

World Anti-Doping Program

GUIDELINE

REPORTING AND MANAGEMENT OF ELEVATED T/E RATIOS

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1. Objective

This guideline has been developed to ensure a harmonized approach in the reporting and management of elevated ratios of testosterone to epitestosterone (T/Es). An elevated T/E may be an indicator of the use of a prohibited substance, and this guideline aims to assist Anti-Doping Organizations (ADOs) to make that determination.

This guideline is intended to assist with the standardized reporting of elevated T/Es, the management of previous data on the athlete's test history, application of Isotope Ratio Mass Spectrometry (IRMS), and the actions required following the reporting of a T/E greater than 4.

2. Scope

This guideline follows the existing rules established in the World Anti-Doping Program's *International Standards* and Technical Documents, which already address provisions regarding T/E ratio. These requirements are still fully applicable and must be respected. This guideline contains additional recommendations to facilitate the result management of such T/E cases.

Unlike the International Standards and Technical Documents, this guideline is not mandatory, and *Anti-Doping Organizations (ADOs)* are free to decide how to incorporate it into their current rules and procedures. The Guideline can be incorporated in whole or in part and can be amended, reworded, or an alternative approach adopted to best fit the *ADOs* needs.

The sections of Level 2 (mandatory) documents of the World Anti-Doping Program relative to T/E ratio are listed below. ADOs should refer to the latest versions of these documents:

- **International Standard: 2006 Prohibited List:**

Section S1b on Endogenous Anabolic Steroids:

- **Technical Document 2004EEAS:**

Reporting and Evaluation Guidance for testosterone, epitestosterone, T/E ratio and other endogenous steroids

3. Responsibility

This guideline applies to WADA-accredited laboratories and to *Anti-Doping Organizations (ADOs)* with result management responsibility.

4. Definitions

'Adverse Analytical Finding': a report from a laboratory or other approved testing entity that identifies in a specimen the presence of a Prohibited Substance or its metabolites or markers, (including elevated quantities of endogenous substances) or evidence of the use of a prohibited method.

'Anti-Doping Organization': a Signatory (of the World Anti-Doping Code) that is responsible for adopting rules, for initiating, implementing or enforcing any part of the doping control process. This includes, for example, the International Olympic Committee, the International Paralympic Committee, or other major event organizations that conduct testing at their events, WADA, International Federations, and National Anti-Doping Organizations.

'Athlete': for purposes of doping control, any person who participates in sport at the international level (as defined by each International Federation), or national level (as defined by each National Anti-Doping Organization) and any additional person who participates in sport at the lower level if designated by the person's National Anti-Doping Organization. For purposes of anti-doping information and education, any person who participates in sport under the authority of any signatory, government, or other sports organization accepting the Code.

Endogenous: refers to a substance with is capable of being produced by the body naturally.

Exogenous: refers to a substance which is not ordinarily capable of being produced by the body naturally.

'International Standard': a standard adopted by WADA in support of the Code. Compliance with an International Standard (as opposed to another alternative standard), practice of procedure shall be sufficient to conclude that the procedures addressed in the standard were performed properly

IRMS (Isotope Ratio Mass Spectrometry): a technique for measuring the quantity of stable isotopes in a sample in order to determine the characteristics of the sample, including composition and origin.

'Prohibited List': the List identifying the Prohibited Substances and Prohibited Methods.

'Threshold substance': a substance listed in the Prohibited List for which the detection of an amount in excess of a stated threshold is considered an adverse analytical finding.

5. Laboratory reporting guideline

In order to achieve harmonization in laboratory reporting and avoid confusion, it is recommended that elevated T/E ratios are reported according to the following principles on the certificate of analysis:

