



## **IAAF BETA-2-AGONISTS PROTOCOL**

In response to a generally recognised increase in the use of beta-2 agonists by athletes in the past, the IAAF decided to implement a protocol for the authorisation of its use on the occasion of the IAAF World Athletics Championships in Paris-Saint Denis in 2003. The aim was controlling and limiting the misuse of beta-2-agonists. Lately, at the time the IOC Medical Commission established a Beta-2-agonist for Athens 2004 Olympic Games the above mentioned IAAF protocol was amended and expanded. IOC recently modified its protocol for Beijing 2008 Olympic Games. This lately modified IOC protocol has taken seriously into account the guidelines and recommendations stated at the IOC Consensus Statement on Asthma in Elite Athletes from January 2008, namely:

- There was consensus that the diagnosis of asthma could not be made in elite athletes on the basis of respiratory symptoms alone and spirometric evidence of reversible airways obstruction or airway hyper responsiveness was needed to confirm the diagnosis.
- The use of national and international guidelines for treatment was recommended with a note that there are special issues for elite athletes. One of these issues relates to the tolerance that can develop with frequent use of inhaled beta 2 agonists and that those who use them daily may find them less effective against exercise-induced bronchoconstriction (EIB).
- The use of inhaled glucocorticosteroids was encouraged for treatment of asthma and EIB. The use of long acting beta 2 agonists as monotherapy was discouraged.
- The importance of athletes receiving education with respect to asthma, EIB and correct use of their medications was stressed.

In addition to all the above, the new International Standard for Therapeutic Use Exemption states at its Rule 7.13 that the use of beta-2-agonists by inhalation must have a medical file justifying the use. That file should meet a minimum of requirements that are in accordance with our IOC Consensus Statement. Taking all that into consideration the IAAF Medical and Anti-doping Commission issues the new IAAF Beta-2-Agonists Protocol as it follows:

Applicants seeking the use inhaled beta-2 agonists will be required to submit

- (i) A TUE Application Form, see [www.iaaf.org/antidoping/athlete/therapeutic/index.html](http://www.iaaf.org/antidoping/athlete/therapeutic/index.html)
- (ii) Objective evidence of asthma and/or exercise-induced asthma (EIA) or EIB through the provision of test results (and supporting documentation, if available), as set out below
- (iii) All tests should have been performed from 1<sup>st</sup> October 2008 and within 3 months of the TUE Form Application Date.

Note: all TUE Application Forms and supporting documentation must be submitted to the IAAF in either English or French.

## **1. Detailed Medical Records**

Medical records should include (accordingly with the enclosed form):

- A precise diagnosis of the individual's condition requiring the use of inhaled beta-2 agonists.
- All relevant information concerning the individual concerned and his condition:
  - age of onset
  - symptoms suggesting airway obstruction following exercise, upper respiratory infection, at rest and at night and/or during the pollen season
  - identified triggering factors
  - past history of atopic disorders and/or childhood asthma
  - past physical examinations
  - results of skin prick tests or RAST to document the presence of allergic hypersensitivity
- Any specific information concerning the individual's coughing during or post-exercise, dyspnoea, shortness of breath, wheezing, chest tightness or excess sputum.
- Details of all consultations with physicians qualified in the treatment of asthma and details of any attendance in hospital emergency departments for treatment or admission to hospital for treatment of acute exacerbation of asthma.
- Details of the individual's currently prescribed medication and any other medication prescribed in the last 6 months. Details of medication in the 3 months prior to provocation tests (see below) must also be notified.

## **2. Provocation Test Results**

The measures of forced expiratory volume (FEV1) at rest, as well as changes in FEV1 in response to either an inhaled bronchodilator or to a bronchial provocation test, are the essential criteria that must be sent together with the application form for inhaled beta2 agonists (see below for further details on these tests).

**Peak Expiratory Flow (PEF) measurements are unacceptable.**

In the application form, information must be provided for at least one of the tests below.

Only tests performed after 1<sup>st</sup> October 2008, and within 3 months of the TUE Form Application Date, will be taken into consideration by the IAAF TUE Sub-commission.

Flow volume curves are not mandatory any more. However, [they may be requested at any time during the evaluation period by the IAAF TUE Subcommission. Therefore, the medical files should record them in order to allow the athlete to send them if requested.](#)

Athletes must also present a positive test result from one of the following recognised provocation tests:

## **BRONCHODILATOR TEST:**

After administering a “permitted” beta2 agonist by inhalation, a bronchial reversibility test is considered positive if the increase in FEV1 is 12% or more of the baseline FEV1 or the predicted FEV1 and exceeds 200 ml.

## **BRONCHIAL PROVOCATION TESTS:**

Recommendation for withholding medications prior to tests

To provide the optimal test circumstances, some medications must be withheld for 8 to 96 hours before the bronchial provocation tests:

- No short-acting bronchodilators, sodium cromoglycate, nedocromil sodium, or ipratropium bromide for 8 hours.
- No long-acting bronchodilators or antihistamines for 48 hours.
- No leukotriene antagonists for four days.
- Steroids should not be inhaled on the day of the test.
- No caffeine should be taken on the morning of the test.
- Avoid vigorous exercise for at least four hours prior to the start of the test and avoid any exercise on the day of testing.

