

PROJECT REVIEW

"Investigation into Metabolism and Detection in Urine of New Substances Specified in the WADA 2005 List"

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The WADA lists for 2004 and 2005 have added a large number of new substances that require detection. WADA will require a number of these to be studied for inclusion into the WADA-accredited laboratories routine testing schemes. From the 2004 list the new additions were corticosteroids and a project to study the metabolism and detections of these is currently funded by WADA. The new list 2005 has a variety of new substances and the metabolism and detection of these must also be studied. Before introduction into testing standards, metabolism and funding will be required in order to investigate cost-effective procedures. This is presently undertaken over a lengthy period by a few laboratories that investigate new substances and publish the results for all laboratories to use. The longer the anti-doping community waits for such data the longer athletes can use the substance with impunity.

Currently there are over 20 such compounds to be investigated including some new classes such as the 5α -reductase inhibitors eg. Finasteride, the selective estrogen receptor modulators eg. Raloxifene and anti-estrogenic compounds such as fulvestrant.

The aim of this project is to study the metabolism of a selected number of these substances and then to determine procedures to allow them to be introduced into the current schemes across all WADA-accredited laboratories.

Investigations into the Metabolism and Detection in Urine of New Substances Specified in the WADA 2005 List

Results and Conclusions

The WADA list since 2004 has had a large number of new substances added to the various classes that require detection by the WADA-accredited laboratories. WADA will eventually require most of these new substances to be studied and included in the WADA-accredited laboratories routine testing schemes. The 2004 list saw new additions such as corticosteroids and a project to study the metabolism and detection of these in several laboratories that is currently being funded by WADA. The recent lists introduced in 2005 and 2006 had a variety of new substances added. Before the introduction of detection methods for all of these substances in the laboratory programmes for routine testing, both research and ongoing testing will be required in order to initiate cost-effective testing procedures. Such studies are presently undertaken over a lengthy period by a few laboratories that investigate new substances and publish the results for all laboratories to use. However, the longer the anti-doping community waits for such data the longer athletes can use the substances with impunity.

The aim of this project was to obtain as many of the compounds added to the list as possible, to study the metabolism of a select number of these substances and then to determine procedures to allow them to be introduced into current detection schemes across all WADA-accredited laboratories. All substances were obtained but not all had metabolic studies undertaken.

The substances that can be considered as "new" additions are:

Aromatase inhibitors (Formestane and testolactone); **Selective estrogen receptor modulators** (Raloxifine and toremifine); **Anti-estrogenic substances** (Cyclofenil and fulvestrant); **5 α -reductase inhibitors** (Finasteride and dutasteride); **Anabolic agents** (18 α -homo-17 β -hydroxyestr-4-ene-3-one, boldione, 4-hydroxy-19-nortestosterone, methyldienolone, methyltrienolone, methasterone, methyl-1-testosterone, methylnortestosterone, prostanazol, tibolone, zilpaterol and norclostebol); **Stimulants** (Famprofazone, benzylpiperazine, cyclazodone, fenbutrazate, fencamine, isometheptene, p-methylamphetamine, norfenefrine, octopamine, ortetamine, oxilofrine, phenpromethamine, sibutramine and tuaminoheptane).

One of the biggest challenges of the project was to obtain the substance suitable for the studies. These were either purchased, often with difficulty in finding a supplier, or synthesised at NMIA's Chemical Reference Materials group. Most of the substances on the WADA list could be analysed by one of two analytical techniques, both used within NMIA and most other WADA-accredited laboratories. These techniques use either solid-phase extraction or solvent-solvent extraction followed by measurement using either Gas Chromatography – Mass Spectrometry (GCMS) or Liquid Chromatography – Mass Spectrometry (LCMS). Many of the materials or excretion studies have been provided to laboratories through cooperation with WAADS.