- T/Es above the threshold of 4 are reported as *Adverse Analytical Findings* (AAFs), and are therefore reported separately from negative samples in the same batch. The actual T/E value is clearly stated, including the actual estimation of testosterone to epitestosterone (equivalent to glucuronide).
- T/Es above the threshold of 4 are reported to the ADO and to WADA.
- The results of IRMS analysis, if carried out, are included in the report. If IRMS has not been carried out, the report may carry a recommendation for IRMS analysis in the opinion section of the report.
- To avoid unnecessary effort and analysis costs (for example for samples from athletes where a naturally elevated T/E has already been determined), the decision of whether or not to proceed with IRMS analysis shall be made by the ADO, rather than the laboratory.
- Laboratories without the capacity to conduct IRMS analysis, shall be in a position to arrange analysis at another WADA-accredited laboratory, and to arrange transport of the sample to that laboratory, with secure chain of custody.
- IRMS results should not be reported as inconclusive, but reported as either significantly different from the endogenous reference compound(s) (ERC) and therefore consistent with exogenous origin¹, or as not significantly different from the endogenous reference compound and therefore consistent with endogenous origin².
- An IRMS result that is consistent with the endogenous reference compound does not necessarily confirm that the elevated T/E is of endogenous origin. The laboratory is encouraged to include an opinion as to the likelihood of endogenous origin, and recommendations for further follow up, if appropriate.
- 'Positive' IRMS analysis allows the clear qualification of exogenous origin. However, indications that values are consistent with the endogenous reference compound ('Negative' IRMS) can range from relative certainty to uncertainty, depending on delta values and other factors. It is therefore possible for laboratories to provide further detail, and an opinion on the likelihood of endogenous origin.

