

World Anti-Doping Program

**GUIDELINES for the
REPORTING and
MANAGEMENT OF
ELEVATED T/E RATIOS
and ENDOGENOUS
STERIODS**

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1. Objective

These guidelines have been developed to ensure a harmonized approach in the reporting and management of elevated concentration of endogenous steroids and ratios of testosterone to epitestosterone (T/E), the management of previous data on the athlete's test history, application of Gas Chromatography/Carbon/Isotope Ratio Mass Spectrometry (GC/C/IRMS), and the actions required following the reporting. An elevated T/E ratio or elevated concentration of endogenous steroid may be an indicator of the use of a *Prohibited Substance*, and these guidelines aim to assist *Anti-Doping Organizations (ADOs)* to make that determination.

Further, these guidelines incorporate instructions on the reporting of elevated values of endogenous steroids and T/E ratios greater than 4.0 until such time that the new version of the Technical Document on Endogenous Androgenic Anabolic Steroids (TD EAAS) becomes effective (for the sake of clarity until such time as the new version of TD EAAS enters into force the 2004 TD EAAS remains in force and applicable). Between the September 01, 2010 effective date of version 1.0 of the TD2010MRPL and the approval of the new version of the TD EAAS, a documentation gap has been noted regarding the provision of effective instructions to Laboratories and *ADOs* for the analytical findings related to elevated endogenous steroids and T/E ratios. Specific instruction related to GC/C/IRMS testing including those related to TE ratio and Boldenone were initially in the Prohibited List, then moved to the MRPL Technical Document. It was not reproduced again in the latest 2010 MRPL TD since the instructions were scheduled to be noted in the new TD EAAS, which is still under revision at the time of release of this document. Therefore, these guidelines will ensure harmony in the way to proceed with these cases until the revised EAAS TD is released.

Therefore, until such time that a new version of the TD EAAS comes into effect; the following cases shall proceed as described herein.

2. Scope

These guidelines follow the existing rules established in the World Anti-Doping Program's *International Standards* and Technical Documents whose requirements are still fully applicable and shall be respected. These guidelines contain additional recommendations to facilitate the result management of elevated concentrations of endogenous steroid and elevated T/E ratio cases.

Unlike the *International Standards* and Technical Documents, these guidelines are not mandatory and *ADOs* are free to decide how to incorporate them into their current rules and procedures. The guidelines 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 are listed below. ADOs should refer to the latest versions of these documents:

- **International Standard: 2011 Prohibited List:**

Section S1b on Endogenous Anabolic Steroids:

- **Technical Document 2004EAAS:**

Reporting and Evaluation Guidance for Testosterone, Epitestosterone, T/E ratio and other Endogenous Steroids

3. Responsibility

These guidelines are intended for use by WADA-accredited laboratories and by ADOs with result management responsibility.

4. Definitions

'Atypical Finding' (ATF): a report from a Laboratory or other WADA-approved entity which requires further investigation as provided by the *International Standard for Laboratories* or related Technical Documents prior to the determination of an *Adverse Analytical Finding*.

'Adverse Analytical Finding' (AAF): A report from a Laboratory or other WADA-approved entity that, consistent with the *International Standard for Laboratories* and related Technical Documents, identifies in a *Sample* 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' (ADO): A *Signatory* 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, other *Major Event Organizations* that conduct *Testing* at their *Events*, WADA, International Federations, and *National Anti-Doping Organizations*.

'Athlete': Any *Person* who participates in sport at the international level (as defined by each International Federation), the national level (as defined by each *National Anti-Doping Organization*, including but not limited to those *Persons* in its *Registered Testing Pool*), and any other competitor in sport who is otherwise subject to the jurisdiction of any *Signatory* or other sports organization accepting the *Code*. All provisions of the *Code*, including, for example, *Testing* and therapeutic use exemptions, must be applied to international- and national-level competitors. Some *National Anti-Doping Organizations* may elect to test and apply anti-doping rules to recreational-level or masters competitors who are not current or potential national caliber competitors. *National Anti-Doping Organizations* are not required, however, to apply all aspects of the *Code* to such *Persons*. Specific national rules may be established for *Doping Control* for non-international-level or non-national-level

competitors without being in conflict with the *Code*. Thus, a country could elect to test recreational-level competitors but not require therapeutic use exemptions or whereabouts information. In the same manner, a *Major Event Organization* holding an *Event* only for masters-level competitors could elect to test the competitors but not require advance therapeutic use exemptions or whereabouts information. For purposes of Article 2.8 (Administration or *Attempted Administration*) and 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* is an *Athlete*.

