Athlete Biological Passport Operating Guidelines

Version 9.0
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Content

This document is divided into four parts.

Part One provides background and context for the creation of the *Athlete Biological Passport (ABP)*, introduces the Hematological, Steroidal, and Endocrine Modules of the Passport and explains the role of the *ABP* Operating Guidelines in supporting *Anti-Doping Organizations (ADOs).*

Part Two describes the Modules and explains the principles for the implementation of the *ABP* by an *ADO*.

Part Three contains Annexes of the *International Standard* for *Results Management* (ISRM), the *International Standard* for *Testing* and Investigations (ISTI) in connection with *Technical Documents* and Laboratory Guidelines that specify mandatory protocols to be followed by *ADOs, Laboratories,* and *Athlete* Passport Management Units (APMUs) in order to run an *ABP* program.

Part Four includes a template agreement developed by *WADA* for the sharing of Passport information between multiple *ADOs* (supported by *ADAMS*).

[For the purpose of these Guidelines, *Code* definitions are in *Italics*. *International Standard* definitions are Underlined.]

Part 1: Introduction and Objectives

1.1. Introduction to the *Athlete Biological Passport*

The term “athlete biological passport” was first proposed in the early 2000s by the scientific community when monitoring of select hematological variables (*Markers* of blood doping) was identified as a means to define an individual’s hematological profile. In conjunction with several stakeholders and medical experts, the World Anti-Doping Agency *(WADA)* began to further develop, harmonize and validate the utility of within-individual serial monitoring of biological parameters to identify physiological patterns of doping. The result was a formal operating Guideline and mandatory Standards formalizing the *Athlete Biological Passport* (*ABP*), first published in 2009, which concerned exclusively the Hematological Module.

In 2014, the initial system was complemented with the Steroidal Module, which aims to establish longitudinal profiles of an *Athlete*’s steroid variables in urine *Samples*. Additional steroid variables measured in blood (serum) *Samples* were added in 2023 to complement the urine steroid profile.

The Endocrine Module was also added in 2023 to monitor *Markers* of human Growth Hormone (hGH).

The framework proposed in these Guidelines builds on existing anti-doping infrastructure to promote harmonization amongst *ABP* Programs, to facilitate the exchange and mutual recognition of relevant information between stakeholders involved in the *ABP* process and, consequently, to enhance efficiencies in the operation of *Anti-Doping Activities*.

These Guidelines provide a harmonized process for the Hematological, Steroidal and Endocrine Modules of the *ABP*, which follow similar administrative procedures and utilize *WADA’s Anti-Doping Administration and Management System (ADAMS)*.

As with all Guidelines, this document is subject to ongoing review to ensure it continues to reflect best practice moving forward. *WADA* encourages feedback on this document and recommends stakeholders to consult *WADA’s* website (http://www.wada-ama.org) for the latest version.

1.2. Objectives

The principal objectives of integrating the *ABP* into the larger framework of a robust anti-doping program are the following:

a) The *ABP* can be used to flag *Athletes* and *Samples* requiring further attention through intelligent, timely interpretation of Passport data, which can lead to an Anti-Doping Rule Violation (ADRV) through establishment of the presence of a *Prohibited Substance* or its *Metabolite* or *Marker* in an *Athlete’s Sample* according to World Anti-Doping Code (*Code*) Article 2.1. The *ABP* provides valuable information that can be used to direct *Target Testing*, *Sample* storage and further analysis of previously collected *Samples* more effectively. The

ABP can notably be used as a complement to Analytical *Testing* Procedures to further refine and strengthen overall anti-doping strategies:

- For the Hematological Module, this could be, for example, by directing *Testing* for Agents Affecting Erythropoiesis (AAEs) or homologous blood transfusion (HBT).
- For the Steroidal Module, this could be, for example, the use of Gas Chromatography-Combustion-Isotope Ratio Mass Spectrometry (GC/C/IRMS) to detect endogenous steroids administered exogenously, or for the analysis of steroid esters on atypical *Samples* targeted by using the *ABP*.
- For the Endocrine Module, an example of this approach could be the application of the hGH Isoform Differential Immunoassay to *Samples* with atypical hGH *Marker* values.

b) Through changes in biological *Markers* of doping collated over time, a Passport can be used to establish '*Use'* per *Code* Article 2.2 without necessarily relying on traditional analytical approaches for the detection of a particular *Prohibited Substance* or *Prohibited Method*. As some *Prohibited Substances* and *Prohibited Methods* can be undetectable despite causing lasting physiological changes on the body, the *ABP* is a powerful and necessary tool to complement traditional analytical testing.

c) The *ABP* can also be used to assist investigations, for example by flagging *Athletes* and/or groups of *Athletes* for further investigation, or by providing complementary information during ongoing investigations. In particular, as *Marker* data are linked to the time and location of *Sample* collection within the *ABP*, spatiotemporal analysis of suspicious *Marker* profiles can provide a rich dataset that can be merged with other forms of intelligence.

d) The Steroidal Module of the *ABP* can assist in identifying the substitution of an *Athlete's urine Sample* with the urine of another individual (urine exchange). When a urine *Sample* steroid profile is not consistent with other *Sample*(s) from the *Athlete's* Passport, urine exchange may be suspected and confirmed using DNA analysis across multiple *Samples*, leading to an ADRV under *Code* Article 2.2 and/or 2.5.

e) The *ABP* can be used by *Anti-Doping Organizations* (*ADOs*) to help optimize their Test Distribution Plan and the cost efficiency of their overall *Testing* strategy. For example, Passport status can be used as part of a larger risk assessment in order to flag *Athletes*, teams, sports or nationalities requiring increased or decreased Testing frequency. Passport status can also be used to select *Samples* for long-term storage.

f) The *ABP* is an effective doping deterrent that complements multi-faceted anti-doping programs by adding to aspects such as *Athlete Education*, whereabouts, traditional testing strategies and *Results Management* thereby having the potential to improve deterrence of athletes and their entourage from engaging in doping behaviour.

Part 2: Modules, Management and Administration

2.1. Modules

2.1.1. Hematological Module

The Hematological Module collects information on *Markers* of blood doping. This module aims to identify the *Use* of *Prohibited Substances* and/or *Prohibited Methods* for the enhancement of oxygen transport or delivery, including the *Use* of AAEs and any form of blood transfusion or manipulation.

In addition to identifying the use of AAEs included under section S2 of the *Prohibited List* (Peptide Hormones, Growth Factors, Related Substances, and Mimetics), the Hematological Module also seeks to identify the *Use of Prohibited Methods* categorized under section M1 of the *Prohibited List* (Manipulation of Blood and Blood Components).

The following blood variables are considered within the *ABP* Hematological Module:

- ABPS: Abnormal blood profile score
- HCT: Hematocrit
- HGB: Hemoglobin
- IRF: Immature reticulocyte fraction
- MCH: Mean corpuscular hemoglobin
- MCHC: Mean corpuscular hemoglobin concentration
- MCV: Mean corpuscular volume
- OFFS: OFF-score
- PLT: Platelet count
- RBC: Red blood cell (erythrocyte) count
- RDW-SD: Red cell distribution width (standard deviation)
- RET#: Reticulocytes count
- RET%: Reticulocytes percentage
- WBC: White blood cells

2.1.2. Steroidal Module

The Steroidal Module collects information on *Markers* of steroid doping measured in urine and/or serum *Samples*. The module aims to identify endogenous anabolic androgenic steroids (EAAS) when administered exogenously. The Steroidal Module is also an effective means to identify urine *Samples* which may have been tampered with or exchanged with the urine of another individual.

The following urinary *Markers* are considered within the *ABP* Steroidal Module, as detailed in the *Technical Document* on Measurement and Reporting of Endogenous Anabolic Androgenic Steroid (EAAS) Markers of the Urinary Steroid Profile (TD EAAS, see Section 3.6 below):

- A: Androsterone
- Etio: Etiocholanolone (Etio)
- 5αAdiol: 5α-Androstane-3α,17β-diol
- 5βAdiol : 5β-Androstane-3α,17β-diol
- T: Testosterone
- E: Epitestosterone

In addition to the following ratios:

- T/E
- A/T
- A/Etio
- 5αAdiol/5βAdiol
- 5αAdiol/E

As detailed in the Laboratory Guidelines for Quantification of Endogenous Steroids in Blood for the *Athlete Biological Passport* (see section 3.5 below), one additional *Marker* and one ratio are considered in blood:

- T: Testosterone
- T/A4: Ratio between the concentrations of Testosterone and Androstenedione (A4)

2.1.3. Endocrine Module

The Endocrine Module collects information on *Markers* of hGH doping. The module aims to identify hGH use and as well as use of hGH analogs, fragments and releasing factors categorized under Section S2.2 of the *Prohibited List*. This module may also indicate use of insulin-like growth factor-I (IGF-I), categorized under Section S2.3 of the *Prohibited List.*

The following *Markers* are considered within the Endocrine Module, as detailed in the Laboratory Guidelines for the Analytical Requirements for the Endocrine Module of the *Athlete Biological Passport* (see Section 3.4 below):

- GH-2000 Score
- IGF-I: Insulin-like Growth Factor-I
- P-III-NP: N-terminal Pro-peptide of Type III Collagen

2.2. Resources, Partner Roles and Responsibilities

The roles and responsibilities of the various partners involved in the *ABP* process include, in particular, test planning, conducting the *Sample* collection, *Sample* analysis, profile assessment and *Results Management*. These activities are carried out through an administrative process involving the coordination of different stakeholder groups, namely *ADOs*, Laboratories, APMUs, and Experts. Consequently, the success of an *ABP* program depends on the mutual recognition of stakeholder roles and the efficient exchange of relevant information between stakeholders involved in the *ABP* process.

2.2.1. Resources

The following resources are required to implement the *ABP*:

- Dedicated resources within an *ADO* to effectively manage both testing and *Results Management* requirements for the *ABP*, including the implementation of *ABP*-related requirements in the *Technical Document* for Sport Specific Analysis (TDSSA).
- Access to a network of Doping Control Officers (DCOs) and Blood Collection Officers (BCOs) where necessary, operating in locations where target *Athletes* will be present, with access to materials required for collection and transport of *ABP Samples*.
- An effective whereabouts management system to facilitate *Athlete* location (i.e. *ADAMS*).
- Access to *ADAMS*, to administer the *ABP* Program.
- Laboratories to analyse *Samples* and report the results into *ADAMS.*
- A *WADA*-approved *Athlete* Passport Management Unit (APMU) for the management of specific *ABP* processes.
- An Expert panel managed by the APMU qualified for the review of Passports.

2.2.2. Specific Partner Responsibilities

2.2.2.1. *Anti-Doping Organization* (*ADO*)

The *ADO* is responsible for:

- Implementing and administrating an *ABP* program in accordance with these Guidelines, including compliance with applicable *International Standards* and *Technical Documents*.
- Contracting a *WADA*-approved APMU to manage the *ABP* program.

  [Comment: The list of WADA-approved APMUs is available at the following link:

https://www.wada-ama.org/en/resources/athlete-biological-passport/list-of-athlete-passport-management-units-apmu]

- Ensuring that recommendations received from the APMU are followed by effective, targeted, timely and appropriate follow up actions, including further *Testing* and/or *Sample* Analytical Testing.
- Establishing and implementing a Test Distribution Plan for the *ABP*, in consultation with the APMU, and ensuring adaptive *Testing* throughout the year depending on changes in Passport status or other relevant intelligence.
- Sharing of relevant information with internal investigations personnel and other *ADOs* (when appropriate).
- Managing Passport custody and ensuring efficient Passport sharing with other *ADOs* having shared *Testing* jurisdiction over the *Athlete*.
- Providing APMU and Experts with supplementary information requested during Passport evaluation.
- When the *ADO* is the Passport *Custodian*, following up on *Adverse Passport Findings* (*APFs*) in accordance with *Code* and ISRM requirements.
- When necessary, informing the *Athlete* to seek independent medical advice in case the Passport indicates a "likely medical condition", as determined by the Experts.

2.2.2.2. Athlete Passport Management Unit (APMU)

In compliance with the *Technical Document* related to Athlete Passport Management Unit Requirements and Procedures (TD APMU, section 3.8 below), the APMU is responsible for:

- Timely management of Passports in *ADAMS* on behalf of the Passport Custodian.
- Performing Passport assessments to make timely *Target Testing* and *Sample* analysis recommendations to the *Anti-Doping Organization* (*ADO)* via the APMU Report in *ADAMS* when appropriate.
- Managing the review of atypical Passports according to Annex C of the *International Standard* for *Results Management* (ISRM) (Section 3.7 below), including, but not limited to, the following:
  - Issuing and updating APMU Reports in *ADAMS*,
  - In case of an *Atypical Passport Finding* (*ATPF)*, or when a review is otherwise justified, assigning and liaising with the Expert panel as required,
  - Compiling all necessary information to establish an *Athlete* Biological Passport Documentation Package, and
  - Declaring *Adverse Passport Findings* (*APFs*) to the Passport Custodian and *WADA*.
- Assessing and managing Passport *Sample* validity in *ADAMS*, in consultation with the Experts or Laboratories when necessary.

- Collating and providing additional information requested by Experts (such as competition schedule or whereabouts information) to assist with Passport evaluation.
- Providing support to the Passport Custodian in defining priorities in order to optimize the efficiency of their *ABP* program. These priorities may include, but are not limited to, cost efficiency, special analyses, Test Distribution Plans, and *Target Testing*.

2.2.2.3. Laboratory

The Laboratory is responsible for:

- Urine analysis: perform urine analysis in compliance with the *Technical Document* on Measurement and Reporting of Endogenous Anabolic Androgenic Steroid (EAAS) Markers of the Urinary Steroid Profile (TD EAAS, Section 3.6 below) for the measurement and reporting of urinary steroid profiles.
- Blood (serum) *Sample* analysis: perform blood *Sample* analysis in compliance with the Laboratory Guidelines for the Analytical Requirements for the Endocrine Module of the *Athlete Biological Passport* and the Laboratory Guidelines for the Quantification of Endogenous Steroids in Blood for the *Athlete Biological Passport*.

The Laboratory or *ABP* Laboratory is responsible for:

- Blood *ABP Sample* analysis: perform blood *ABP Sample* analysis in compliance with the *Technical Document* on Analytical Requirements for the Hematological Module of the *Athlete Biological Passport* (TD BAR, Section 3.3 below).
- Issuing a Certificate of Analysis or Laboratory Documentation Package as applicable, in accordance with the *Technical Document* for the production of Laboratory Documentation Packages (TD LDOC).
- Collating and providing additional information for interpretation of results and for complementary analysis.

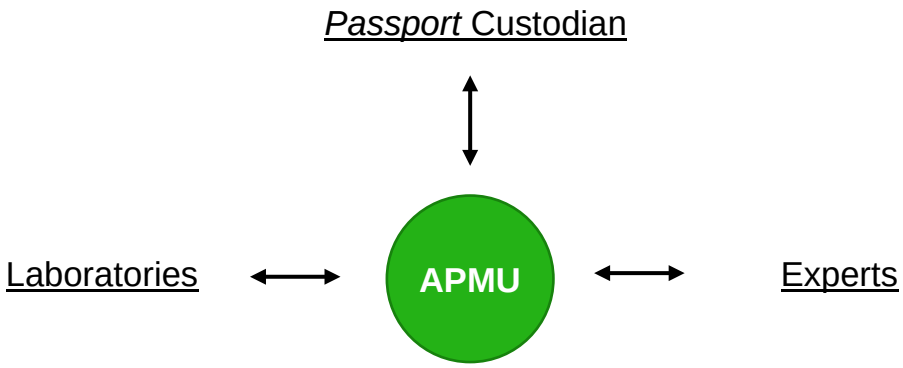
2.2.2.4. Experts

Experts are responsible for:

- Reviewing Passport data and results from the Adaptive Model in *ADAMS* provided by the APMU in order to assess the likelihood that the Passport is the result of normal physiological variation, the result of the *Use* of a *Prohibited Substance* or *Prohibited Method*, or the result of other potential causes.
- Recommending follow-up *Testing*, *Sample* analysis, and/or, when justified, recommending clinical testing that may be required to confirm their assessment.
- Reviewing any explanations given by the *Athlete* and providing an opinion on whether the Passport is “Normal”, “Suspicious”, “Likely doping” or “Likely medical condition” per Annex C of the ISRM.
- Working with the relevant APMU as required and providing support as necessary throughout the *Results Management* and hearing process.