Various bronchial provocation tests may be used:

- a) eucapnic voluntary hyperpnea test
- b) exercise challenge in the laboratory or an exercise test in the field
- c) hyperosmolar aerosols i.e. 4.5gm% saline or dry powdered mannitol
- d) methacholine test

### **a) Eucapnic voluntary hyperpnea test**

The eucapnic voluntary hyperpnea test is considered positive when a fall in FEV1 of 10% or more from baseline is recorded after a 6 minutes period of hyperpnea in dry air. To overcome the problem of any post-test respiratory muscle fatigue, the FEV1 should first be recorded at least 3 minutes after challenge. It is usual for the reduction to be sustained over the next five minutes to be consistent with hyperpnea-induced bronchoconstriction.

### **b) Exercise challenge in the laboratory or an exercise test in the field**

The response to the exercise challenge is considered positive when there is a fall in FEV1 of 10% or more compared to baseline during the first 30 minutes post exercise.

To maximise the opportunity for a positive test, the exercise test should be performed breathing dry air for 8 minutes with the intensity of exercise close to maximal for the last 4 minutes. To overcome the problem of any post-test respiratory muscle fatigue, the FEV1 should first be recorded at least 3 minutes after challenge. It is usual for the reduction to be sustained over the next 5 minutes to be consistent with exercise-induced bronchoconstriction (EIB).

### **c) Hyperosmolar aerosols**

A fall in FEV1 of 15% or more from baseline after inhaling 22.5 ml of 4.5 gm% saline (e.g. 4.5 g NaCl/100 ml water) or a dose of 635 mg of dry powdered mannitol is a positive response and is consistent with a diagnosis of currently active asthma or EIA/EIB. The response to 4.5% saline and the

response to mannitol is usually reported as the dose required to provoke a 15% fall in FEV<sub>1</sub> (PD<sub>15</sub>) but should also be reported as the maximum fall after the final dose of aerosol .

#### **d) Methacholine test**

A test is considered positive if there is a fall in FEV<sub>1</sub> of 20% or more from baseline at a dose (PD<sub>20</sub>) less than or equal to 400 microgram / 2 micromoles (cumulative dose) or 200 micrograms / 1 micromole (non cumulative dose) or a concentration (PC<sub>20</sub>) less than or equal to 4mg/ml (tidal breathing technique American Thoracic Society guidelines 1999) **when the subject is not taking inhaled corticosteroids or has taken them for less than one month.**

**For applicants taking inhaled corticosteroids for at least one month,** the PD<sub>20</sub> should be less than or equal to 1600 micrograms /8.0 micromoles (cumulative dose) or 800 micrograms / 4.0 micromoles (non cumulative dose), or a PC<sub>20</sub> less than or equal to 16.0mg/ml (tidal breathing ATS guidelines 1999) to be accepted as proof of airway hyperresponsiveness (AHR).

It should be noted that a negative response to methacholine does not exclude exercise-induced asthma/bronchoconstriction in an athlete and in the event of a negative response, an alternative bronchial provocation test is recommended. The method of delivery of methacholine may influence the outcome. If the values for PC<sub>20</sub> or PD<sub>20</sub>, during methacholine challenge are in excess of the thresholds mentioned above, the athlete may undergo an EVH test or an exercise test or a hyperosmolar aerosol provocation test.

IAAF TUE Sub-commission strongly encouraged to submit athletes preferably either an EVH test or a Mannitol test.

For a better understanding of the disease's physiopathology and adequate subsequent treatments, the assessment of eosinophils and/or neutrophils on the provoked sputum is highly recommended and will be especially welcome.

**IMPORTANT NOTE: The results of bronchial provocation tests using pharmacological agents other than methacholine (e.g. carbachol, histamine or adenosine monophosphate) WILL NOT BE ACCEPTED.**

**WELL-CONTROLLED ASTHMA** with negative response to all the tests In the case of an athlete with known, but well-controlled, asthma recording a negative result to the bronchial provocation test(s), but still seeking approval for the use of inhaled beta2 agonist(s), the following documentation must be included in the medical file: consultations with their physician for treatment of asthma, hospital emergency department attendance or admission for acute exacerbations of asthma or treatment with oral corticosteroids. Additional information that may assist includes those quoted at point 1 above (Detailed Medical Records).

#### Abbreviations:

FEV<sub>1</sub> = Forced expired volume in one second.

PD<sub>15</sub> FEV<sub>1</sub> = Is the provocative dose of 4,5% saline or mannitol causing a 15% fall in FEV<sub>1</sub>

PC<sub>20</sub> FEV<sub>1</sub> = Is the provocative concentration of methacholine causing a 20% fall in FEV<sub>1</sub>

PD<sub>20</sub> FEV<sub>1</sub> = Is the provocative dose of methacholine causing a 20% fall in FEV<sub>1</sub>

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