Endogenous: refers to a substance which 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 or procedure) shall be sufficient to conclude that the procedures addressed by the *International Standard* were performed properly. *International Standards* shall include any Technical Documents issued pursuant to the *International Standard*.

GC/C/IRMS (Gas Chromatography/Carbon/Isotope Ratio Mass Spectrometry or "IRMS"): 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 and quantification of an amount in excess of a stated threshold is considered an *Adverse Analytical Finding*.

5. Laboratory reporting guidelines

5.1 Application of GC/C/IRMS analysis to determine exogenous origin of Endogenous Steroids

In all cases, and at any concentration, the *Athlete's Sample* will be deemed to contain a *Prohibited Substance* and the Laboratory will report an *Adverse Analytical Finding* if, based on any reliable analytical method (e.g. GC/C/IRMS), the Laboratory can show that the *Prohibited Substance* is of exogenous origin. In such case, no further investigation is necessary.

- If GC/C/IRMS (or other reliable analytical method) has been carried out and is "positive", thereby proving exogenous production of the *Prohibited Substance*, the *Sample* shall be reported as an *AAF*. However, in cases where values are consistent with the endogenous reference compound (ERC) (e.g. "Negative" GC/C/IRMS result) the *Sample* shall be reported to indicate that no *Prohibited Substances* were found (e.g. "Negative").
- GC/C/IRMS results shall be reported in a way to conclude that the result is either significantly different from the ERC(s) and therefore consistent with exogenous origin¹, or not significantly different from the ERC(s) and therefore consistent with endogenous origin².
- The results of GC/C/IRMS analysis are to be included in the Laboratory test report.
- Laboratories unable to conduct the GC/C/IRMS analysis for technical reason(s) shall be in a position to arrange the analysis at another WADA-accredited laboratory, and to arrange transport of the *Sample* to that Laboratory with secure chain of custody upon request of the *Testing* authority.

¹ In layman's terms - a "positive" GC/C/IRMS

² In layman's terms - a "negative" GC/C/IRMS

(it is recommended that the terms "negative" and "positive" are not used in reporting since these words may be confused with the determination of the status of the finding.)

Boldenone:

In extremely rare individual cases, boldenone of endogenous origin can be consistently found at very low nanograms per milliliter (ng/mL) levels in urine. When such a very low concentration of boldenone is reported by a Laboratory and the application of any reliable analytical method (e.g. GC/C/IRMS) has not determined the exogenous origin of the substance, the *Sample* shall be reported as negative. If, based on any reliable analytical method (e.g. GC/C/IRMS), the Laboratory can show that the *Prohibited Substance* is of exogenous origin, the Laboratory will report an *AAF*. When a GC/C/IRMS analysis (or other reliable analytical method) has not been performed, further collections and analyses shall be performed by the relevant *ADO*.

5.2 Cases when GC/C/IRMS analysis to determine exogenous/endogenous origin of Endogenous Steroids has not been applied

In order to achieve harmonization in Laboratory reporting, the following steps are recommended in cases of elevated values of endogenous steroids and T/E ratios (e.g. TE ratio greater than 4.0) for which GC/C/IRMS has not been applied.

Where an Anabolic Androgenic Steroid is capable of being produced endogenously, a *Sample* will be deemed to contain such *Prohibited Substance* and an *Adverse Analytical Finding* will be reported where the concentration of such *Prohibited Substance* or its *metabolites* or *markers* and/or any other relevant ratio(s) in the *Athlete's Sample* so deviates from the range of values normally found in humans that it is unlikely to be consistent with normal endogenous production. A *Sample* shall not be deemed to contain a *Prohibited Substance* in any such case where an *Athlete* proves that the concentration of the *Prohibited Substance* or its *metabolites* or *markers* and/or the relevant ratio(s) in the *Athlete's Sample* is attributable to a physiological or pathological condition.