2.3. *ABP* Management and Administration

The daily management of an *ABP* program is carried out through the cooperation of the Passport Custodian and the APMU. While the Passport Custodian oversees test distribution for the *ABP*, Passport management is carried out by the APMU on behalf of the Passport Custodian. In the administrative sequence of the *ABP*, the APMU provides a link between the Passport Custodian, the Laboratories, and the Expert panel. Within each Passport in *ADAMS*, the APMU Report provides a record of these various interactions for efficient follow-up by the Passport Custodian, *WADA* and other *ADOs* with whom the Passport is shared though *ADAMS*.



2.3.1. Defining, *Testing* and Target *Athletes*

An *ABP Testing* Program must be managed in accordance with the ISTI, the ISRM, the *Technical Document* for Sport Specific Analysis (TD SSA) and applicable *Technical Documents* specific to the *ABP* (Part Three below).

Without limitation, the criteria listed in ISTI Articles 4.2 and 4.5 are factors that may be considered in determining the target population for the *ABP* in the context of an *ADO's* overall Test Distribution Plan (TDP).

Targeted tests that follow the recommendations of the APMU should be privileged over Random Selection *Testing* to improve the effectiveness of the *ABP*. Importantly, *ADOs* should have an internal procedure in place to ensure that rapid reactive follow up *Testing* can be carried out for atypical Passports when appropriately recommended by the APMU, regardless of the level of the *Athlete*. *ADOs* should also ensure they can implement an adaptive *Testing* strategy during the year that can allocate tests to *Athletes* with Passports containing suspicious features. As such, a small contingency of reactive tests dedicated to the *ABP* should be part of an *ADOs* Test Distribution Plan.

In general, the effectiveness of the *ABP* to detect doping is improved where both *In-* and *Out-of Competition Testing* are distributed strategically throughout the year. As a single test represents a snapshot in time, it is generally recognized that the *ABP* is more efficient when at least three (3) tests

are planned per *Athlete* in a calendar year, across the athlete's training, competition, and off-season periods, where additional reactive tests may be included should the Passport demonstrate abnormal features. A Test Distribution Plan for the *ABP* should therefore seek to favor increased test numbers per *Athlete*, as opposed to *Testing* many *Athletes* 1-2 times a year. This point is formalized for the Hematological Module, where the TDSSA requires *ADOs* to plan to test endurance *Athletes* annually, at a minimum, an average of three (3) times across all endurance *Athletes* in their *Registered Testing Pool* (*RTP*).

[Comment: The exceptional use of Advance Notice Testing can also be considered in specific situations (ex. to establish baseline values in athletes at a competition).]

When a blood *ABP Sample* is collected, the *ADO* must consider whether the collection of concomitant urine or blood *Samples* is warranted, under the circumstances, to perform additional analysis. For the Hematological Module, it is recommended to collect urine *Samples* together with blood *ABP Sample*(s) in order to permit Analytical Testing for AAEs when required. Similarly, when collecting blood (serum) *Samples* for the Steroidal Module, it is recommended to collect urine *Samples* in order to provide additional information based on steroid profile or the presence of potential confounding factors from the urine *Sample* in addition to the possibility to carry out GC/C/IRMS analysis.

[Comment: For the Hematological Module, it is recommended to use data from samples collected 5 days apart or more to optimize the statistical significance of the data. This does not preclude Testing an Athlete less than five (5) days apart, notably and without limitation, when a potential risk of doping practices has been identified, or when recommended by the APMU. The validity of the Samples and their inclusion in the Expert review is, in any event, not put in question by the collection frequency.]

2.3.2. *Sample* Collection and Transportation

While urine *Samples* have no specific requirements for collection and transport beyond those outlined in the Guidelines for *Sample* Collection, blood (serum) and blood *ABP Samples* shall be collected and transported according to defined conditions to ensure reliable measurement of the relevent *Markers*.

Sample type	Collection		Transport	
	Time after exercise	Supplementary form	Temperature logger	Time
Urine	---	No	No	Should be performed as soon as possible.
Blood ABP	>120 min (2 hours)	Yes (ISTI Article I.2.9)	Yes (ISTI Article I.2.7)	Using the Blood Stability Score (BSS). (ISTI Article I.4)
Blood (serum)	>60 min (1 hour)	No	Yes (ISTI Article D.4.16)	As soon as possible, and up to 72h.*

**Blood (serum) Samples may be analyzed by different methods with varying requirements for collection to analysis time. Best practice dictates that a Sample should arrive at the Laboratory as soon as possible. A maximum of 72h of transportation time is generally recommended as it ensures the potential application of the hGH Isoform Differential Immunoassay to Sample following analysis for the Endocrine Module. An additional*

24h is permitted in the case of analysis for the Endocrine Module or the hGH Biomarkers Test. Both cases assume 24h of handling time for Samples in the Laboratory in an unfrozen state.

2.3.3. *Sample* Storage

As part of a comprehensive strategy for long term storage of *Samples*, *ADOs* are recommended to consider Passport information as part of the criteria for long term storage in order to decide which *Samples* to store and for how long.

The longitudinal nature of the *ABP* can uncover atypical features that may warrant further Analytical *Testing* in the most recent *Sample*, but also in previous *Samples*. For example, an *ATPF* for low T/E in a steroidal Passport may indicate that a GC/C/IRMS analysis should be performed not on the most recent *Sample*, but on a previous *Sample*. Therefore, such a *Sample* storage strategy should consider the general frequency of *Sample* collection in order to improve the chance of such *Samples* being available for retroactive analysis.

Passport status can also be used to drive *Sample* storage decisions. For example, an *ADO* may wish to store all *Samples* for which there is a "suspicious" APMU recommendation in *ADAMS*. Similarly, an APMU may directly recommend that an *ADO* consider storing *Samples* for a given *Athlete* displaying abnormal features in their Passport.

With regards to *Sample* type, given that blood (serum) *Samples* now have the possibility of retroactive analysis for the Endocrine and Steroidal Modules, it is recommended to consider systematically storing such blood *Samples* for a longer period than the minimum three months that is required by Lanoratories (for example, 12 months).

2.3.4. *Athlete* Information

Given that additional information is required from *Athletes* beyond what is collected in traditional *Doping Control* documentation pursuant to the ISTI, supplemental documentation may be required. Such documentation may be collected as appropriate, both prior to and after *Testing*, for APMU assessment and Expert review, as required.

For blood *ABP Samples*, in addition to the mandatory information set out in ISTI Article 7.4.5, which must be recorded as a part of all Sample Collection Sessions, the information listed in ISTI I.2.9 (Section 3.2 below) shall be recorded in a specific *ABP* Supplementary Form or a related form to be signed by the *Athlete*.

> *[Comment: See the available ABP Supplementary Form template: https://www.wada-ama.org/en/resources/world-anti-doping-program/athlete-biological-passport-supplementary-report-form]*

2.3.5. Standardization through *ADAMS*

The *ABP* Program is administered through *ADAMS,* a secure online database management tool for data entry, storage, sharing, and reporting, designed to assist stakeholders and *WADA* in their anti-

doping operations. An essential element of the *ABP*, the Adaptive Model, is fully integrated into *ADAMS*. Only programs that fully utilize *ADAMS* can be considered *ABP* Programs.

Standardization and harmonization of *ABP* programs is achieved through the use of *ADAMS*. This ensures that all mandatory requirements are met and that the *Athlete* Passports are shared and stored securely, all in accordance with the *International Standard* for the Protection of Privacy and Personal Information (ISPPPI). Furthermore, *ADAMS* facilitates prompt exchange of information between *ADOs*, APMUs, Laboratories and/or *ABP* Laboratory, Sample Collection Personnel, and *WADA*.

2.3.6. The APMU Report

The APMU Report is a central element in the administrative sequence of the *ABP* that shall be entered and maintained by the APMU in *ADAMS.* The APMU Report provides an up-to-date overview of the current status of an *Athlete's* Passport together with recommendations, as appropriate, for efficient follow-up by the Passport Custodian. The APMU Report serves to update the Passport Custodian*, WADA* and other *ADOs* with whom the Passport is shared. In addition, it provides a record of events associated with a Passport in *ADAMS*.

As detailed in the TD APMU (see section 3.8), the APMU Report may include, without limitation:

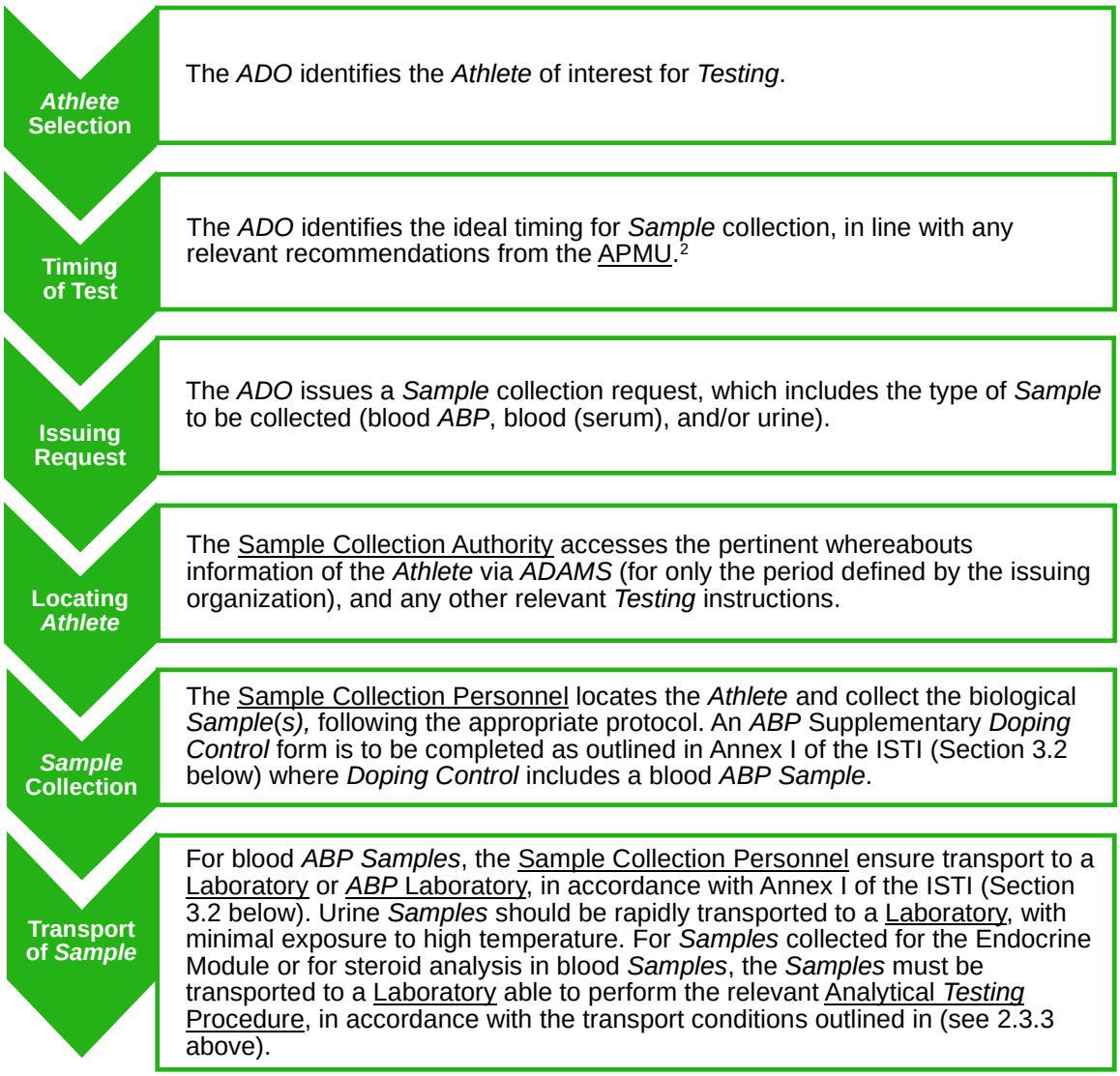
- Assessments of *Sample* validity by the APMU and/or Experts;
- Recommendations for complementary Analytical *Testing* (*e.g.,* ESAs, HIF stabilizers, confirmation of steroid profile, GC/C/IRMS, long-term steroid *Metabolites*, IGF-I, etc.) on *Samples* collected;
- Recommendations for further Analytical *Testing* on *Samples* collected previously;
- Recommendations for storing of *Samples* for extended periods of time for Further Analysis;
- *Target Testing* recommendations based on available data and Experts' recommendations; and a summary of any recent Expert reviews.

2.3.7. Recommended Administrative Sequence

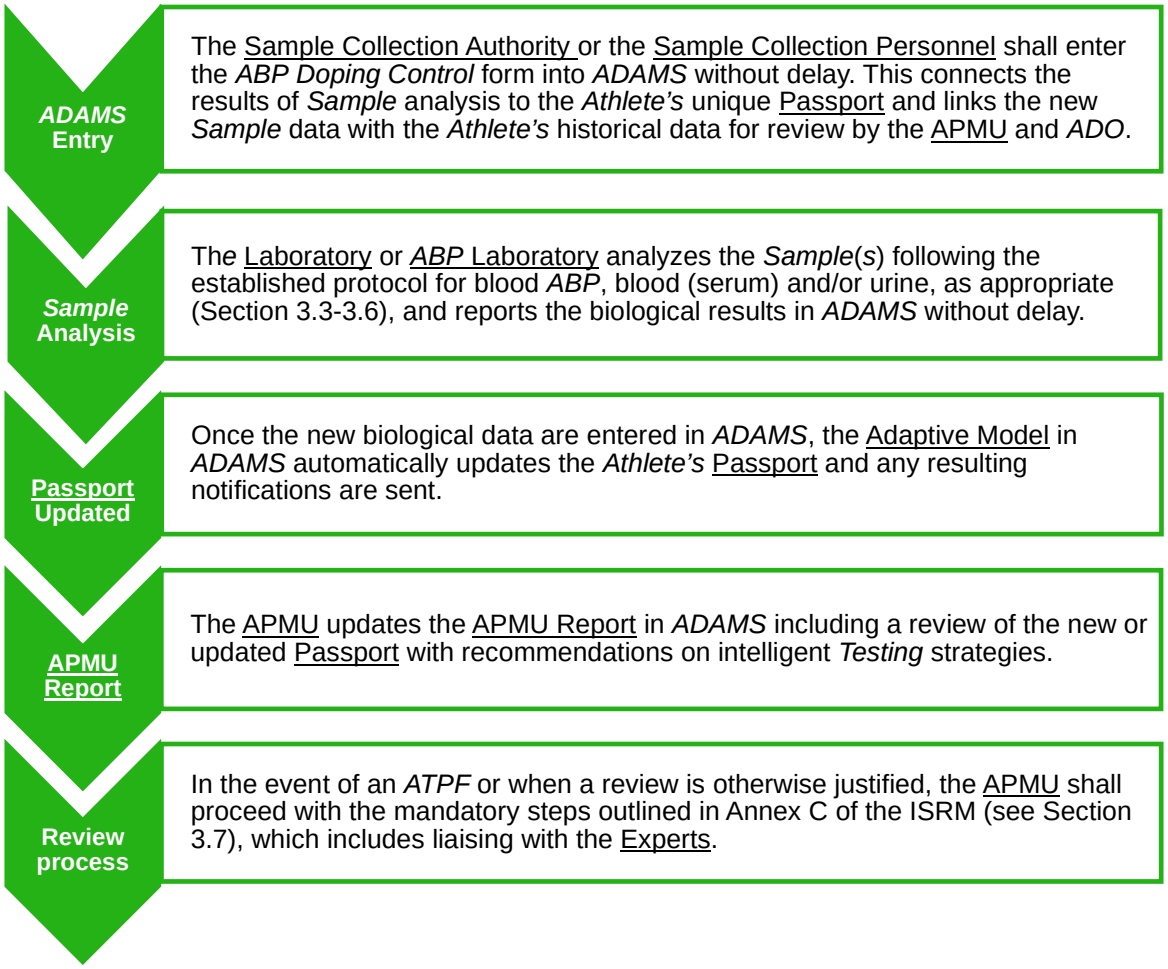
The following outlines the suggested sequence of interactions between the *Athlete,* Sample Collection Personnel*, ADOs,* Laboratory(ies)*, ADAMS,* APMUs, and Expert panels to establish, follow up and review an individual *Athlete*'s Passport in an effective and efficient manner.

