlete%20advisory-yasmin[1].pdf) (emphasis added).

n85. United States Anti-Doping Agency, Athlete Advisory - YASMIN (Jan. 27, 2005), [http://www.usantidoping.org/files/active/athletes/athlete%20advisory%20-%20yasmin\[3\].pdf](http://www.usantidoping.org/files/active/athletes/athlete%20advisory%20-%20yasmin[3].pdf). The Advisory merely stated: "On January 25, 2005, the World Anti-Doping Agency (WADA) List Committee considered the status of Yasmin, an oral contraceptive. Today, WADA notified USADA that the medication, Yasmin, is allowed in-or out-of-competition, effective immediately." Id.

n86. See Current Good Manufacturing Practice in Manufacturing, Packing, or Holding Dietary Ingredients and Dietary Supplements, 68 Fed. Reg. 12,158 (Mar. 13, 2003) (to be codified at 21 C.F.R. pts. 111, 112) (presenting several examples of contaminated dietary supplements). Under the Dietary Supplement Health Education Enhancement Act (DSHEA), pre-market approval is not required for dietary ingredients intended for use in dietary supplements. Id. at 12,915.

n87. See id. at 12,158.

n88. Parts per billion (nanograms) or parts per trillion (picograms).

n89. IOC Rules, *supra* note 11, 3.1.

n90. Savulescu et al., *supra* note 19, at 669.

n91. Id. ("The rule of strict liability - under which athletes have to be solely and legally responsible for what they consume - must remain supreme. We cannot, without blinding reason and cause, move one millimetre from strict liability - if we do, the battle to save sport is lost.") (quoting Sebastian Coe, We Cannot Move from Strict Liability Rule, Daily Telegraph (UK), Feb. 25, 2004, Sports, at 5, available at <http://www.telegraph.co.uk/sport/main.jhtml?xml=/sport/2004/02/25/socoe25.xml>).

n92. Id.

n93. David Allen & Hakan Westerblad, Lactic Acid - The Latest Performance-Enhancing Drug, 305 Science 1112, 1112-13 (2004). Using isolated frog muscle preparations, it was shown in 1929 that lactic acid accumulation, caused by electrical stimulation, decreased mechanical performance. Id. at 1112. When the accumulated lactic acid was removed by immersing the muscle preparation in a suitable saline solution, muscle performance improved. Id. For more details, see generally Thomas H. Pedersen et al., Intracellular Acidosis Enhances the Excitability of Working Muscle, 305 Science 1144 (2004).

n94. Cathy M. Fomous et al., Symposium: Conference on the Science and Policy of Performance-Enhancing Products, 34 Med. & Sci. Sports & Exercise 1685, 1685-86 (2002). Creatine, though not a prohibited substance, has been reported to improve performance by five to ten percent "during short duration, high intensity types of exercise." Id. at 1688. However, not all studies have been able to show this improvement. Id.

n95. See Restoring Faith in America's Pastime, *supra* note 3.

n96. See Savulescu et al., *supra* note 19, at 667 (noting that Beta blockers, which lower blood pressure and heart rates, have been used by classical musicians to enhance performance by combating physical effects of stress).

n97. *Id.* at 668.