- To avoid unnecessary effort and analysis costs (for example for *Samples* from *Athletes* where naturally elevated values of endogenous steroids or T/E ratio have already been determined), the decision of whether or not to proceed with GC/C/IRMS analysis shall be made by the relevant *Testing* authority or *WADA*.
- In cases for which endogenous steroids show elevated values or the T/E ratio is greater than 4.0 and GC/C/IRMS has not been applied, the *Sample* shall be reported as an *Atypical Finding* based on the results of a Confirmation Procedure. The *Atypical Finding* report shall include a recommendation for the GC/C/IRMS analysis in the comment/opinion section of the test report³.
- When, upon decision by the relevant *Testing* authority or *WADA*, a GC/C/IRMS analysis (or other reliable analytical method) for a *Sample* reported as an *Atypical Finding* has not been performed, and a minimum of 3 previous results showing the longitudinal range of endogenous steroid values or T/E ratios found for the *Athlete* are not available, further collections and analyses shall be performed by the relevant *ADO*. At any time, relevant *ADOs* may conduct any additional investigations as they deem appropriate in assessing a *Sample* with an *Atypical Finding*.
- All "A" and "B" *Samples* associated with an *Atypical Finding* shall be stored appropriately and with secure chain of custody (in the same manner as *Samples* with an *AAF*).

³ In cases where the *Testing* authority requests a GC/C/IRMS analysis on a *Sample* reported as an *Atypical Finding*, the *Sample's* test report shall be re-issued based on the GC/C/IRMS result and reported as an *AAF* or "Negative" as indicated in section 5.1 of this Guideline.

6. Interpretation and follow up

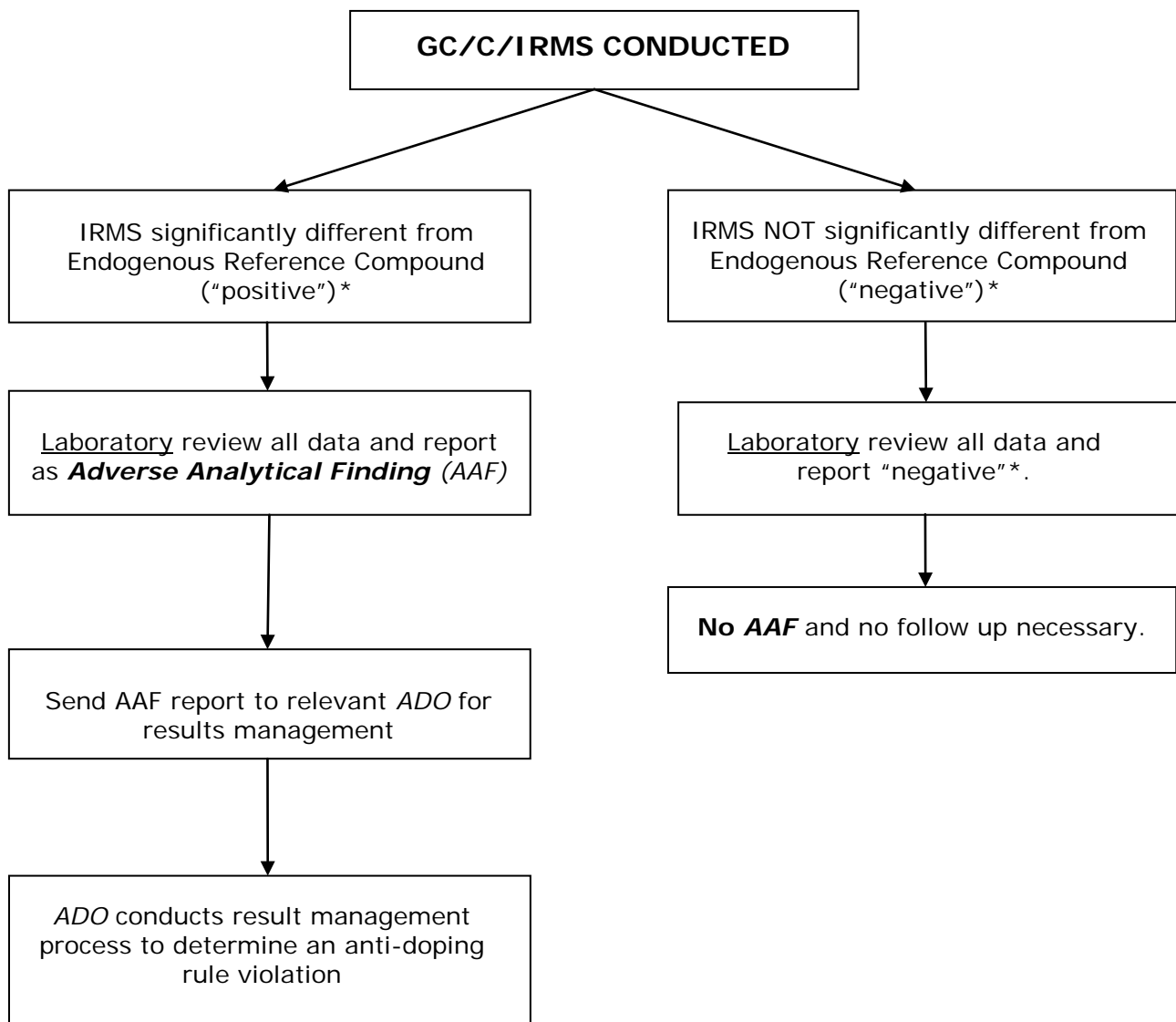
The *Athlete* is not to be informed of an *Atypical Finding*. At the end of the follow up *Testing* and/or investigation, the *Athlete* should be informed of the final outcome (AAF or "Negative"), i.e., whether or not the determination is that an anti-doping rule violation (ADRV) is alleged to have occurred, with explanation.