The recommended administrative sequence outlined below may be modified or adapted to fit with existing anti-doping infrastructure, procedures and mechanisms as required. However these Guidelines aim to ensure that *ADOs* establish a process that demonstrates transparency in the planning, interpretation and *Results Management* aspects of an *ABP* program.

2.3.8. *ABP* Administrative Sequence Graphic



ABP Administrative Sequence Graphic, *cont.*



2.4. Passport Custody and Sharing

For any individual *Athlete,* only one Passport is to be established. Using *ADAMS* for the management of Passport information, *ADOs* enhance efficiency and program effectiveness through exchange of information and mutual recognition of program outcomes. Such coordination and reciprocal agreement reduce unnecessary duplication in resource expenditure and foster enhanced confidence among *ADO*s and *Athletes* alike.

All *Doping Control* biological results obtained for an *Athlete* are collated in their Passport regardless of the *Testing* Authority. Only a complete *Athlete's* Passport allows the correct determination of *Atypical Passport Findings* in *ADAMS*. Passport administration and possible *Results Management* can then follow in compliance with the *Code* with the assurance that the Passports are complete.

Within the framework provided by the ISPPPI and as required by the ISTI (Article 4.9.1)*, ADOs* shall coordinate their activities where multiple *ADOs* have *Testing* jurisdiction over a single *Athlete* and multiple *ADO*s may wish to perform Passport *Testing*. In the interests of a "one *Athlete* – one

Passport" principle, *ADOs* shall work cooperatively to see that *Testing* is coordinated appropriately with all results collated in the *Athlete*'s Passport in *ADAMS* and that the Passport Custodian shares the Passport with other *ADOs* having shared *Testing* jurisdiction over the *Athlete*.

2.4.1. Role of the Passport Custodian

Each individual *Athlete* has a Passport Custodian that ensures that all *ADOs* that have *Testing* jurisdiction over the *Athlete* do not work in isolation. The Passport Custodian is responsible for sharing Passport information with other *ADOs* to ensure proper coordination and best use of resource expenditure. *WADA* has developed a template agreement for the sharing of Passport information between multiple *ADOs* (supported by *ADAMS*), which is included herein in Part Four.

In addition to sharing Passport information with ADOs directly via *ADAMS*, the Passport Custodian is also responsible for ensure the sharing of relevant Passport-related information with *Major Event Organizers (MEO)* who are planning *Testing* around an upcoming competition. Prior to the event, the Passport Custodian is responsible for providing relevant testing recommendations to the *MEO* including Passport status and/or recent APMU recommendations in order assist *MEOs* to prioritize their test distribution. During the event, the Passport Custodian should ensure that rapid communication of APMU recommendations can be made during the competition in response to *MEO* testing, which will allow the *MEO* to conduct any follow up testing or additional analysis that may be required as a result of the *MEOs* testing.

The Passport Custodian is responsible for *Results Management* of *Athlete* Passports under their custody. In the case of an *ATPF*, or when a review is otherwise justified, the APMU contracted by the Passport Custodian is responsible for initiating the Passport review process on behalf of the Passport Custodian. If an *APF* is declared, the Passport Custodian is responsible for *Results Management* of the Passport in compliance with Annex C of the ISRM (Section 3.7 below), regardless of whether another *ADO* was the *Testing* Authority of the test that triggered the *ATPF*.

As outlined in ISTI Article 10.4, where the *Testing* Authority is not the Passport Custodian, the *Testing* Authority that initiated and directed the *Sample* collection maintains the responsibility for additional Analytical *Testing* of the *Sample*, including the performance of further Confirmation Procedure(s) upon requests generated automatically by the Adaptive Model of the *ABP* in *ADAMS* (*e.g.* GC/C/IRMS triggered by elevated T/E) or as requested by the APMU (*e.g.* GC/C/IRMS requested due to abnormal secondary *Markers* of the urinary "longitudinal steroid profile"; AAE tests due to suspicious hematological *Marker* values) and *Results Management* of the *Sample* Analytical *Testing* results.

2.4.2. Attribution and Transfer of Passport Custody

In *ADAMS*, Passport custody is attributed to the *Testing* Authority that first tests the *Athlete*, independently of whether it is a blood *ABP* test, a blood (serum) test, a urine test, or a combination of these. This process ensures that the custody will most likely automatically be assigned to the organization that has a real interest in the *Athlete*. When the *Athlete* is first tested by a *Major Event Organization* (*MEO*), Passport custody is attributed to the IF. When a *NADO* first tests an *Athlete* with

a different sport nationality, Passport custody is attributed to the IF. This can later be reassigned to the NADO of the sport nationality of the *Athlete* if appropriate.

Passport custody can be transferred in *ADAMS* by the *Passport* Custodian to another *ADO* with *Testing* jurisdiction over the *Athlete*. *ADOs* should have a procedure in place to monitor their pool of Passports at regular intervals (ex. quarterly) using the reporting functionalities in *ADAMS* in order to identify Passports potentially more suitable for management by another *ADO*. Reasons for transferring *Passport* custody may include a change in *Athlete* level, more frequent *Testing* by another *ADO*, or be based on a strategic agreement between *ADOs* with *Testing* jurisdiction over the *Athlete*. The *Passport* Custodian should make requests in writing regarding any transfers of *Passport* custody to the recipient *ADO*. If no agreement can be found on the Passport custody, *WADA* shall determine which *ADO* is the *Athlete's Passport* Custodian. *WADA* shall not rule on this without consulting the *ADOs* involved.

Part 3: Mandatory Protocols

3.1. Scope

ADOs implementing an *ABP* Program shall follow mandatory protocols documented in Annexes of the *International Standard* for *Results Management* (ISRM) and *International Standard* for *Testing* and Investigations (ISTI). Included herein for the ease of reference, these requirements have been established to harmonize the results of monitored biological *Markers* within the *ABP* to ensure both legal fortitude and scientific certainty. This standardization of procedure allows for the sharing and mutual recognition of Passport data between the anti-doping programs of multiple *ADOs*. Only programs that fully adhere to these protocols and fully utilize *ADAMS* can be considered *ABP* Programs. These protocols are linked to *Technical Documents* and Laboratory Guidelines that a Laboratory or *ABP* Laboratory shall follow for the analysis of *Samples* collected within the framework of the *ABP* (included herein for the sake of completeness).

Section 3.2 sets out the minimum requirements for *Sample* collection and *Sample* transport that an *ADO* shall fulfil to run the Hematological Module of the *ABP* program (Annex I of the ISTI). Sections 3.3-3.6 are *Technical Documents* and Laboratory Guidelines intended for *Laboratory* or *ABP* Laboratory personnel that aim to harmonize the analysis of blood ABP, blood or urine *Samples* collected for the measurement of the *Markers* of the Hematological, Endocrine and Steroidal Modules of the *ABP*. Section 3.7 sets out the requirements and procedures that the Passport Custodian and its APMU shall follow for *Result Management* for the *ABP* (Annex C of the ISRM). Finally, Section 3.8 outlines the requirements and procedures for WADA-approved APMUs.

3.2. Collection, Storage and Transport of Blood Athlete Biological Passport Samples (ISTI Annex I)

I.1 Objective

To collect an *Athlete's* blood *Sample* by venipuncture, intended for use in connection with the measurement of individual *Athlete* blood variables within the framework of the hematological module of the *Athlete Biological Passport* program, in a manner appropriate for such use. The requirements of this Annex are additional requirements to those contained in Annex D - Collection of Venous Blood *Samples*.

I.2 Requirements

I.2.1 Planning shall consider the *Athlete*'*s* whereabouts information to ensure *Sample* collection does not occur within two (2) hours of the *Athlete*'*s* training, participation in *Competition* or other similar physical activity. If the *Athlete* has trained or competed less than two (2) hours before the time the *Athlete* has been notified of their selection, the DCO or other designated *Sample* Collection Personnel shall chaperone the *Athlete* until this two-hour period has elapsed.

I.2.2 If the *Sample* was collected within two (2) hours of training or *Competition*, the nature, duration and intensity of the exertion shall be recorded by the DCO to make this information available to the APMU.

I.2.3 Although a single blood *Sample* is sufficient within the framework of the hematological module of the *Athlete Biological Passport*, it is recommended to collect an additional (B) *Sample* for a possible subsequent analysis of *Prohibited Substances* and *Prohibited Methods* in whole blood (e.g., detection of homologous blood transfusion (HBT) and/or erythropoietin receptor agonists (ERAs)).

I.2.4 For *Out-of-Competition Testing*, A and B urine *Samples* should be collected together with the blood *Athlete Biological Passport Sample(s)* in order to permit Analytical *Testing* for ERAs unless otherwise justified by a specific intelligent *Testing* strategy.

[Comment to I.2.4: WADA's Guidelines for Sample Collection reflect these protocols and include practical information on the integration of Athlete Biological Passport Testing into "traditional" Testing activities. A table has been included within WADA's Guidelines for Sample Collection that identifies which particular timelines for delivery are appropriate when combining particular types of analysis (e.g, blood Athlete Biological Passport and growth hormone (GH), blood Athlete Biological Passport and HBT, etc.), and which types of Samples may be suited for simultaneous transport.]

I.2.5 The *Sample* shall be refrigerated from its collection until its analysis with the exception of when the *Sample* is analyzed immediately following collection. The storage procedure is the DCO's responsibility.

I.2.6 The storage and transport device shall be capable of maintaining blood *Athlete Biological Passport Samples* at a cool temperature during storage. Whole blood *Samples* shall not be allowed to freeze at any time. In choosing the storage and transport device, the DCO shall take into account the time of storage, the number of *Samples* to be stored in the device and the prevailing environmental conditions (hot or cold temperatures). The storage device shall be one of the following:

a) Refrigerator;

b) Insulated cool box;

c) Isotherm bag; or

d) Any other device that possesses the capabilities mentioned above.

I.2.7 A temperature data logger shall be used to record the temperature from the collection to the analysis of the *Sample* except when the *Sample* is analyzed immediately following collection. The temperature data logger shall be able to:

a) Record the temperature in degrees Celsius at least once per minute;

b) Record time in GMT;

c) Report the temperature profile over time in text format with one line per measurement following the format "YYYY-MM-DD HH:MM T"; and

d) Have a unique ID of at least six characters.

I.2.8 Following notification to the *Athlete* that they have been selected for Sample collection and following the DCO/BCO's explanation of the *Athlete's* rights and responsibilities in the *Sample* collection process, the DCO/BCO shall ask the *Athlete* to remain still, in an upright, stationary seated position, with feet on the floor for at least ten (10) minutes prior to providing a blood *Sample*. If the *Athlete's* feet cannot reach the floor and/or the *Athlete's* impairment does not allow feet on the floor, the *Athlete* shall remain in an upright, stationary seated position.

[Comment to I.2.8: The Athlete shall not stand up at any time during the ten (10) minutes prior to Sample collection. To have the Athlete seated during ten (10) minutes in a waiting room and then to call the Athlete into a blood collection room is not acceptable.]

I.2.9 The DCO/BCO shall collect and record the following additional information on an *Athlete Biological Passport* supplementary form, *Athlete Biological Passport* specific *Doping Control* form or other related report form to be signed by the *Athlete* and the DCO/BCO:

a) Has the *Athlete* been seated for at least ten (10) minutes with their feet on the floor prior to blood collection, as per Annex I.2.8?

b) Was the *Sample* collected immediately following at least three (3) consecutive days of an intensive endurance *Competition*, such as a stage race in cycling?

c) Has the *Athlete* had a training session or *Competition* in the two (2) hours prior to the blood collection?

d) Did the *Athlete* train, compete or reside at an altitude greater than 1,500 meters within the prior two (2) weeks? If so, or if in doubt, the name and location of the place where the *Athlete* had been, and the dates and the duration of their stay shall be recorded.

The estimated altitude shall be entered, if known.

e) Did the *Athlete* use any form of altitude simulation such as a hypoxic tent, mask, etc. during the prior two (2) weeks? If so, as much information as possible on the type of device and the manner in which it was used (e.g., frequency, duration, intensity) should be recorded.

f) Did the *Athlete* receive any blood transfusion(s) during the prior three (3) months? Was there any blood loss due to accident, pathology or donation in the prior three (3) months? If so, the estimated volume should be recorded.

g) Has the *Athlete* been exposed to any extreme environmental conditions during the last two (2) hours prior to blood collection, including any sessions in any artificial heat environment, such as a sauna? If so, the details should be recorded.

I.2.10 The DCO/BCO shall start the temperature data logger and place it in the storage device. It is important to start recording the temperature before *Sample* collection.

I.2.11 The storage device shall be located in the *Doping Control* Station and shall be kept secure.

I.2.12 The DCO/BCO instructs the *Athlete* to select the *Sample* Collection Equipment in accordance with Annex D.4.6 and continue the *Sample* Collection Session in accordance with Annex D.4.7.

I.3 The *Sample* Collection Procedure

I.3.1 The *Sample* collection procedure for the collection of blood for the purposes of the *Athlete Biological Passport* is consistent with the procedure set out in Annex D.4, including the ten (10) minute (or more) seated period.

I.3.2 The *Athlete* and the DCO/BCO sign the *Doping Control* and *Athlete Biological Passport* supplementary form(s), when applicable.

I.3.3 The blood *Sample* is sealed and deposited in the storage device containing the temperature data logger.

I.4 Transportation Requirements

I.4.1 Blood *Samples* shall be transported in a device that maintains the integrity of *Samples* over time, due to changes in external temperature.

I.4.2 The transport procedure is the DCO's responsibility. The transport device shall be transported by secure means using a *Sample* Collection Authority authorized transport method.

I.4.3 The integrity of the *Markers* used in the hematological module of the *Athlete Biological Passport* is guaranteed when the Blood Stability Score (BSS) remains below eighty-five (85), where the BSS is computed as:

BSS = 3 * T + CAT

with CAT being the Collection to Analysis Time (in hours), and T the average Temperature (in degrees Celsius) measured by the data logger between *Sample* collection and analysis.

I.4.4 Within the framework of the BSS, the following table can be used by the DCO/BCO to estimate the maximal transport time to a Laboratory or *ABP* Laboratory, called the Collection to Reception Time (CRT), for a given average temperature (T), e.g., if shipped at 4°C, the maximal CRT is 60 h.:

T [°C]	CRT [h]
15	27
12	36
10	42
9	45
8	48
7	51
6	54
5	57
4	60

I.4.5 The DCO/BCO shall as soon as possible transport the *Sample* to a Laboratory or *ABP* Laboratory.

I.4.6 The *Testing* Authority or *Sample* Collection Authority shall report without delay into *ADAMS*:

a) The *Doping Control* form, as per Article 4.9.1 b);

b) The *Athlete Biological Passport* supplementary form, and/or the additional information specific to the *Athlete Biological Passport* collected on a related report form;

c) In the Chain of Custody, the temperature data logger ID (without any time reference) and the time zone of the *Testing* location in GMT.

3.3. Analytical Requirement for the Hematological Module of the *Athlete Biological Passport*

***WADA Technical Document* – TD2021BAR**

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Written by: Reviewed by:	*WADA* Science *WADA* Laboratory Expert Group	Approved by:	*WADA* Executive Committee
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1.0 Introduction

The purpose of this *Technical Document* (*TD*) is to harmonize the analysis of *ABP* blood *Sample*s collected, both *In-Competition* and *Out-of-Competition*, for the measurement and reporting of individual *Athlete* blood *Markers* within the framework of the hematological module of the *Athlete Biological Passport* (*ABP*).

The *International Standard* for Laboratories (ISL) [1] is applicable to the analysis of *ABP* blood *Sample*s carried out in connection with the measurement of individual *Athlete* blood *Markers* within the framework of the *ABP*. This *TD* describes certain specificities of blood analysis related to the *ABP*.

In order to standardize analytical results in the *ABP*, *ABP* blood *Sample*s shall only be analyzed with analyzers of comparable technical characteristics in the dedicated network of laboratories (*i.e. WADA*-accredited laboratories or *ABP* Laboratories). The Analytical Method for measuring *ABP* blood variables shall be included within the Laboratory or *ABP* Laboratory's Scope of ISO/IEC (17025 or 15189) Accreditation, and the Laboratory or *ABP* Laboratory shall satisfactorily participate in the relevant *WADA* External Quality Assessment Scheme (EQAS), as determined by *WADA*, prior to applying the Analytical Method to *ABP* blood *Sample*s.