1. In layman's terms - a positive IRMS

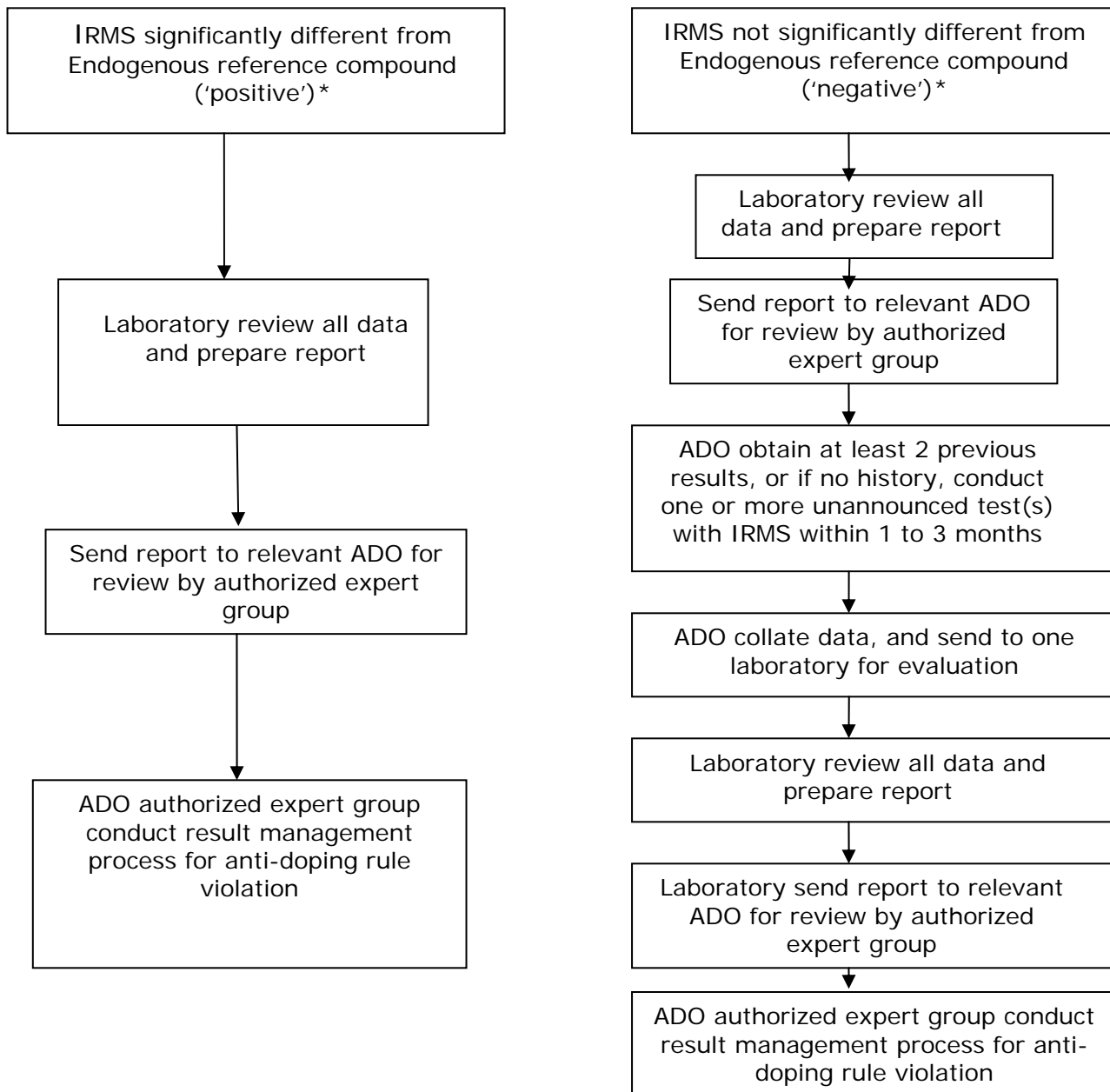
2. In layman's terms - a negative IRMS

(it is recommended that the terms negative and positive are not used in relation to IRMS analysis, since these words may be confused with the determination of the status of the finding.)

6. Interpretation of data and follow up

Flow charts, with a description of appropriate courses of action to be followed when an elevated T/E ratio is found, are presented below:

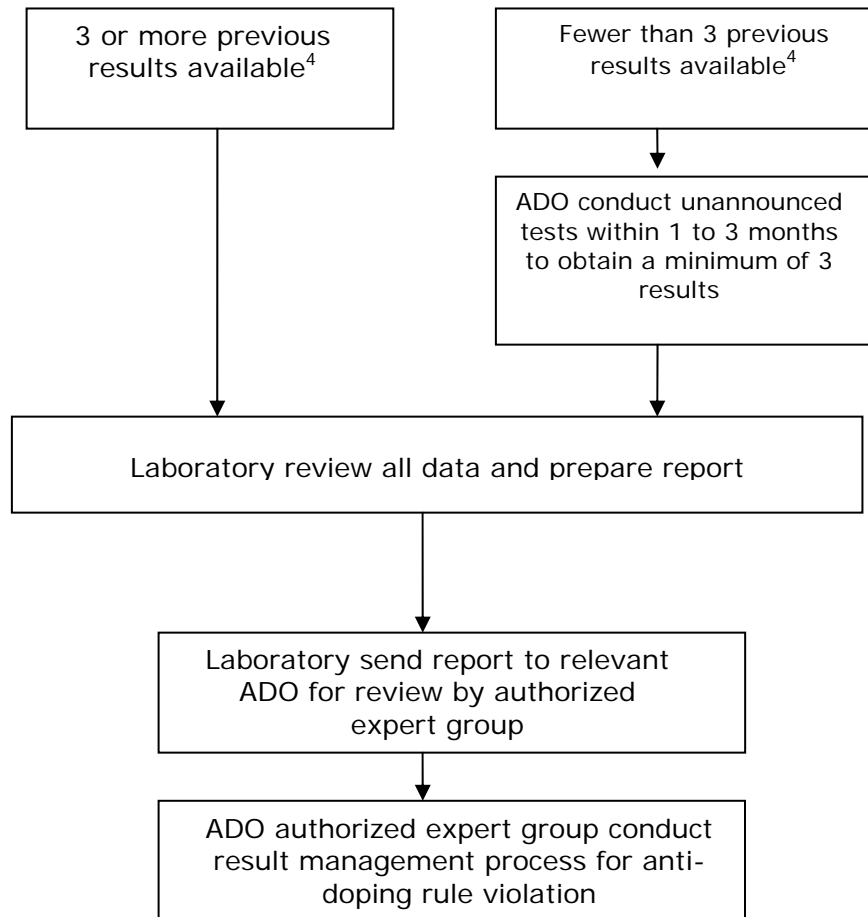
T/E >4
Chart A: IRMS conducted



* See footnote at bottom of page 5

T/E >4

Chart B: No IRMS conducted



⁴ A combination of previous and future data may also be used. For example if two test results are available, only one follow up test need be carried out. If one result is available, a minimum two follow up tests are required.

