

Reprint from

RECENT ADVANCES
IN DOPING ANALYSIS
(7)

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Banned Agents and Related Compounds - How many?
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Banned agents and related compounds - how many?

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The I.O.C. Medical Code defines the doping agents by classes of prohibited substances, and instead of a complete list of agents some examples are listed with the supplement "... and related substances". The last update (Jan 31, 1999) emphasises again the fact, that the lists of examples are not at all exhaustive and a substance missing on the list may not be considered to be permitted.

Although the extension "...and related substances" was additionally explained since 1994 "...related by the pharmacological action and/or the chemical structure", the lists of examples have lead to several controversial arguments, whether an agent would be prohibited or not.

On the other hand, there have been reasons against a complete list of banned agents:

- postulated frequent appearance of new agents
- possible support of misuse by extensive information.

But the development of (mostly pharmaceutical) agents is very much slowed down by the scrutinous regulations for toxicological and clinical evaluation, before new compounds are registered and marketed.

The "criminal energy" of doping offenders does not require – as practical experience shows – our lists to trigger their misbehaviour: underground and official literature, Internet and "mouth-to-mouth"-advertising provide a wealth of information about real and illusionary doping substances and methods.

Goodwilling people lack detailed information about prohibited substances and therefore about pharmaceuticals to be avoided, because the pharmacological or chemical relationship is not easily recognised by non-experts.

Last but not least: decisions of the I.O.C. and international federations have sometimes been inconsequent insofar, as the use of compounds undoubtedly related – like clenbuterol, bromantan, carphedone – has been sanctioned only after their explicit listing as examples for the prohibited class.

In addition, there exists a grey zone of compounds, whose relation to a banned class remains questionable even for experts.

Therefore it does not surprise, when complete lists of banned substances have been frequently demanded during the recent past (as during the I.O.C. World Conference on Doping in Lausanne Febr. 2-4, 1999).

We have tried to select all compounds related to the prohibited classes of doping agents of the I.O.C. Medical Code from an international register of defined pharmaceutical agents (M. Negwer 1994). This register comprises 12 111 compounds, including thousands of newly synthesised agents, which have not yet been on market in 1994. Each compound monograph of this register contains the registration number, sum formula, CAS-number, IUPAC chemical name, structure formula, synonyms and pharmacological/clinical indication(s).

The endeavour was sponsored by the German Federal Institute of Sports Science (Bundesinstitut für Sportwissenschaft (BISp) Köln) and adopted as an initiative according to the Antidoping Convention of the Council of Europe by its Monitoring Group on Science.

A first selection based on relatively wide criteria for any relation to doping intentions yielded about 4000 compounds. Their further critical check, selection and distribution to the different classes has diminished this number, but resulted in surprisingly large groups surrounding the prohibited classes and their comparatively few examples.

While the Narcotics, Anabolics and Diuretics can be limited fairly easy, the class Stimulants is very heterogeneous. This is obvious already when looking onto the lists of examples, - varying among the annual updates of the I.O.C. Medical Commission, and comprising 43 agents in the 1999 version, exactly the double number some years ago.

The term “stimulant” is explicit or implicit part of a whole series of indications (Table 1).

On the other hand, already the given examples of the IOC Medical Commission for this class have fairly differing chemical structure types (like amphetamine, caffeine, strychnine etc.).

One might easily agree to consider compounds with the indications listed in table 1 part 1 as stimulating agents (closely related substances to class I A), but even this would increase the total number of prohibited stimulants to 290.

The inclusion of agents with the indications table 1 part 2 would further increase the total number, but probably the majority of those compounds can be considered as irrelevant or less relevant.

Narcotics stem also from definitely different chemical classes, and the distinction between narcotic and nonnarcotic analgesics is somewhat unsharp. But this could be easily overcome; the present list of examples distinguishes explicitly between prohibited and permitted agents.

Table 2 shows the numbers of substances according to the prohibited classes of the I.O.C. definition, standing behind the term "... and related substances".

Table 3 presents as an example one page of the completed "stimulants 1" class (based on the closer related indications of Table 1 part 1) with the few marked examples of the I.O.C. list.