Sample handling shall be conducted in compliance with the *TD* on Laboratory Internal Chain of Custody (TD LCOC) [2].

If not reasonably possible for *ABP* blood *Sample*s to be analyzed in a Laboratory or *ABP* Laboratory for technical and/or geographical reasons, *ABP* blood *Sample*s can be analyzed at a satellite facility of a Laboratory or using mobile units operated by a Laboratory under their applicable ISO/IEC accreditation (17025 or 15189). Satellite facilities and mobile units shall also be ISO/IEC (17025 or 15189) accredited and participate in the *WADA* EQAS for blood *Markers* for the *ABP* prior to analysis of *ABP* blood *Sample*s.

2.0 *ABP* blood *Sample* Reception and Timing of Analysis

Upon reception at the Laboratory or *ABP* Laboratory, the *ABP* blood *Sample* shall be analyzed as soon as possible and no later than twelve (12) hours after reception unless the *Sample* Collection Authority (SCA) provides specific information regarding the *Sample* collection and transportation

conditions (for example, the SCA provides a projected time window for analysis during which the projected Blood Stability Score (BSS) should remain acceptable) that would allow the Laboratory or *ABP* Laboratory to analyze the *Sample* beyond twelve (12) hours after reception without compromising the *ABP* blood *Sample* validity.

In cases when the Laboratory or *ABP* Laboratory is unable to analyze the *ABP* blood *Sample* immediately after reception, the Laboratory or *ABP* Laboratory is responsible for maintaining the *ABP* blood *Sample(s)* at a cool temperature (approximately 4°C) between reception and the start of the analysis. The temperature data logger shall accompany the *ABP* blood *Sample(s)* until homogenization.

The *ABP* blood *Sample* shall not be aliquoted before the *ABP* analysis is satisfactorily conducted. Only after the analysis for the *ABP* has been satisfactorily completed may the Laboratory or *ABP* Laboratory aliquot the *ABP* blood *Sample* for the performance of other Analytical *Testing* Procedures (*e.g.* test for homologous blood transfusion, EPO and agents affecting erythropoiesis).

If there is a Laboratory or *ABP* Laboratory deviation from the aforementioned procedure, the Laboratory or *ABP* Laboratory shall proceed with the analysis and report the results into *ADAMS* with a detailed description of the deviation. If the *ABP* blood *Sample* cannot be analyzed, the Laboratory or *ABP* Laboratory shall report the *Sample* as “Not Analyzed” and provide a description of why it could not be analyzed in *ADAMS*.

3.0 Instrument Check

The Laboratory or *ABP* Laboratory shall maintain an instrument maintenance schedule to ensure proper performance; particularly if an analysis has not been recently conducted and the instrument remains idle for an extended period of time.

The analyst shall ensure that all reagents are within their expiration dates and comply with the reagent manufacturer’s recommendations before performing an analysis. Operational parameters of the instrument (background level, temperature of the incubation chambers, pressure, etc.) shall be verified as compliant with manufacturer’s specifications.

In each analysis session:

- All internal quality controls (QC levels 1, 2 and 3) shall be analyzed twice, following the specifications provided by the manufacturer, prior to the analysis of *Samples*.
- If more than 30 *Samples* are analyzed, at least one internal QC from the manufacturer (either level 1, 2 or 3) shall be analyzed in the middle of the analytical session, and every 30 - 50 *Samples* for larger batches.
- At the end of each analysis session and after all blood *Sample* analyses are completed, one internal QC (either level 1, 2 or 3) shall be analyzed once again to demonstrate the continuous stability of the instrument and the quality of the analyses done.

All results relevant to the *ABP* shall be in agreement with the reference value ranges of the manufacturer. These internal QCs shall be furnished exclusively by the instrument manufacturer and handled in strict accordance with the manufacturer specifications (*e.g.* expiration dates, storage

conditions). The analysis of internal QCs shall be monitored via QC-charts with appropriate control limits.

At least once a month, following the satisfactory analysis of all internal QCs (levels 1, 2 and 3) as described above, one fresh blood sample shall be homogenized for a minimum period of fifteen (15) minutes on an appropriate mixer (*e.g.* roller mixer). The fresh blood sample shall be analyzed at least seven (7) consecutive times under Repeatability conditions. The Repeatability of the determinations, expressed as coefficients of variation (CV %), shall be below 1.5% for Haemoglobin (HGB) and Haematocrit (HCT), and below 15% for Reticulocyte percentage (RET%).

[Comment: Samples from Athletes shall not be used as a fresh blood sample to conduct the Repeatability analysis.]

4.0 External Quality Assessment Scheme (EQAS)

The Laboratories or *ABP* Laboratories shall participate in and meet the requirements of *WADA's* EQAS for blood *Markers* for the *ABP*. *WADA's* EQAS program is the only EQAS relevant to the Laboratory's or *ABP* Laboratory's compliance with the requirements for the analysis of blood *Markers* within the framework of the hematological module of the *ABP* (in case of discrepancy with other blood EQAS programs).

All internal QCs (levels 1, 2 and 3) shall be analyzed twice following the specifications provided by the manufacturer prior to the analysis of EQAS samples. All results relevant to the *ABP* shall be in agreement with the reference value ranges of the manufacturer. The EQAS sample shall be homogenized for a minimum period of fifteen (15) minutes using an appropriate mixer (*e.g.* roller mixer) prior to analysis. The external QCs shall be analyzed multiple times consecutively (based on the EQAS rules), and the mean results of the following blood variables (full blood count) shall be returned:

Red Blood Cell (Erythrocyte) Count	RBC
Mean Corpuscular Volume	MCV
Haematocrit	HCT
Haemoglobin	HGB
Mean Corpuscular Haemoglobin	MCH
Mean Corpuscular Haemoglobin Concentration	MCHC
White Blood Cell (Leukocyte) Count	WBC
Platelet (Thrombocyte) Count	PLT
Reticulocytes Percentage	RET%

Laboratories or *ABP* Laboratories may also participate in ring tests with other laboratories (hospitals, clinics, etc.) using the same technology and the same procedure.

5.0 Analysis of *ABP* Blood *Samples*

5.1 Temperature Data Logger

The temperature data logger shall be stopped before *ABP* blood *Sample* homogenization, upon removal of the *ABP* blood *Sample(s)* from the cooling device or refrigerator. The *ABP* blood *Sample* shall be homogenized prior to analysis and for a minimum period of fifteen (15) minutes using an appropriate mixer (*e.g.* roller mixer).

In cases when the temperature data logger accompanies multiple *ABP* blood *Samples*, and these *ABP* blood *Samples* are analyzed in the same batch by the Laboratory or *ABP* Laboratory, the temperature data logger shall be stopped before the homogenization of the first *ABP* blood *Sample*. The Laboratory shall proceed with the analysis of all *ABP* blood *Samples* associated with the same temperature data logger without delay.

5.2 *ABP* Blood *Sample* Analysis

The *ABP* blood *Sample* shall be analyzed twice. The Laboratory's or *ABP* Laboratory's procedure should minimize the delay between the two analyses. Absolute differences between the two (2) analyses shall be equal or less than (≤) each of the following criteria in order to accept the results:

- 0.1 g/dL for HGB;
- 0.15% for RET% if either the first or second measurement is lower or equal to 1.00%; otherwise 0.25% absolute difference.

The data from the second injection is used to confirm the first injection data. Therefore, if the absolute differences between the results of the analyses are within the criteria above, then only the first injection data is reported into *ADAMS*.

If the absolute differences between the results of the two analyses are greater than (>) those defined above, then the *ABP* blood *Sample* shall be analyzed twice again in accordance with Article 5.2. In cases of repeated analysis, the *ABP* blood *Sample* shall be mixed prior to re-analysis using the automated mixing feature of the blood analyzer or by appropriate manual inversion. This reanalysis procedure shall be repeated until the absolute differences between the results of the two (2) most recent analyses are within the criteria specified above.

The requirements for an Initial *Testing* Procedure (ITP), an "A" *Sample* Confirmation Procedure (CP) and a "B" *Sample* CP, as defined in the ISL [1], shall not be applicable to *ABP* blood *Samples* analyzed for the purposes of the *ABP*.

6.0 Reporting

6.1 Temperature Report

The Laboratory or *ABP* Laboratory shall promptly submit into *ADAMS* the raw temperature profile report recorded by the temperature data logger. The filename shall consist in the concatenation of the data logger ID with the date of *Sample* reception by the Laboratory or *ABP* Laboratory ("YYYY-MM-DD" in local time) separated by an underscore. For example, for a data logger ID "KG34V10" and a

date of *Sample* reception "2015-03-25", the Laboratory or *ABP* Laboratory shall report the temperature profile under the filename "KG34V10_2015-03-25.txt". The Laboratory or *ABP* Laboratory shall report the temperature profile into *ADAMS* before the test results of the *Sample*, when temperature data can be retrieved from the logger.

[Comment: Where the Sample meets the requirements of the ISTI Annex I, Article I.2.7, and is analyzed at the Sample collection site without delay, a temperature data logger is not necessary and the Laboratory shall proceed to reporting the test results of the Sample.

In cases that the Laboratory is unable to upload a suitable temperature profile report from the temperature data logger into ADAMS, the Laboratory shall proceed to upload the test results of the relevant Sample(s).]

6.2 Reporting *ABP* Blood *Sample* Test Results

The Laboratory or *ABP* Laboratory should report the *ABP* blood *Sample* test results as soon as possible and within three (3) days after *Sample* reception. The following shall be reported into *ADAMS*:

- Status ("Submitted" or "Not Analyzed");
- *ABP* blood *Sample* code;
- Type of test (*Out-of-Competition* / *In-Competition*);
- Sport and discipline;
- Date and time of receipt of the *ABP* blood *Sample*;
- Date and time of analysis of the *ABP* blood *Sample*;
- The name of the *Testing* Authority;
- The name of the *Sample* Collection Authority;
- Type of *Sample* (blood Passport);
- Type of analyzer;
- Test results (other variables may be included for quality purposes):

Blood Variable		Unit(s)
Haemoglobin	HGB	g/dL
Hematocrit	HCT	%
Immature Reticulocyte Fraction	IRF	%
Mean Corpuscular Haemoglobin	MCH	pg
Mean Corpuscular Haemoglobin Concentration	MCHC	g/dL
Mean Corpuscular Volume	MCV	fL
OFF-Score	-	-
Platelets	PLT	$10^3/\mu L$
Red Blood Cell Distribution Width	RDW-SD	fL
Red Blood Cells	RBC	$10^6/\mu L$
Reticulocytes – in absolute number	RET	$10^6/\mu L$
Reticulocytes Percentage	RET%	%
White Blood Cells	WBC	$10^3/\mu L$

- Include a comment describing any relevant deviation as part of the *ABP* blood *Sample*'s *ADAMS* record.

7.0 References

[1] The World Anti-Doping *Code International Standard* for Laboratories (ISL).

[2] *WADA Technical Document* TD LCOC: Laboratory Internal Chain of Custody.

[Comment: Current versions of WADA ISL and Technical Documents may be found at https://www.wada-ama.org/en/what-we-do/science-medical/laboratories]

3.4. Laboratory Guidelines – Analytical Requirements for the Endocrine Module of the *Athlete Biological Passport*

1.0 Objective

These Laboratory Guidelines have been developed to ensure a harmonized application of Analytical *Testing* Procedures for the measurement of *Markers* of human Growth Hormone (hGH) as part of the Endocrine Module of the *Athlete Biological Passport* (*ABP*). The document provides guidance on the pre-analytical details, *Sample* preparation procedure, the performance of the analyses and the reporting of the test results.

2.0 Scope

These Laboratory Guidelines contain requirements for the implementation of the Analytical *Testing* Procedures for the quantification of hGH *Markers* as part of the Endocrine Module of the *ABP*, which allows the detection of hGH doping and may also have utility in detecting GH secretagogues and IGF-I abuse in sport [1,2]. These Laboratory Guidelines follow the rules established in the *WADA International Standard for* Laboratories (ISL) [3] and relevant *Technical Documents* (*TDs*) regarding the Analytical *Testing* of blood *Samples*.

3.0 Introduction to the Analytical *Testing* Procedures

The Analytical *Testing* Procedures for the Endocrine Module involve the measurement of two (2) *Markers* of hGH biological activity, namely Insulin-like Growth Factor-I (IGF-I) and N-terminal Pro-peptide of Type III Collagen (P-III-NP), which are naturally present in blood and whose concentrations are increased following hGH administration [4–11]. The measured concentrations of these two (2) *Markers* are then combined in a discriminant function formulae to calculate a GH-2000 score, which is gender-specific and includes an adjustment for age to reflect the age-related decline in hGH and *Marker* concentrations [4].

In order to generate individual *Athlete* longitudinal data that are comparable between Laboratories, a specific IGF-I / P-III-NP assay pairing is applied for the measurement of concentrations of IGF-I and P-III-NP in blood (serum) for the purposes of the *ABP*. The assays used for the Endocrine Module of the *ABP* are limited to:

- Intact IGF-I quantification by top-down Liquid Chromatography-(tandem) Mass Spectrometry (LC-MS^n; $n \geq 1$) [12], as detailed in Table 2 below.
- P-III-NP quantification using Siemens ADVIA Centaur P-III-NP chemiluminescence immunoassay (Siemens Healthcare Laboratory Diagnostics, Camberley, UK). The Siemens ADVIA Centaur P-III-NP assay is an automated, two-site sandwich, chemiluminescent

immunoassay [13]. The assay uses two (2) monoclonal mouse antibodies: the first antibody is an acridinium ester-labeled anti-P-III-NP antibody. The second antibody is a biotin-labeled anti-P-III-NP antibody. The solid phase contains streptavidin-coated paramagnetic particles and during the reaction, the light emitted by the acridinium label is directly proportional to the concentration of P-III-NP in the sample. The Siemens P-III-NP assay is calibrated by the manufacturer using a standard derived from bovine P-III-NP.

For the purposes of the *ABP*, an initial quantification of the "A" *Sample* is performed. When requested, a confirmatory quantification of the "A" *Sample* may additionally be performed using the same assay pairing (see, Article 6.2) to confirm the concentrations and to perform identification of IGF-I (as per TD IDCR[14]).

The concentrations of IGF-I and P-III-NP reported by the Laboratories, as well as the GH-2000 score automatically calculated in *ADAMS*, are integrated in the Endocrine Module of *ADAMS* using a similar Bayesian approach to that applied in the Steroidal and Hematological Modules of the *ABP* [15].

4.0 Assay Pre-Analytical Procedure

- The Laboratory should (usually) receive refrigerated (not frozen[i]) "A" and "B" blood *Samples*, which have been collected in blood tubes containing an inert polymeric serum separator gel and a clotting activation factor (for example: BD Vacutainer® SST™-II Plus tubes, EU ref 367955; BD Vacutainer® SST™-II Plus Advance tubes, EU ref 367954; BD Vacutainer® SST™ tubes, US ref 367986) in accordance with the *International Standard* for *Testing* and Investigation (ISTI) [16];

  [Comment: Previous studies have demonstrated that IGF-I and P-III-NP concentrations remain stable if the Sample is maintained at a refrigerated temperature for up to 5 days [17].]

- Alternatively, if the clotting and centrifugation of the *Sample* is performed prior to reception at the Laboratory (for example, at the site of *Sample* collection), *Samples* may be received at the Laboratory as frozen/refrigerated blood *Samples* either in the same *Sample* collection tubes or as separated serum in new tubes;

- The Laboratory shall check the status of the *Sample(s)* (*e.g.,* evidence of hemolysis) and the integrity of the collection tubes (*e.g.,* evidence of breakage of the separating gel). The Laboratory shall note any unusual condition of the *Sample* and record such condition(s) in the Test Report in *ADAMS*;

- Any *Samples* delivered to the Laboratory in tubes containing an anti-coagulant (for example, *ABP* blood *Samples* collected in EDTA tubes), or as separated plasma, shall not be analyzed for *Markers* of the Endocrine Module;

[i] unless the blood matrix components have been separated before shipment to the Laboratory.

- The Laboratory shall notify and seek advice from the *Testing* Authority regarding rejection or Analytical *Testing* of *Samples* for which irregularities are noted (see ISL [3]).