- 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 that *ADOs* go back to the relevant Laboratories to request the actual T/E values, steroid profile information and other documentation.
- Previous, or follow up data, shall be collated by the *ADO*, and shall be provided to one *WADA*-accredited laboratory (one that was involved in the analysis of at least one of the results in question) for the analysis of the longitudinal data. Only one Laboratory must be responsible for the analyses and be provided with all the relevant data necessary to conduct the investigation
- *Samples* showing indications of bacterial activity should be excluded from the data set of a longitudinal study.
- 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 *NADO* for an *Athlete's* test history, and vice-versa.
- For follow-up *Testing*, GC/C/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 GC/C/IRMS analysis be conducted even on follow up *Samples* showing a T/E ratio of less than 4.
- The Laboratory Director 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 relevant *ADO* for their review and determination of whether an ADRV has occurred. It is strongly recommended that the interpretation of longitudinal data be signed off by the Director of the Laboratory. To facilitate this, follow-up *Samples* may be sent to the same Laboratory that reported the *Atypical Finding* where possible. At a minimum, the results of all related tests shall be provided to one Laboratory for the interpretation of longitudinal data.
- Prior or subsequent *Samples* with T/E values less than 4.0 do not require a quantitative confirmation in order to be utilized in longitudinal studies to determine an AAF.
- The expert body of the *ADO* should consist of individuals with the appropriate competence in the relevant field, i.e. endocrinology.
- If the *ADO* decides to prosecute the *Athlete* on the basis of an AAF and at the *Athlete's* request, a full documentation package shall be provided including test results used in the results management of the case including the *Atypical Finding*.