The completed lists are thought to be a basis for discussion; they are intended to be published during the near future in a suitable form. In the meantime, they have been submitted to the responsible bodies (I.O.C. Medical Commission, Monitoring Group of the Antidoping Convention of the Council of Europe, in Germany Antidoping Commission of the German Sports Federation and the National Olympic Committee, Ministry of the Interior and Federal Institute of Sports Science).

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Table 1 **Pharmacological actions of agents related
to the prohibited class STIMULANTS**

above: agents directly related;
 compiled to „Stimulants 1“
 of Table 2

below: questionably related agents,
 to be discussed in detail,
 compiled to „Stimulants 2“
 of Table 2

STIMULANTS 1

analeptic

anorexic

stimulant

central stimulant

CNS stimulant

cardiac stimulant

psychostimulant

respiratory stimulant

sympathomimetic

tonic

STIMULANTS 2

antidepressant

cardiotonic

cardioenergetic

cerebral vasodilator

cerebrotonic

cognition activator, - enhancer

nootropic

Table 2 **Related compounds to the prohibited classes of substances**

Classes	Numbers of examples IOC 1999	Numbers of related compounds of this compilation	
Stimulants 1	49	290	(315)
(Stimulants 2)	-	396	(526)
Beta-2-agonists	6	125	(156)
Narcotics	8	134	(137)
Anabolics	36	141	(146)
Diuretics	13	137	(177)

Anabolics include the derivatives (esters) of parent compounds

Numbers in brackets include registered compounds still under test

4979	22232-71-9	Mazindol		anorexic, antidepressant
2988	51-68-3	Meclofenoxate		central stimulant, metabolic
4188	107555-96-4	Meclo sulfonate		psycho-analeptic
3090	17243-57-1	Mefenorex	X	anorexic
4859	1227-61-8	Mefexamide		central stimulant
2601	100-92-5	Mephentermine	X	sympathicomimetic, vasoconstrictor
7621	17854-59-0	Mepixanox		respiratory stimulant
6326	34262-84-5	Mesocarb	X	psychostimulant
623	87-89-8	Mesoinositol		tonic, lipotropic
2053	5001-33-2	Metadrenaline		sympathomimetic
2497	15351-09-4	Metamfepramone		anorexic, analeptic
3611	13898-68-5	Metamivanum		analeptic, cardiogenic
2038	537-46-2	Metamphetamine	X	sympathomimetic, central stimulant
1540	54-49-9	Metaraminol		sympathomimetic, hypertensive
2609	3571-71-9	Metaterol		sympathomimetic, broncholytic
3450	721-19-7	Methastyrindone		central stimulant
1934	28521-94-0	Methcathinone		stimulant
2615	390-28-3	Methoxamine		sympathicomimetic, vasoconstrictor
2507	530-54-1	Methoxyphedrine		sympathicomimetic, vasoconstrictor
2607	93-30-1	Methoxyphenamine	X	sympathicomimetic, bronchodilator
2052	6032-14-0	Methyladrenaline		sympathomimetic, vasoconstrictor
2604	552-79-4	Methylephedrine	X	sympathicomimetic
934	105-41-9	<i>Methylhexamine</i>		sympathomimetic
2619	20168-80-3	Methylnicethamide		analeptic
4117	113-45-1	Methylphenidate	X	central stimulant
3660	29559-00-0	Methylphenamin		sympathomimetic, broncholytic
3142	1212-03-9	Metiprenaline		sympathicomimetic, anti-allergic
3424	17692-22-7	Metizoline		sympathicomimetic, vasoconstrictor
3114	97476-58-9	Midodrine		sympathicomimetic, hypertensive (alpha1-agonist)
4519	68693-11-8	Modafinil		psychostimulant, thymoleptic
4851	41152-17-4	Morforex		anorexic
4526	102791-47-9	Nanterinone		cardiac stimulant
3895	835-31-4	Naphazoline		sympathomimetic, vasoconstrictor, ansal decongestant
2111	76-26-6	Natrii camsilas		analeptic
8365	509-52-4	<i>Natrium strychninicum</i>	X	strychnine depot prepartate
6120	509-08-0	Neobornylval		analeptic, sedative

Table 3 **Sample page of the extended class „Stimulants 1“**
(examples given to the I.O.C. doping definition marked)