4.1 *Samples* received as non-separated blood in tubes containing an inert polymeric serum separator gel and a clotting activation factor:

Reception	Both *Samples* "A" and "B" shall be centrifuged for 10-15 min at 1300-1500 g as soon as possible after reception at the Laboratory. The "A" *Sample* shall be used for the initial and confirmatory (if needed) quantifications (see below). The "B" *Sample* shall be step-frozen and stored until use, if needed (see below).
Aliquoting and analysis	Two (2) Aliquots of the "A" *Sample* serum shall be taken for initial quantification. The remaining "A" serum fraction may be kept in the *Sample* collection tube or aliquoted into new vials with label(s) ensuring that Laboratory Internal Chain of Custody is maintained. For initial quantification: • the Aliquots may be analyzed immediately after aliquoting; or • the Aliquots shall be stored at approximately 4 °C if analyzed within 24h (within a maximum of five (5) days from *Sample* collection); or • the Aliquots shall be frozen (-20°C) if the analysis will be conducted more than 24h after aliquoting. For the confirmatory quantification, two (2) new Aliquots of the "A" *Sample* shall be analyzed immediately after aliquoting. *[Comment: When analyses specific to the ABP are requested for blood (serum) Samples (i.e., Markers of the Endocrine Module or blood steroid Markers as part of the Steroidal Module), only the "A" Sample should be considered for the initial and the confirmatory quantifications of the Markers. In cases where the "A" Sample is not suitable for the performance of ABP Markers quantification (e.g., there is insufficient Sample volume; the Sample container has not been properly sealed or has been broken; the Sample's integrity has been compromised in any way; the "A" Sample is missing), a splitting procedure of the "B" Sample could be performed, as detailed in the ISL[3].]*
Storage [The same storage conditions apply for *Samples* received in conditions described in section 4.2]	Storage for up to three (3) months → at approximately -20 °C. Storage for more than three (3) months → freeze at approximately -20 °C and transfer to approximately -70 to -80 °C. *[Comment: If the separated serum fraction is kept in the Sample collection tube, it shall be step-frozen for storage according to the tube manufacturer's instructions until analysis.* *If the Laboratory transfers the Aliquot into new vials for frozen storage, the vials should ensure proper sealing for optimal storage (cryovials with an "O-ring").* *Thawing of Sample(s) for analysis should also be done stepwise. Samples shall not be thawed under hot water or any other similar process that risks raising the temperature of the Sample above room temperature. Thawing overnight at 4°C is recommended.]*

4.2 *Samples* received as frozen/refrigerated centrifuged blood/serum *Samples*:

Reception	If *Samples* are received frozen, they should remain frozen until analysis as described in this Article 4.2. If *Samples* are received refrigerated, they should be processed as soon as possible as per Article 4.1.

Aliquoting and analysis	Once the *Sample* "A" is thawed, two (2) Aliquots shall be taken for initial quantification. These Aliquots may be stored at approximately 4 °C for a maximum of 24h before analysis. The remaining "A" serum fraction may be kept in the *Sample* collection tube or aliquoted into new vial(s) with label(s) ensuring Laboratory Internal Chain of Custody is maintained. For the confirmatory quantification, two (2) new Aliquots of the "A" *Sample* shall be analyzed immediately after aliquoting.

5.0 *Analytical Testing Procedure* Requirements

5.1 Analytical *Testing* Procedure Validation Requirements

Prior to the implementation of the Analytical *Testing* Procedures for the quantification of IGF-I and P-III-NP in routine *Doping Control* analysis, the Laboratory shall fulfil the following requisites:

- Validate the Analytical *Testing* Procedures, including the determination of the assays' Limit of Quantification (LOQ), Repeatability (s_r), Intermediate Precision (s_w), Bias and Measurement Uncertainty (u_c);
- The Analytical *Testing* Procedures shall meet the acceptance values for the parameters of IGF-I and P-III-NP assay performance, as specified in Table 1 and Table 2 (as applicable).

Table 1: Acceptance Criteria for Parameters of Assay Performance for the Endocrine Module

Validation Parameters	IGF-I	P-III-NP
Maximum LOQ	≤ 50 ng/mL	≤ 1 ng/mL
Maximum Relative Combined Standard Measurement Uncertainty (u_{c_Max}, %)	≤ 20%	≤ 15%

5.2 Analytical *Testing* Procedure Accreditation Requirements

- Demonstrate readiness for assay implementation through method validation data and successful participation in at least one *WADA*-approved educational External Quality Assessment Scheme (EQAS) round or inter-Laboratory collaborative study. In cases of identified deficiencies, proper corrective action(s) shall be documented and implemented;
- Obtain ISO/IEC 17025 accreditation for the Analytical *Testing* Procedures for the quantification of hGH *Markers* in blood as part of the Endocrine Module from an Accreditation Body that is a full member of the International Laboratory Accreditation Cooperation (ILAC) and a signatory to the ILAC Mutual Recognition Agreement (ILAC MRA).

5.3 Quality Controls (QCs) and Reagents

- QC samples: Laboratories shall implement well-characterized and stable internal QC sample(s), which are not subject to assay lot variations, for the performance of the tests under different assay conditions (different assay lots, different analysts, *etc*.). Following preparation/reception by the Laboratory, all QC material should be aliquoted and stored frozen (preferably at – 80°C for long-term storage) until use. These QC samples should include:
    - QC_{low}: Serum obtained from healthy individual(s), which is demonstrated to contain concentrations of IGF-I not greater than (≤) 200 ng/mL and P-III-NP not greater than (≤) 5 ng/mL;
    - QC_{high}: Serum obtained from hGH administration studies or another appropriate source that has been demonstrated to contain concentrations of IGF-I greater than (≥) 500 ng/mL and P-III-NP greater than (≥) 10 ng/mL.

  [Comment: Four (4) separate QC samples may also be used, as long as they contain IGF-I and P-III-NP at the necessary concentrations (e.g., $QC_{IGF\text{-}I\_low}$, $QC_{IGF\text{-}I\_high}$, QC_{PIIINP_low} and QC_{PIIINP_high}).]
- Reagents: With every new batch of reagents (new lot number), the following evaluation steps should be implemented before including the new batch into routine operations for P-III-NP quantification:
    - Each of the QC samples shall be determined at least three (3) times whenever a new batch of reagents is obtained. The number of replicates per determination shall be conducted as stipulated by the assay manufacturers. The QCs may be measured in a single assay or over a range of assays. If, for any QC, the difference between the mean concentration for the new batch and that for the preceding batch is more than 20%, the new batch shall not be implemented into routine operations and an investigation of the new batch shall be conducted.
    - In order to detect small but systematic changes over time, it is recommended that the performance of a new batch of reagents is controlled, for example, through a cumulative sum (CUSUM) chart/table, which is established for each QC based on the difference between the mean(s) of the new batch and the initial value(s). When using the CUSUM, results should be assessed using customary procedures as detailed at *http://itl.nist.gov/div898/handbook/pmc/section3/pmc323.htm*

6.0 Analytical *Testing* Procedure and Reporting of Test Results

6.1 Initial Quantification of the *Markers*

- Two (2) Aliquots taken from the original "A" *Sample* shall be analyzed once (x1) to quantify intact IGF-I and P-III-NP;

- QC Sample(s), at low- and high-levels of the *Marker*s (see Article 5.3), shall be included in each initial quantification analytical batch;
- The coefficient of variation (CV%) between the duplicate determinations of the IGF-I and P-III-NP concentrations shall not be higher (≤) than the associated u_{c_Max} (see Table 1). If the CV% between duplicate determinations of only one *Marker* (IGF-I or P-III-NP) exceeds the respective u_{c_Max}, the analysis of only that *Marker* shall be repeated;
- The mean *Marker* concentration from the duplicate measurement of IGF-I and P-III-NP shall be reported in *ADAMS* in nanograms per milliliter (ng/mL);

  [Comment: for the purposes of the Endocrine Module of the ABP, the GH-2000 score does not need to be calculated or reported by the Laboratory since it will be automatically calculated in ADAMS [15]*].*
- If the measured *Marker* concentration is below the LOQ of the assay, the Laboratory shall report a value of "-1" for its concentration in *ADAMS* and the Laboratory shall make a comment in the Test Report on why the *Marker* could not be quantified (e.g., the measurement of the *Marker* is not possible due to unusual matrix interferences);
- An observation of hemolysis of the *Sample* should be recorded in the comments section of the Laboratory Test Report in *ADAMS*.

6.2 Confirmatory Quantification of the *Markers*

If requested by the *Testing* Authority (TA), *Results Management* Authority (RMA) or *WADA*, the Laboratory shall proceed with the confirmatory quantification of the *Markers* of the Endocrine Module.

[Comment: An APMU or Passport Custodian (PC), where the PC is not the TA, may request a confirmatory quantification on behalf of the TA or RMA. In such cases, the APMU or PC shall copy the relevant TA or RMA, as applicable, on all written requests to the Laboratory for confirmatory quantifications.]

When a confirmatory quantification analysis is requested:

- Two (2) new Aliquots taken from the original "A" *Sample* shall be analyzed once (x1) to:
  - quantify intact IGF-I and P-III-NP; and
  - identify IGF-I (as per the TD IDCR [14]);
- At least one QC Sample (see Article 5.3), depending on initial quantification results, shall be included in each confirmatory quantification analytical batch;
- The CV (%) between the duplicate determinations of the IGF-I or P-III-NP concentrations shall not be higher (≤) than the associated u_{c_Max} (see Table 1). If the CV% between duplicate determinations of only one *Marker* (IGF-I or P-III-NP) exceeds the respective u_{c_Max}, the analysis of only that *Marker* shall be repeated;

- The mean *Marker* concentration from the duplicate measurement of IGF-I and P-III-NP shall be reported in *ADAMS* in nanograms per milliliters (ng/mL);
- If the measured *Marker* concentration is below the LOQ of the assay, the Laboratory shall report a value of "-1" for its concentration in *ADAMS* and the Laboratory shall make a comment in the Test Report on why the *Marker* could not be quantified (e.g., the measurement of the *Marker* is not possible due to unusual matrix interferences);
- An observation of hemolysis of the *Sample* should be recorded in the comments section of the Laboratory Test Report in *ADAMS*.

Table 2. Analytical *Testing* Procedure Validation and Performance Requirements for the initial and confirmatory quantification of IGF-I in blood (serum) *Samples* by top-down LC-MS^n for the Endocrine Module of the *ABP*.

Method and Instrumentation	Top-down (intact IGF-I) Liquid Chromatography combined with (Tandem) Mass Spectrometry based on triple quadrupole or HRMS (LC-MS^n; n ≥ 1).
Range of the Method	Shall cover the ranges of IGF-I concentrations normally found in males and females and demonstrate linearity between **50–1000 ng/mL**, at least.
Limit of Quantification (LOQ)	The LOQ shall not be greater than (≤) **50 ng/mL**.
Maximum Relative Combined Standard Measurement Uncertainty u_c (%)	The estimated u_c (%) shall not be greater than (≤) **20%**.
Sample	IGF-I quantification shall be conducted in duplicate (using two Aliquots of the "A" *Sample*) using a volume not greater than (≤) **50 µL** of serum per replicate.
Internal Standard	Stable isotope-labeled IGF-I (*e.g.,* NIST[ii] or ProSpec[iii] ^{15}N-IGF-I).
Calibration	A freshly prepared single point calibrator (SPC) shall be included in each analytical batch. The Recombinant Human IGF-I calibrator from NIST (SRM 2926[iv]) should be used to prepare the SPC. Any other calibration material shall be validated against the NIST SRM 2926 calibrator.

Applicable links

[ii] https://shop.nist.gov/ccrz__ProductDetails?sku=2927&cclcl=en_US

[iii] https://www.prospecbio.com/igf1_n15_human

[iv] https://shop.nist.gov/ccrz__ProductDetails?sku=2926&cclcl=en_US

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3.5. Laboratory Guidelines - Quantification of Endogenous Steroids in Blood for the *Athlete Biological Passport*

1.0 Objective

These Laboratory Guidelines have been developed to ensure a harmonized application of the Analytical *Testing* Procedure for the quantification of endogenous steroid *Markers* measured in blood (serum) as part of the Steroidal Module of the *Athlete Biological Passport* (*ABP*). The document provides guidance on the pre-analytical details, *Sample* preparation procedure, the performance of the analyses and the reporting of the test results.

2.0 Scope

These Laboratory Guidelines contain requirements for the implementation of the Analytical *Testing* Procedure for the quantification of endogenous *steroid Markers* in blood (serum) as part of the Steroidal Module of the *ABP* to uncover use of endogenous anabolic androgenic steroids (EAAS) administered exogenously. These Laboratory Guidelines follow the rules established in the *WADA International Standard for* Laboratories (ISL) [1] and relevant *Technical Documents* (*TDs*) regarding the Analytical *Testing* of blood *Samples*.

3.0 Introduction to the Analytical *Testing* Procedure

The Analytical *Testing* Procedure involves the measurement of two (2) *Markers*, namely Testosterone (T) and Androstenedione (Androst-4-ene-3,17-dione, A4), which are naturally present in blood, and the calculation of the T/A4 ratio. While the endogenous levels of these *Markers* are gender-specific, they have been identified as relevant target Analytes to detect T abuse with an increased sensitivity in female *Athletes* [2,3], as well as the transdermal application of T-related drugs in both genders [4–6].

The quantification of T and A4 concentrations is based on Liquid Chromatography (LC) combined with tandem Mass Spectrometry ($LC\text{-}MS^n$; $n \geq 1$). For the purposes of the *ABP*, an initial quantification from the "A" *Sample* is performed. When requested, a confirmatory quantification of the "A" *Sample* may additionally be performed (see Article 6.2) to confirm the concentrations and to perform identification of the *Markers* (as per TD IDCR[7]).

The concentrations of T and A4 in blood reported by the Laboratories are integrated in the Steroidal Module of *ADAMS*, using a similar Bayesian approach to that applied in the other Steroidal (urine), Hematological and Endocrine Modules of the *ABP*.

4.0 Assay Pre-analytical Procedure

- The Laboratory should (usually) receive refrigerated (not frozen[i]) "A" and "B" blood *Samples*, which have been collected in blood tubes containing an inert polymeric serum separator gel and a clotting activation factor (for example: BD Vacutainer® SST™-II Plus tubes, EU ref 367955; BD Vacutainer® SST™-II Plus Advance tubes, EU ref 367954; BD Vacutainer® SST™ tubes, US ref 367986) in accordance with the *International Standard* for *Testing* and Investigation (ISTI) [7];
- Alternatively, if the clotting and centrifugation of the *Sample* is performed prior to reception at the Laboratory (for example, at the site of *Sample* collection), *Samples* may be received at the Laboratory as frozen/refrigerated blood *Samples* either in the same *Sample* collection tubes or as separated serum in new tubes;
- The Laboratory shall check the status of the *Sample(s)* (*e.g.,* evidence of hemolysis) and the integrity of the collection tubes (*e.g.,* evidence of breakage of the separating gel). The Laboratory shall note any unusual condition of the *Sample* and record such condition(s) in the Test Report in *ADAMS*;
- Any *Samples* delivered to the Laboratory in tubes containing an anti-coagulant (for example, *ABP* blood *Samples* collected in EDTA tubes), or as separated plasma, shall not be analyzed for *Markers* of the Endocrine Module;
- The Laboratory shall notify and seek advice from the *Testing* Authority regarding rejection or Analytical *Testing* of *Samples* for which irregularities are noted (see ISL [1]).

4.1 *Samples* received as non-separated blood in tubes containing an inert polymeric serum separator gel and a clotting activation factor:

Reception	Both *Samples* "A" and "B" shall be centrifuged for 10-15 min at 1300-1500 g as soon as possible after reception at the Laboratory. The "A" *Sample* shall be used for the initial and confirmatory (if needed) quantifications (see below). The "B" *Sample* shall be step-frozen and stored until use, if needed (see below).
Aliquoting and analysis	An Aliquot of the "A" *Sample* serum shall be taken for initial quantification. The remaining "A" serum fraction may be kept in the *Sample* collection tube or aliquoted into new vials with label(s) ensuring that Laboratory Internal Chain of Custody is maintained.

[i] unless the blood matrix components have been separated before shipment to the Laboratory.