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

Elevated T/E ratios and elevated values of Endogenous Steroids

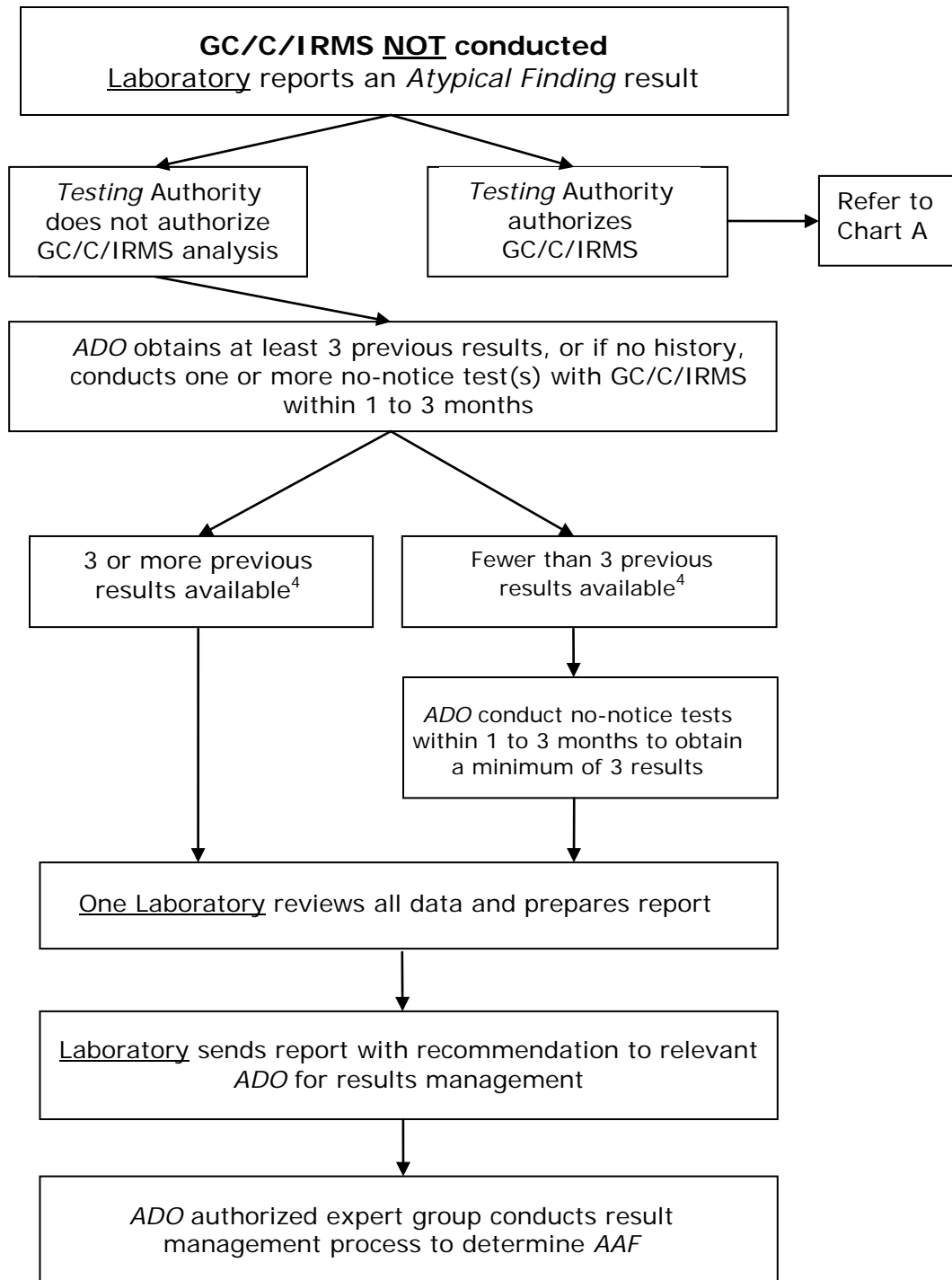
Chart A: GC/C/IRMS conducted



* See footnotes on page 6

Elevated T/E ratios and elevated values of Endogenous Steroids

Chart B: GC/C/IRMS NOT conducted – *Atypical Finding* reported



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 needed.

7. Results Management

Confirmation of exogenous origin

- Once it is determined that elevated values of endogenous steroid or elevated T/E is consistent with exogenous origin and reported as an *AAF*, the results management process is followed, as in the case of the use of other *Prohibited Substances* or *Methods*.

No confirmation of exogenous origin

- When an *Athlete* is identified with a possibly naturally elevated endogenous steroid or T/E ratio, i.e. an *Atypical Finding* consistent with endogenous origin, a dossier including all data should be reviewed by one Laboratory and transferred to the relevant *ADO*. The Laboratory Director 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 the elevated value of endogenous steroid or T/E ratio is of natural origin, this determination shall be documented in the dossier of the *Athlete* concerned, preventing systematic follow-up for future anti-doping tests which show similar elevated ratios or values. This information will also be shared with other *ADOs* as relevant. In the case of subsequent anti-doping *Testing* of an *Athlete* with a naturally elevated T/E ratio, the T/E ratio should be carefully monitored to ensure that it 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, *GC/C/IRMS Testing* should be requested. In the absence of *GC/C/IRMS Testing*, a follow-up, no-notice anti-doping test should be triggered immediately by the relevant *ADO*.
- 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
- A copy of the report confirming a naturally elevated value of endogenous steroid or T/E ratio, including the results of the related initial and subsequent follow-up tests, and any related analytical information, shall be forwarded to *WADA* results management.