- As for other AAFS, the athlete should be informed of the original adverse analytical finding. At the end of the follow up testing and/or investigation, the athlete should be informed of the final outcome, ie whether or not the determination is that an anti-doping rule violation is alleged to have occurred, with explanation.
- At the athlete request, a full documentation package including data on tests both prior and subsequent to the initial finding should be provided to the athlete.
- Previous data, including T/E ratios from past tests conducted on the athlete, and any related documentation should be gathered by the ADO. It may be necessary to go back to the relevant laboratories to request the actual T/E values and other documentation.
- The ADO can request that additional information is provided by the anti-doping laboratory in support of the T/E ratio above the threshold of 4 (testosterone concentration, epitestosterone concentration, steroid profiles, etc).
- Samples showing indications of bacterial activity (pH higher than 7.0 and presence of 5-alpha or 5-beta-androstandione) should be excluded from the data set of a longitudinal study.
- T/E data gathered by different *ADOs* for one athlete may be shared to gain the necessary test history for that athlete. For example, an International Federation can ask a National Anti-Doping Organization for an athlete's test history, and vice-versa.
- For follow-up testing; IRMS analysis will reduce the total number of follow-up tests required, especially if it has not been conducted for the initial sample. It is recommended that IRMS be conducted even on follow up samples showing a T/E ratio of less than 4.
- Previous, or follow up data, shall be collated by the ADO, and shall be provided to one WADA-accredited laboratory for the analysis of the data.
- It is strongly recommended that the interpretation of longitudinal data be signed off by the Head of an anti-doping laboratory, if necessary using other relevant parameters of the steroid profile, for example, A/Etio ratio, testosterone concentration, epitestosterone concentration, etc. To facilitate this, follow-up samples may be sent to the same laboratory as the initial sample where possible or, as a minimum, the results of all related tests shall be provided to one laboratory for the interpretation of longitudinal data.
- The Head of the anti-doping laboratory shall then provide a full report, including his/her opinion on the possibility of exogenous origin, with all relevant data, to the authorized expert body of the ADO for their review and determination of whether an anti-doping rule violation has occurred.

- The expert body of the ADO should consist of individuals with the appropriate competence in the relevant field, i.e. endocrinology.

7. Results Management

Confirmation of exogenous origin

- Once it is determined that an elevated T/E is consistent with exogenous origin, the results management process is followed, as in the case of the use of other prohibited substances or methods.
- If medical information is provided by the athlete to support the claim that the result is due to a physiological or pathological explanation, such information must be taken in to account in the result management of the case.

No clear confirmation of exogenous origin

- When an athlete is identified with a possibly naturally elevated T/E ratio, ie consistent with endogenous origin, a dossier including all data should be reviewed by one anti-doping laboratory and transferred to the relevant ADO. The Head of the anti-doping laboratory shall provide an interpretation of the data. The authorized expert body of the relevant ADO will then determine whether the data provided supports the conclusion that the elevated T/E value is of natural origin, or not.
- If it is determined that an anti-doping rule violation is alleged to have occurred, the results management process is followed, as in the case of the use of other prohibited substances or methods.
- If it is determined that the elevated T/E value is of natural origin, a note will be added to the dossier of the athlete concerned, preventing systematic follow-up for future anti-doping tests which show similar elevated T/E values. This information will also be shared with other ADOs as relevant.
- A copy of the report confirming a naturally elevated T/E ratio, including the results of the related initial and subsequent follow-up tests, and any related analytical information, will be forwarded to the WADA Medical Director.
- When subsequent anti-doping tests for an athlete with a naturally elevated T/E ratio are reported, the T/E ratio should be carefully monitored to ensure that the T/E ratio remains within the range of values normally found in humans (30% variation from the mean value in males and 60% variation in females), thus confirming the natural origin. If the result of a new test were to differ by more than those acceptable variations, a follow-up, unannounced anti-doping test should be triggered immediately by the relevant ADO.