	For initial quantification: • the Aliquot may be analyzed immediately after aliquoting; or • the Aliquot shall be stored at approximately 4 °C°C if analyzed within 24h (within a maximum of five (5) days from *Sample* collection); or • the Aliquot shall be frozen (-20°C) if the analysis will be conducted more than 24h after aliquoting. For the confirmatory quantification, a new Aliquot of the "A" *Sample* shall be analyzed immediately after aliquoting. *[Comment: When analyses specific to the ABP are requested for blood (serum) Samples (i.e., Markers of the Endocrine Module or blood steroid Markers as part of the Steroidal Module), only the "A" Sample should be considered for the initial and the confirmatory quantifications of the Markers. In cases where the "A" Sample is not suitable for the performance of ABP Markers quantification (e.g., there is insufficient Sample volume; the Sample container has not been properly sealed or has been broken; the Sample's integrity has been compromised in any way; the "A" Sample is missing), a splitting procedure of the "B" Sample could be performed, as detailed in the ISL[1].]*
Storage [The same storage conditions apply for *Samples* received in conditions described in section 4.2]	Storage for up to three (3) months → at approximately -20 °C. Storage for more than three (3) months → freeze at approximately -20 °C and transfer to approximately -70 to -80 °C. *[Comment: If the separated serum fraction is kept in the Sample collection tube, it shall be step-frozen for storage according to the tube manufacturer's instructions until analysis.* *If the Laboratory transfers the Aliquot into new vials for frozen storage, the vials should ensure proper sealing for optimal storage (cryovials with an "O-ring").* *Thawing of Sample(s) for analysis should also be done stepwise. Samples shall not be thawed under hot water or any other similar process that risks raising the temperature of the Sample above room temperature. Thawing overnight at 4°C is recommended.]*

4.2 *Samples* received as frozen/refrigerated centrifuged blood/serum *Samples*:

Reception	If *Samples* are received frozen, they should remain frozen until analysis as described in this Article 4.2. If *Samples* are received refrigerated, they should be processed as soon as possible as per Article 4.1.
Aliquoting and analysis	Once the *Sample* "A" is thawed, an Aliquot shall be taken for initial quantification. This Aliquot may be stored at approximately 4 °C for a maximum of 24h before analysis. The remaining "A" serum fraction may be kept in the *Sample* collection tube or aliquoted into new vial(s) with label(s) ensuring Laboratory Internal Chain of Custody is maintained. For the confirmatory quantification, a new Aliquot of the "A" *Sample* shall be analyzed immediately after aliquoting.

5.0 Analytical *Testing* Procedure Requirements

5.1 Analytical *Testing* Procedure Validation Requirements

Prior to the implementation of the Analytical *Testing* Procedure for the quantification of blood endogenous steroids in routine *Doping Control* analysis, the Laboratory shall fulfil the following requisites:

- Validate the Analytical *Testing* Procedure, including the determination of the assays' Limit of Quantification (LOQ), Repeatability (s_r), Intermediate Precision (s_w), Bias and Measurement Uncertainty (u_c);
- The Analytical *Testing* Procedure shall meet the acceptance values for the parameters of assay performance applicable to the separate determination of T and A4 concentrations as specified in Table 1 below.

5.2 Analytical *Testing* Procedure Accreditation Requirements

- Demonstrate readiness for assay implementation through method validation data and successful participation in at least one *WADA*-approved educational External Quality Assessment Scheme (EQAS) round or inter-Laboratory collaborative study. In cases of identified deficiencies, proper corrective action(s) shall be documented and implemented;
- Obtain ISO/IEC 17025 accreditation for the Analytical *Testing* Procedure for quantification of endogenous steroids in blood from an Accreditation Body that is a full member of the International Laboratory Accreditation Cooperation (ILAC) and a signatory to the ILAC Mutual Recognition Agreement (ILAC MRA).

6.0 Analytical *Testing* Procedure and Reporting of Test Results

6.1 Initial Quantification of the *Markers*

- One (1) Aliquot taken from the original "A" *Sample* shall be analyzed once (x1) to quantify T and A4;
- QC Sample(s), at low- and high-levels of the *Marker*s (see Table 1), shall be included in each initial quantification analytical batch;
- The T and A4 *Marker* concentrations shall be reported in *ADAMS* in nanograms per milliliter (ng/mL);

  [Comment: for the purposes of the Steroidal Module of the ABP, the T/A4 ratio does not need to be calculated or reported by the Laboratory; it will be automatically calculated in ADAMS].
- If the measured *Marker* concentration is below the LOQ of the assay, the Laboratory shall report a value of "-1" for its concentration in *ADAMS* and the Laboratory shall make a comment in the Test Report on why the *Marker* could not be quantified (e.g., the measurement of the *Marker* is not possible due to unusual matrix interferences);
- An observation of hemolysis of the *Sample* should be recorded in the comments section of the Laboratory Test Report in *ADAMS*.

6.2 Confirmatory Quantification of the *Markers*

If requested by the *Testing* Authority (TA), *Results Management* Authority (RMA) or *WADA*, the Laboratory shall proceed with the confirmatory quantification of the *Markers* of the blood Steroidal Module.

[Comment: An APMU or Passport Custodian (PC), where the PC is not the TA, may request a confirmatory quantification on behalf of the TA or RMA. In such cases, the APMU or PC shall copy the relevant TA or RMA, as applicable, on all written requests to the Laboratory for confirmatory quantification.]

When a confirmatory quantification analysis is requested:

- One (1) new Aliquot taken from the original "A" *Sample* shall be analyzed once (x1) to identify (as per the TD IDCR [8]) and to quantify T and A4.
- At least one QC Sample (see Table 1), depending on initial quantification results, shall be included in each confirmatory quantification analytical batch;
- The T and A4 *Marker* concentrations shall be reported in *ADAMS* in nanograms per milliliter (ng/mL).
- If the measured *Marker* concentration is below the LOQ of the assay, the Laboratory shall report a value of "-1" for its concentration in *ADAMS* and the Laboratory shall make a comment in the Test Report on why the *Marker* could not be quantified (e.g., the measurement of the *Marker* is not possible due to unusual matrix interferences);
- An observation of hemolysis of the *Sample* should be recorded in the comments section of the Laboratory Test Report in *ADAMS*.

Table 1: Analytical *Testing* Procedure Validation and Performance Requirements for the initial and confirmatory quantification of blood (serum) endogenous steroid *Markers*.

Markers	**Testosterone (T)**, total unconjugated fraction **Androstenedione** (Androst-4-ene-3,17-dione, **A4**), total unconjugated fraction
Method and Instrumentation	Liquid Chromatography combined with tandem Mass Spectrometry based on triple quadrupole or HRMS analyzer (LC-MS^n; n ≥ 1).
Range of the Method	Shall cover the ranges of *Marker* concentrations normally found in males and females and demonstrate linearity between **0.1 – 10 ng/mL (~ 0.35 – 35 nmol/L)**, at least.
Limits of Quantification (LOQ)	The LOQ shall be determined during method validation and is defined as the lowest concentration with an associated u_c (%) not greater than (≤) 30% and shall be not greater than (≤) **0.1 ng/mL (~ 0.35 nmol/L)**.
Relative Standard Combined Measurement Uncertainty, u_c (%)	The estimated u_c (%) shall be no greater than (≤) **30%** at the LOQ; and not greater than (≤) **20%** when the *Marker* concentration is greater than (>) 0.3 ng/mL.
Sample	*Marker* quantification shall be conducted on one serum Aliquot of no greater than (≤) **100 µL**.
Internal Standards	Adequate isotopic-labelled internal standards shall be used for both *Markers* (*e.g.,* Testosterone-d3 (16,16,17-d3)[ii] and Androstenedione-d3 (19-d3)[iii]).
Calibration	Calibration standard(s) shall be included in each sequence of analysis. The "*Multilevel Serum Calibrator Set*" from Chromsystem[iv] is recommended. Other calibrators may be used as long as the method performance criteria are met.
Quality Control	At least two (2) quality control (QC) samples in serum containing representative low (*e.g*., 0.5 ng/mL) and high (*e.g.,* 5 ng/mL) concentrations of the *Markers* shall be included in each analytical batch. The QCs should be prepared from authentic samples, or by spiking with a standard solution independent from that used for the calibrator(s).

Applicable links:

[ii] https://www.lipomed-usa.com/en/testosterone-d3, for example.

[iii] https://www.lgcstandards.com/US/en/Androstenedione-d3/p/TRC-A637552-1MG, for example.

[iv] https://chromsystems.com/en/6plus1r-multilevel-serum-calibrator-set-masschromr-steroid-panel-2-72039.html

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3.6. Measurement and Reporting of Endogenous Anabolic Androgenic Steroid (EAAS) *Markers* of the Urinary Steroid Profile

***WADA Technical Document* – TD2021EAAS**

Document Number:	TD2021EAAS	Version Number:	2.0
Written by: Reviewed by:	*WADA* Science/EAAS Working Group *WADA* Laboratory Expert Group	Approved by:	*WADA* Executive Committee
Date:	20 May 2021	Effective Date:	1 June 2021

1.0 Introduction

The purpose of this *Technical Document* (*TD*) is to harmonize the measurement and reporting of the "steroid profile" of urine *Samples* in support of the steroidal module of the *Athlete Biological Passport* (*ABP*) (the steroidal Passport).

1.1 The Steroid Profile

The measurement of steroidal *Markers* [concentrations and ratios of defined Endogenous Anabolic Androgenic Steroids (EAAS)] in a urine *Sample* form the steroid profile for that *Sample* (see Table 1).

The steroid profiles of a series of urine *Samples* collected from an *Athlete* over a period of time constitute the steroidal Passport of that *Athlete*.

The administration of synthetic forms of EAAS can alter one or more of the *Markers* of the urinary steroid profile, resulting in increased or decreased concentrations and/or ratios of specific pairs of steroid *Markers* [1-3]. This effect forms the basis for the use of the steroidal Passport as a tool for the detection of doping with EAAS, in particular testosterone (T), its precursors (for example, 4-androstenediol, androstenedione and prasterone), its active *Metabolite* [dihydrotestosterone (DHT)], or its epimer epitestosterone (E).

The steroidal module of the *ABP* utilizes the Adaptive Model in *ADAMS* to trigger *Atypical Passport Findings* (*ATPFs*), which can lead to the performance of Confirmation Procedures (CP), *Target Testing* of an *Athlete*, or to establish *Use* of a *Prohibited Substance* and/or *Prohibited Method* as per *Code* Article 2.2 (see *International Standard* for *Results Management*, Annex C [4]).

1.2 Procedure for Determination of the Steroid Profile

Each urine *Sample* shall be analyzed to determine its steroid profile. The determination and reporting of a *Sample*'s steroid profile follows a two-step procedure:

i. An Initial *Testing* Procedure (ITP) is conducted to estimate the steroid profile of the *Sample*, and

ii. A subsequent CP is performed when the reported steroid profile constitutes an *ATPF*, as determined by the Adaptive Model, or upon request from the *Athlete* Passport Management Unit (APMU), the *Testing* Authority or *WADA*.

Table 1. *Markers* of the Urinary Steroid Profile.

Type of *Marker*	Steroid Profile *Markers*	Determination
Concentrations of Steroids	- Androsterone (A); - Etiocholanolone (Etio); - 5α-Androstane-3α,17β-diol (5αAdiol); - 5β-Androstane-3α,17β-diol (5βAdiol); - Testosterone (T); and - Epitestosterone (E).	Determined by the Laboratory by GC-MS^n from the combination of the free steroid fraction and the conjugated fraction released after hydrolysis with β-glucuronidase from *E. coli*.
Ratios of Steroids	- T/E	As reported by the Laboratory in *ADAMS.*
	- A/T; - A/Etio; - 5αAdiol/5βAdiol; and - 5αAdiol/E	Automatically computed in *ADAMS* from respective steroid concentrations after the reporting of the steroid profile by the Laboratory.

1.3 Factors Impacting the Steroid Profile

In addition to the effects mediated by the administration of EAAS, alteration of the urinary steroid profile can occur for a number of other reasons including, but not limited to, the following factors [1-3]:

- Intake of alcohol (ethanol);
- The administration of other anabolic androgenic steroids (*e.g.* stanozolol);
- The administration of human chorionic gonadotrophin (hCG) in males;
- The administration of aromatase inhibitors and anti-estrogenic substances;
- The administration of inhibitors of 5α-reductase (*e.g.* finasteride, dutasteride);
- The administration of ketoconazole or other similar compounds (*e.g.* fluconazole, miconazole);
- The use of masking agents (*e.g.* probenecid) and diuretics;
- Microbial activity;
- *Sample* manipulation.

2.0 Initial *Testing* Procedure (ITP)

2.1 ITP Method Requirements

The quantification of the *Markers* of the steroid profile shall be based on gas chromatography combined with mass spectrometry (GC-MS^n; $n \geq 1$).

Table 2. Requirements of the ITP for Quantification of the *Markers* of the Steroid Profile.

<table>
<tr><td colspan="8">2.1.1 ITP Validation Requirements</td></tr>
<tr><td>Range of the Method</td><td colspan="7">Shall cover the ranges of Marker concentrations normally found in males and females.</td></tr>
<tr><td>Enzymatic Hydrolysis</td><td colspan="7">Assess the efficiency of the enzymatic hydrolysis using β-glucuronidase from E. coli</td></tr>
<tr><td>Derivatization</td><td colspan="7">Assess the efficiency of the trimethylsilyl (TMS) derivatization</td></tr>
<tr><td>Limits of Quantification (LOQ)</td><td colspan="7">The LOQ shall be determined during method validation as the lowest concentration that can be measured with an u_c (%) not greater than (≤) 30% and shall meet the following criteria:
T, E ≤ 1 ng/mL;
5αAdiol, 5βAdiol ≤ 10 ng/mL;
A, Etio ≤ 500 ng/mL</td></tr>
<tr><td rowspan="6">Measurement Uncertainty, u_c (%)</td><td rowspan="2">Level</td><td>A</td><td>Etio</td><td>T</td><td>E</td><td>Adiols
(5α-, 5β-)</td><td>T/E</td></tr>
<tr><td colspan="6">The estimated u_c (%) shall be not greater than (≤) the u_{c_Max} (%) value given below</td></tr>
<tr><td>at LOQ</td><td colspan="5">≤ 30%</td><td></td></tr>
<tr><td>at 5 x LOQ</td><td colspan="4">≤ 20%</td><td>≤ 25%</td><td></td></tr>
<tr><td>(T, E) > 5 ng/mL</td><td colspan="5"></td><td>≤ 15%</td></tr>
<tr><td>(T, E) ≤ 5 ng/mL</td><td colspan="5"></td><td>≤ 30%</td></tr>
<tr><td colspan="8">2.1.2 ITP Analysis Requirements</td></tr>
<tr><td>Sample</td><td colspan="7">The ITP for the quantification of the Markers of the steroid profile shall be conducted on a single Aliquot. When needed, the volume of the Aliquot may be adjusted as a function of its specific gravity (SG) and of the sex of the Athlete.</td></tr>
<tr><td>Calibration</td><td colspan="7">Calibration standard(s) or a calibration curve shall be included in each sequence of analysis.</td></tr>
<tr><td>Quality Control</td><td colspan="7">At least two (2) quality control (QC) urine samples containing representative low and high concentrations of the Markers of the steroid profile shall be included in each sequence of analysis.</td></tr>
<tr><td>Enzymatic Hydrolysis</td><td colspan="7">Purified β-glucuronidase from E. coli shall be used for the hydrolysis of the glucuroconjugated urinary steroids, and the completeness of hydrolysis shall be monitored in each Aliquot with isotopically labeled A-glucuronide (or an equivalent scientifically recognized alternative). H. pomatia mixtures shall not be used.</td></tr>
<tr><td>Derivatization</td><td colspan="7">The Markers of steroid profile shall be analyzed as TMS derivatives (TMS enol ethers and/or TMS ethers).</td></tr>
</table>

	Completeness of the derivatization shall be controlled in each Aliquot through the monitoring of mono-O-TMS vs. di-O-TMS derivative of A.
T/E Ratio	The T/E ratios shall be determined from the ratios of chromatographic peak areas or peak heights after correction against a calibrator or a calibration curve.
Factors Impacting the Steroid Profile	The Laboratory shall: • Monitor for signs of microbial activity [*e.g.* presence of indicators of 3α-hydroxysteroid dehydrogenase (HSD) activity]; *[Comment: The direct enzymatic hydrolysis of urine Samples may increase the effects of microbial contamination.]* Test for the presence of conjugated *Metabolite(s)* of ethanol [*e.g.* ethanol glucuronide (EtG)], 5α-reductase inhibitors (*e.g.* finasteride, dutasteride) and ketoconazole (and similar substances).

2.2 Reporting the *Sample*'s Steroid Profile from the ITP

Following the performance of the ITP, the Laboratory shall report in *ADAMS* the steroid profile for each *Sample* analyzed.

The Laboratory shall report in *ADAMS*:

i. The SG of the *Sample,* as determined by the Laboratory (see TD DL [5]);

ii. The uncorrected concentrations of T, E, A, Etio, 5αAdiol and 5βAdiol, and the T/E ratio;

[Comment: When the ITP measurement of a steroid profile Marker is not possible due to, for example, dilution, unusual matrix interferences, inhibition of the enzymatic hydrolysis or incomplete derivatization, the Laboratory should repeat the analysis with an alternative Sample preparation procedure (e.g. changing Aliquot volumes, application of solid phase extraction, or extraction with a different solvent).

If, however, a Marker of the steroid profile cannot be quantified, the concentration of the affected Marker shall be reported as "-1". The Laboratory shall make a comment in the Test Report on why this Marker could not be quantified (e.g. < LOQ, incomplete derivatization).

When the chromatographic peak signal for a Marker cannot be detected (i.e. is below the detection capability of the assay), the concentration of the Marker shall be reported as "-2" (See Table 3 for reporting of specific situations for [T], [E], and T/E).

The Laboratory may also provide information on other steroidal parameters such as prasterone (DHEA), dihydrotestosterone (DHT) and 6α-hydroxy-androstenedione (6α-OH-AD) at the request of the Testing Authority, Results Management Authority or the APMU.]

iii. Any signs of microbial activity in the *Sample*, *e.g.* ratios of 5α-androstanedione (5αAND) to A and 5β-androstanedione (5βAND) to Etio, as determined from the respective steroid concentrations;

iv. The presence or absence in the *Sample* of substance(s) that may alter the steroid profile (see Article 1.3). The Laboratory shall report the estimated levels of:

- EtG if ≥ 5 μg/mL;
- Carboxy-finasteride if ≥ 5 ng/mL;
- 4-hydroxy- and/or 6-hydroxy-dutasteride if ≥ 5 ng/mL;
- Ketoconazole if ≥ 100 ng/mL;

- Fluconazole if ≥ 500 ng/mL;
- Miconazole if ≥ 1,000 ng/mL.

2.2.1 Validity of the *Sample* Steroid Profile

The validity of the *Sample* will be determined automatically upon reporting of the steroid profile in *ADAMS.* A *Sample* will be invalid only when the *Sample* shows signs of extensive degradation, as determined by:

- 5αAND/A ≥ 0.1, and/or
- 5βAND/Etio ≥ 0.1

[Comment: In addition, following the reporting of the steroid profile in ADAMS by the Laboratory, the Sample may be evaluated as "invalid" by the APMU upon review of the steroid profile data, for example, by considering the presence of substances that may alter the steroid profile in the Sample.]

Table 3. Summary of conditions for reporting T and E concentrations and T/E ratio.

<table>
<tr><th>Concentration of T</th><th>Concentration of E</th><th>T/E ratio</th></tr>
<tr><td rowspan="3">Chromatographic peak signal of T measured at or above (≥) the LOQ.

[T] ≥ $LOQ_{(T)}$

Report T as measured</td><td>Chromatographic peak signal of E measured at or above (≥) LOQ.

[E] ≥ $LOQ_{(E)}$
Report E as measured.</td><td rowspan="2">Report T/E
(as determined by the Laboratory from corrected peak heights/areas)</td></tr>
<tr><td>Chromatographic peak signal of E detected, but below (<) LOQ.

$LOD_{(E)}$ ≤ [E] < $LOQ_{(E)}$
Report E as "-1"</td></tr>
<tr><td>Chromatographic peak signal of E not detected.

[E] < $LOD_{(E)}$
Report E as "-2"</td><td>Report T/E as "-1"
Report the $LOD_{(E)}$

Comment in ADAMS:
T/E ratio could not be measured accurately because E could not be detected.</td></tr>
<tr><td rowspan="2">Chromatographic peak signal of T detected, but below (<) the LOQ.

$LOD_{(T)}$ ≤ [T] < $LOQ_{(T)}$

Report T as "-1"</td><td>Chromatographic peak signal of E measured at or above (≥) LOQ.

[E] ≥ $LOQ_{(E)}$
Report E as measured</td><td rowspan="2">Report T/E
(as determined by the Laboratory from corrected peak heights/areas)</td></tr>
<tr><td>Chromatographic peak signal of E detected, but below (<) LOQ.

$LOD_{(E)}$ ≤ [E] < $LOQ_{(E)}$
Report E as "-1"</td></tr>
</table>

	Chromatographic peak signal of E not detected. [E] < LOD(E) **Report E as "-2"**	**Report T/E as "-1"** *Comment in ADAMS:* *T/E ratio could not be measured accurately because the concentration of T could not be measured, and E could not be detected*
Chromatographic peak signal of T not detected. [T] < LOD(T) **Report T as "-2"**	Chromatographic peak signal of E measured at or above (≥) LOQ. [E] ≥ LOQ(E) **Report E as measured**	**Report T/E as "-1"** Report the LOD(T) *Comment in ADAMS:* *T/E ratio could not be measured accurately because T could not be detected*
	Chromatographic peak signal of E detected but below (<) LOQ. LOD(E) ≤ [E] < LOQ(E) **Report E as "-1"**	**Report T/E as "-1"** Report the LOD(T) *Comment in ADAMS:* *T/E ratio could not be measured because T could not be detected, and E could not be measured.*
	Chromatographic peak signal of E not detected. [E] < LOD(E) **Report E as "-2"**	**Report T/E as "-2"** Report the LOD(E) and LOD(T) *Comment in ADAMS:* *T/E ratio could not be measured because T and E could not be detected.*

3.0 Confirmation Procedures (CP)

The CP for the EAAS *Markers* include the GC-MS^n ($n \geq 1$) identification (in compliance with the TD IDCR [6]) and quantification, as well as the GC/C/IRMS analysis [7] of the *Marker(s)* of the steroid profile.

In addition, the Laboratory shall confirm the presence or absence of factors impacting the steroid profile (see Article 1.3).

3.1 CP Requests (CPRs)

3.1.1 CPRs triggered by *Atypical Passport Findings* (*ATPF*) through *ADAMS*

Once the *Sample*'s steroid profile data are entered in *ADAMS* and matched with an *Athlete*, the Adaptive Model automatically updates the steroidal Passport. If an *ATPF* is identified based on an abnormally high T/E value, a CP request (*ATPF*-CPR) is triggered and sent automatically to Laboratories through *ADAMS*.

Upon receipt of an *ATPF*-CPR, the Laboratory shall proceed with the CP of the steroid profile as soon as possible, unless the presence of ethanol or other factors impacting the steroid profile has been detected in the *Sample*. In such cases, the Laboratory shall receive, within fifteen (15) days from the

ATPF-CPR notification, an advice from the Passport Custodian or the *Testing* Authority (or *Results Management* Authority, if different) on whether to proceed or not with the CP of the *Sample*'s steroid profile.

[Comment: In the absence of communication from the Passport Custodian or the Testing Authority (or Results Management Authority) within fifteen (15) days from the ATPF-CPR notification, the Laboratory shall proceed with the CP of the steroid profile (see Article 3.2)].

Any justification from the Passport Custodian or the *Testing* Authority (or *Results Management* Authority) not to proceed with the CP shall be provided in writing and in compliance with the TD APMU [8].

[Comment: In cases when the Laboratory is instructed by the Passport Custodian or the Testing Authority (or Results Management Authority) not to perform the CP, the Laboratory shall update the ADAMS Test Report for the Sample with a comment stating that the Passport Custodian, Testing Authority (or Results Management Authority) requested not to perform the CP, and the reasons given.]

When the Laboratory receives an *ATPF*-CPR for a *Sample* for which *Adverse Analytical Finding*(s) (*AAF*) have been reported for other *Prohibited Substance(s)* or *Method(s)*, the Laboratory shall consult the *Testing* Authority (or *Results Management* Authority, if different) about the need to conduct the CP for the *Markers* of the steroid profile.

3.1.2 CPRs from the APMU, the *Testing* Authority (or *Results Management* Authority, as applicable) or *WADA*.

The Adaptive Model will also determine abnormal values or sequences of the other ratios of the "steroid profile" (A/T, A/Etio, 5αAdiol/5βAdiol, 5αAdiol/E). However, in such cases the Laboratory will not receive an automatic "*ATPF*-CPR" notification through *ADAMS*. Instead, the APMU will advise the *Testing* Authority (or *Results Management* Authority, if different) on whether the *Sample* shall be subjected to CP. Therefore, in these cases the Laboratory shall receive a written request from the *Testing* Authority (or *Results Management* Authority, if different) before proceeding with the CP.

In the absence of an *ATPF*-CPR, requests for CP can be made also by the *Testing* Authority (or *Results Management* Authority, if different), the APMU *, or *WADA*.

* where the respective client of the APMU has agreed to bestow such authority to the APMU.

3.2 CP Test Methods

3.2.1 CP of Steroid Profile *Markers* by GC-MS^n

The Laboratory shall quantify all the *Markers* of the steroid profile in one Aliquot by a validated Fit-for-Purpose GC-MS^n ($n \geq 1$) quantification method. Identification (in compliance with the TD IDCR [6]) of the *Markers* that triggered the CP shall be performed as well.

- In every case, the Laboratory shall confirm quantitatively all the *Markers* of the steroid profile before proceeding with the GC/C/IRMS analysis;

[Comment: This requirement does not apply if the Testing Authority (or Results Management Authority, as applicable) has authorized the Laboratory to proceed directly to GC/C/IRMS analysis without a need for a quantitative confirmation of the steroid Markers (for example, in cases of limited Sample volume).

For T/E values, only T needs to be confirmed if E is not detected or the volume of the Sample is not sufficient.]

- In the case of an *ATPF*-CPR for an abnormally high T/E ratio, GC/C/IRMS analysis is not mandatory when the confirmed T/E value is below the confirmation T/E cut-off calculated by the Adaptive Model and provided within the *ATPF*-CPR notification received from *ADAMS*;

- For other CP requests, when the steroid profile CP does not confirm the ITP values that triggered the CP (*e.g.* 5αAdiol/E value), taking into consideration the expanded uncertainty of the measurement ($U_{95\%}$, k = 2), the Laboratory shall consult the *Testing* Authority to determine if the GC/C/IRMS analysis is necessary. In the event that GC/C/IRMS analysis is deemed unnecessary, the Laboratory shall update the *ADAMS* report for the *Sample* with the confirmed values of all the *Markers* of the steroid profile and include a comment that GC/C/IRMS analysis was not necessary.

[Comment: for ratios other than the T/E, the u_c (%) of the ratio shall be calculated by propagation of uncertainties of the corresponding Marker concentrations.]

The same analytical requirements presented in Table 2 for the ITP shall apply for the GC-MS^n CP, with the following modifications:

- GC-MS^n CP Validation Requirements
  - For determinations of A, Etio, 5αAdiol and 5βAdiol, the u_c (%) shall be not greater than (≤) 15% when the concentrations are five times (5x) the respective LOQ;
  - For determinations of T, E and T/E ratios, the u_c (%) shall be not greater than (≤) 15% when the concentrations of T and E are greater than (>) 5 ng/mL.
- GC-MS^n CP Analysis Requirements
  - A Solid Phase Extraction (SPE) shall be performed prior to the enzymatic hydrolysis of the *Sample*;
  - Calibration standard(s) and at least two (2) QC urine samples containing representative low and high levels of the *Markers* of the steroid profile shall be included.

3.2.2 GC/C/IRMS CP

Technical and reporting requirements for the GC/C/IRMS CP are specified in the TD IRMS [7].

When an *AAF* is reported for the *Marker*(s) of the steroid profile based on the results of a GC/C/IRMS analysis performed on the "A" *Sample*, only the GC/C/IRMS analysis, including the identification of the relevant *Markers* (target compounds and endogenous reference compounds) shall be repeated during the "B" *Sample* CP.

3.3 Reporting Results from the CP

3.3.1 "A" *Sample*

Following the CP performed for the steroid profile on the "A" *Sample*, the Laboratory shall report in *ADAMS*:

i. The SG of the *Sample* (determined from a new Aliquot of the "A" *Sample*);

ii. The confirmed value of the *Markers* of the steroid profile (concentrations, T/E value), without adjustment for the SG of the *Sample*;

iii. The associated u_c (expressed in units);

iv. The GC/C/IRMS confirmation results, if performed (see TD IRMS [7]). The Laboratory shall update the Test Report for the *Sample* in *ADAMS* (as *AAF*, *Atypical Finding* (*ATF*), or Negative Finding) based on the results of the GC/C/IRMS CP;

v. The confirmed results (presence/absence) for signs of microbial activity: 5αAND/A, 5βAND/Etio, and T_{free}/T_{total}; based on concentrations;

[Comment: In addition to the determination of the 5αAND/A and 5βAND/Etio ratios as signs of microbial contamination, the determination during the CP of an elevated ratio of free Testosterone to total Testosterone (T_{free} / T_{total} > 0.05) will also invalidate (the steroid profile of) the Sample. However, this shall not preclude the performance of the GC/C/IRMS CP or invalidate its results.]

vi. The presence or absence in the *Sample* of substance(s) that do not constitute an *AAF* but may alter the steroid profile (see Article 1.3): if detected in the *Sample*, the Laboratory shall report the confirmed estimated levels of EtG, 5α-reductase inhibitors and -azoles as specified in Article 2.2 (without the need to report the u_c for these determinations).

3.3.2 "B" *Sample*

Following the performance of the GC/C/IRMS CP for the steroid profile on the "B" *Sample*, the Laboratory shall report the GC/C/IRMS confirmation results (see TD IRMS [7]) in *ADAMS*.

[Comment: If the Sample has not been reported as an AAF for the Marker(s) of the steroid profile based on the results of the GC/C/IRMS analysis, but the steroid profile CP by GC-MS^n has been requested for the "B" Sample, then the Laboratory shall report in ADAMS the results of the "B" confirmation of the steroid profile as described for the "A" Sample in Article 3.3.1.]

4.0 Reporting *Sample* Manipulation (*Tampering* or *Attempted Tampering*)

Tampering or *Attempted Tampering* aims to alter the integrity and validity of *Samples* collected during *Doping Control*, including, but not limited to *Sample* substitution with another fluid and urine exchange and/or adulteration (*e.g.* addition of proteases to *Sample*).

[Comment: the substitution of an Athlete's urine Sample with the urine of another individual (urine exchange) can be uncovered using the steroidal Passport and confirmed by DNA analysis across multiple Samples, as described in the TD APMU [8].]

In cases when a *Sample* is not consistent with human urine (*e.g.* SG ≤ 1.001, creatinine ≤ 5 mg/dL [9], non-physiological salt concentration, abnormal pH values, absence or abnormally low levels of endogenous steroids, corticosteroids, proteins, etc.), the Laboratory shall:

i. Report the finding as an *AAF* for *Tampering* or *Attempted Tampering* (class M2.1 of the *Prohibited List*) if the Laboratory can determine the general nature/type of the adulterated *Sample,* which is not consistent with human urine (*e.g.* water, liquor, synthetic urine);

OR

ii. Report the finding as an *ATF* for *Tampering* or *Attempted Tampering* and include a comment in *ADAMS* advising the *Testing* Authority to perform further investigations (*e.g.* additional analyses on the *Sample*, *Target Testing* the *Athlete*).

5.0 References

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[5] *WADA Technical Document* TD DL: *Decision Limits* for the Confirmatory Quantification of Exogenous Threshold Substances by Chromatography-based Analytical Methods.

[6] *WADA Technical Document* TD IDCR: Minimum Criteria for Chromatographic-Mass Spectrometric Confirmation of the Identity of Analytes for *Doping Control* Purposes.

[7] *WADA Technical Document* TD IRMS: Detection of Synthetic Forms of *Prohibited Substances* by GC/C/IRMS.

[8] *WADA Technical Document* TD APMU: *Athlete* Passport Management Unit – Requirements and Procedures.

[9] Cook J D *et al*. The Characterization of Human Urine for Specimen Validity Determination in Workplace Drug Testing: A Review. *J Anal Toxicol* **24**: 579-588, 2000

[Comment: Current versions of WADA Technical Documents may be found at https://www.wada-ama.org/en/what-we-do/science-medical/laboratories]

3.7. Results Management Requirements and Procedures for the Athlete Biological Passport (ISRM Annex C)

C.1 Administrative Management

C.1.1 The requirements and procedures described in this Annex apply to all modules of the *Athlete Biological Passport* except where expressly stated or implied by the context.

C.1.2 These processes shall be administered and managed by an *Athlete* Passport Management Unit on behalf of the Passport Custodian. The *Athlete* Passport Management Unit will initially review profiles to facilitate targeting recommendations for the Passport Custodian when appropriate or refer to the Experts as required. Management and communication of the biological data, *Athlete* Passport Management Unit reporting and Expert reviews shall be recorded in *ADAMS* and be shared by the Passport Custodian with other *Anti-Doping Organizations* with *Testing* Authority over the *Athlete* to coordinate further Passport *Testing* as appropriate. A key element for *Athlete Biological Passport* management and communication is the *Athlete* Passport Management Unit Report in *ADAMS*, which provides an overview of the current status of the *Athlete's* Passport including the latest targeting recommendations and a summary of the Expert reviews.

C.1.3 This Annex describes a step-by-step approach to the review of an *Athlete's* Passport:

a) The review begins with the application of the Adaptive Model.

b) In case of an *Atypical Passport Finding* or when the *Athlete* Passport Management Unit considers that a review is otherwise justified, an Expert conducts an initial review and returns an evaluation based on the information available at that time.

c) In case of a "Likely doping" initial review, the Passport is then subjected to a review by three (3) Experts including the Expert who conducted the initial review.

d) In case of a "Likely doping" consensus of the three (3) Experts, the process continues with the creation of an *Athlete Biological Passport* Documentation Package.

e) An *Adverse Passport Finding* is reported by the *Athlete* Passport Management Unit to the Passport Custodian if the Experts' opinion is maintained after review of all information available at that stage, including the *Athlete Biological Passport* Documentation Package.

f) The *Athlete* is notified of the *Adverse Passport Finding* and offered the opportunity to provide explanations.

g) If after review of the explanations provided by the *Athlete*, the Experts maintain their unanimous conclusion that it is highly likely that the *Athlete Used* a *Prohibited Substance* or a *Prohibited Method*, an anti-doping rule violation is asserted against the *Athlete* by the Passport Custodian.

C.2 Initial Review Phase

C.2.1 Review by the Adaptive Model

The requirements and procedures described in this Annex apply to all modules of the *Athlete Biological Passport* except where expressly stated or implied by the context.

C.2.1.1. In *ADAMS*, the Adaptive Model automatically processes data on the biological *Markers* of the *Athlete Biological Passport*. These *Markers* include primary *Markers* that are defined as the most specific to doping and secondary *Markers* that provide supporting evidence of doping in isolation or in combination with other *Markers*. The Adaptive Model predicts for an individual an expected range within which a series of *Marker* values falls assuming a normal physiological condition. Outliers correspond to those values outside of the 99%-range, from a lower limit corresponding to the 0.5^{th} percentile to an upper limit corresponding to the 99.5^{th} percentile (1:100 chance or less that this result is due to normal physiological variation). A specificity of 99% is used to identify *Atypical Passport Findings*. In the case of sequence deviations (sequence *Atypical Passport Findings*), the applied specificity is 99.9% (1:1000 chance or less that this is due to normal physiological variation).

C.2.1.2. An *Atypical Passport Finding* is a result generated by the Adaptive Model in *ADAMS* which identifies either:

a) a primary *Marker(s)* value(s) as being outside the *Athlete's* intra-individual range, or,

b) a longitudinal profile consisting of (up to) the last five (5) valid primary *Marker* values as deviating from expected ranges (sequence *Atypical Passport Findings*), assuming a normal physiological condition.

An *Atypical Passport Finding* requires further attention and review.

C.2.1.3. Primary and Secondary *Markers*

C.2.1.3.1 For the Haematological Module, the Adaptive Model automatically processes in *ADAMS* two primary *Markers*, haemoglobin concentration (HGB) and stimulation index OFF-score (OFFS), and two secondary *Markers,* the reticulocyte percentage (RET%) and the Abnormal Blood Profile Score (ABPS). HGB and RET% are *Markers* measured in blood ABP *Samples* while OFFS and ABPS are calculated using values of *Markers* measured in blood ABP *Samples*.

C.2.1.3.2 The Steroidal Module comprises steroid *Markers* measured in urine and/or blood (serum) *Samples*. For urine *Samples*, the Adaptive Model automatically processes in *ADAMS* one primary *Marker*, the Testosterone to Epitestosterone ratio (T/E), and four (4) secondary *Markers*: the Androsterone to Testosterone ratio (A/T), the Androsterone to Etiocholanolone ratio (A/Etio), the 5α-Androstane-3α,17β-diol to 5β-Androstane-3α,17β-diol ratio (5αAdiol/5βAdiol)

and the 5α-Androstane-3α,17β-diol to Epitestosterone ratio (5αAdiol/E). For blood *Samples*, the Adaptive Model automatically processes in

ADAMS one primary *Marker,* the Testosterone to Androstenedione ratio (T/A4).

C.2.1.3.3 For the Endocrine Module, the Adaptive Model automatically processes in *ADAMS* one primary *Marker*, the GH-2000 score calculated using a formula including two (2) secondary *Markers*, insulin-like growth factor-I (IGF-I) and N-terminal pro-peptide of type III collagen (P-III-NP) measured in blood (serum) *Samples*.

C.2.1.4. Departure from *WADA Athlete Biological Passport* requirements

C.2.1.4.1 If there is a departure from *WADA Athlete Biological Passport* requirements for *Sample* collection, transport and analysis, the biological *Marker* result obtained from this *Sample* affected by the non-conformity shall not be considered in the Adaptive Model calculations (for example, RET% can be affected but not HGB under certain transportation conditions).

C.2.1.4.2 A *Marker* result which is not affected by the non-conformity can still be considered in the Adaptive Model calculations. In such case, the *Athlete* Passport Management Unit shall provide the specific explanations supporting the inclusion of the result(s). In all cases, the *Sample* shall remain recorded in the *Athlete's* Passport. The Experts may include all results in their review provided that their conclusions may be validly supported when taking into account the effects of the non-conformity.

C.2.2 The Initial Expert Review

C.2.2.1 A Passport generating an *Atypical Passport Finding,* or for which a review is otherwise justified, shall be sent by the *Athlete* Passport Management Unit to an Expert for review in *ADAMS*. This should take place within seven (7) days following the generation of the *Atypical Passport Finding* in *ADAMS*. The review of the Passport shall be conducted based on the Passport and other basic information (e.g. *Competition* schedules), which may be available, such that the Expert is blinded to the identity of the *Athlete*. The Expert shall provide the individual report in *ADAMS* and this should take place within seven (7) days after receipt of the request.

C.2.2.2 If a Passport has been recently reviewed by an Expert and the Passport Custodian is in the process of executing a specific multi-*Sample Testing* strategy on the *Athlete*, the *Athlete* Passport Management Unit may delay the review of a Passport generating an *Atypical Passport Finding* triggered by one of the *Samples* collected in this context until completion of the planned series of tests. In such situations, the *Athlete* Passport Management Unit shall clearly indicate the reason for delaying the review of the Passport in the *Athlete* Passport Management Unit Report.

C.2.2.3 If the first and unique result in a Passport is flagged as an *Atypical Passport Finding* by the Adaptive Model, the *Athlete* Passport Management Unit may recommend the collection of an additional *Sample* before initiating the initial Expert review.

C.2.2.4 Review in the absence of an *Atypical Passport Finding*

C.2.2.4.1 A Passport may also be sent for Expert review in the absence of an *Atypical Passport Finding* where the Passport includes other elements otherwise justifying a review.

These elements may include, without limitation:

a) Data not considered in the Adaptive Model;

b) Any abnormal levels and/or variations of *Marker(s)*;

c) Signs of hemodilution in the haematological Passport;

d) *Marker* levels below the corresponding Limit of Quantification of the assay; or

e) Intelligence in relation to the *Athlete* concerned.

C.2.2.4.2 An Expert review initiated in the above-mentioned situations may result in the same *Consequences* as an Expert review triggered by an *Atypical Passport Finding*.

C.2.2.5 Expert Evaluation

C.2.2.5.1 When evaluating a Passport, an Expert weighs the likelihood that the Passport is the result of the *Use* of a *Prohibited Substance* or *Prohibited Method* against the likelihood that the Passport is the result of a normal physiological or pathological condition in order to provide one of the following opinions: “Normal”, “Suspicious”, “Likely doping” or “Likely medical condition”. For a “Likely doping” opinion, the Expert shall come to the conclusion that the likelihood that the Passport is the result of the *Use* of a *Prohibited Substance* or *Prohibited Method* outweighs the likelihood that the Passport is the result of a normal physiological or pathological condition.

[Comment to Article C.2.2.5.1: When evaluating competing propositions, the likelihood of each proposition is evaluated by the Expert based on the evidence available for that proposition. It is acknowledged that it is the relative likelihoods (i.e., likelihood ratio) of the competing propositions that ultimately determine the Expert’s opinion. For example, where the Expert is of the view that a Passport is highly likely the result of the Use of a Prohibited Substance or Prohibited Method, it is necessary for a “Likely doping” evaluation that the Expert consider that it is unlikely that it may be the result of a

normal physiological or pathological condition. Similarly, where the Expert is of the view that a Passport is likely the result of the Use of a Prohibited Substance or Prohibited Method, it is necessary for a "Likely doping" evaluation that the Expert consider that it is highly unlikely that it may be the result of a normal physiological or pathological condition.]

C.2.2.5.2 To reach a conclusion of "Likely doping" in the absence of an *Atypical Passport Finding*, the Expert shall come to the opinion that it is highly likely that the Passport is the result of the *Use* of a *Prohibited Substance* or *Prohibited Method* and that it is highly unlikely that the Passport is the result of a normal physiological or pathological condition.

C.2.3 Consequences of the Initial Review

Depending on the outcome of the initial review, the *Athlete* Passport Management Unit will take the following action:

Expert Evaluation	***Athlete* Passport Management Unit Action**
"Normal"	Continue normal *Testing* plan.
"Suspicious"	Provide recommendations to the Passport Custodian for *Target Testing*, *Sample* analysis and/or requesting further information as required.
"Likely doping"	Send to a panel of three (3) Experts, including the initial Expert, as per section C.2 of this Annex C.
"Likely medical condition"	If recommended by the Expert, inform the *Athlete* as soon as possible via the Passport Custodian (or send to other Experts).

[Comment to Article C.2.3: The Athlete Biological Passport is a tool to detect the possible Use of Prohibited Substance(s) or Prohibited Method(s) and it is not intended as a health check or for medical monitoring. It is important that the Passport Custodian educate the Athletes to ensure that they undergo regular health monitoring and not rely on the Athlete Biological Passport for this purpose. Nevertheless, the Passport Custodian should inform the Athlete in case the Passport indicates a likely pathology as determined by the Experts.]

C.3 Review by Three (3) Experts

C.3.1 In the event that the opinion of the appointed Expert in the initial review, pending other explanation to be provided at a later stage, is that of "Likely doping", the Passport shall then be sent by the *Athlete* Passport Management Unit to two (2) additional Experts for review. This should take place within seven (7) days after the reporting of the initial review. These additional reviews shall be conducted without knowledge of the initial review. These three (3) Experts now constitute the Expert Panel, composed of the Expert appointed in the initial review and these two (2) other Experts.

C.3.2 The review by the three (3) Experts must follow the same procedure, where applicable, as presented in section C.2.2 of this Annex. The three (3) Experts shall each provide their individual reports in *ADAMS*. This should take place within seven (7) days after receipt of the request.

C.3.3 The *Athlete* Passport Management Unit is responsible for liaising with the Experts and for advising the Passport Custodian of the subsequent Expert assessment. The Experts can request further information, as they deem relevant for their review, notably information related to medical conditions, *Competition* schedule and/or *Sample(s)* analysis results. Such requests are directed via the *Athlete* Passport Management Unit to the Passport Custodian.

C.3.4 A unanimous opinion among the three (3) Experts is necessary in order to proceed further towards declaring an *Adverse Passport Finding*, which means that all three (3) Experts render an opinion of "Likely doping". The conclusion of the Experts must be reached with the three (3) Experts assessing the *Athlete's* Passport with the same data.

[Comment to Article C.3.4: The three (3) Expert opinions cannot be accumulated over time based on different data.]

C.3.5 To reach a conclusion of "Likely doping" in the absence of an *Atypical Passport Finding*, the Expert Panel shall come to the unanimous opinion that it is highly likely that the Passport is the result of the *Use* of a *Prohibited Substance* or *Method* and that there is no reasonably conceivable hypothesis under which the Passport is the result of a normal physiological condition and highly unlikely that it is the result of pathological condition.

C.3.6 In the case when two (2) Experts evaluate the Passport as "Likely doping" and the third Expert as "Suspicious", the *Athlete* Passport Management Unit shall promptly confer with the Expert Panel before they finalize their opinion. The group can also seek advice from an appropriate outside Expert, although this must be done while maintaining strict confidentiality of the *Athlete's* Personal Information.

C.3.7 If no unanimity can be reached among the three (3) Experts, the *Athlete* Passport Management Unit shall promptly report the Passport as "Suspicious", update the *Athlete* Passport Management Unit Report, and recommend that the Passport Custodian pursue additional *Testing* and/or gather intelligence on the *Athlete* (refer to Information Gathering and Intelligence Sharing Guidelines), as appropriate.

C.4 Conference Call, Compilation of the *Athlete Biological Passport* Documentation Package and Joint Expert Report

C.4.1 If a unanimous opinion of "Likely doping" is rendered by all three (3) Experts, the *Athlete* Passport Management Unit shall promptly declare a "Unanimous likely doping" evaluation in the *Athlete* Passport Management Unit Report in *ADAMS* and should organize a conference call with the Expert Panel to initiate the next steps for the case, including proceeding with the compilation of the *Athlete Biological Passport* Documentation Package (see *Technical Document* for *Athlete* Passport Management Units) and drafting of the joint Expert report. In preparation for this conference call, the *Athlete* Passport Management Unit should coordinate with the Passport Custodian to compile any potentially relevant information to share with the Experts (e.g. suspicious analytical findings, relevant intelligence and relevant pathophysiological information).

C.4.2 Once completed, the *Athlete Biological Passport* Documentation Package shall be sent by the *Athlete* Passport Management Unit to the Expert Panel, who will review it and provide a joint Expert report to be signed by all three (3) Experts. The conclusion within the joint Expert report shall be reached without interference from the Passport Custodian. If necessary, the Expert Panel may request complementary information from the *Athlete* Passport Management Unit.

C.4.3 At this stage, the identity of the *Athlete* is not mentioned but it is accepted that specific information provided may allow to identify the *Athlete*. This shall not affect the validity of the process.

C.4.4 If after review of the *Athlete Biological Passport* Documentation Package, the Expert Panel is no longer unanimous in their opinion of "Likely doping", the Expert Panel shall update their respective opinions in ADAMS and the *Athlete* Passport Management Unit shall update the *Athlete* Passport Management Unit Report accordingly.

C.5 Issuing an *Adverse Passport Finding*

C.5.1 If the Expert Panel confirms their unanimous position of "Likely doping", the *Athlete* Passport Management Unit shall promptly declare an *Adverse Passport Finding* in *ADAMS* that includes a written statement of the *Adverse Passport Finding*, the *Athlete Biological Passport* Documentation Package and the joint Expert report.

C.5.2 After reviewing the *Athlete Biological Passport* Documentation Package and joint Expert report, the Passport Custodian shall:

a) Notify the *Athlete* of the *Adverse Passport Finding* in accordance with Article 5.3.2;

b) Provide the *Athlete* the *Athlete Biological Passport* Documentation Package and the joint Expert report;

c) Invite the *Athlete* to provide their own explanation, in a timely manner, of the data provided to the Passport Custodian.

C.6 Review of Explanation from *Athlete* and Disciplinary Proceedings

C.6.1 Upon receipt of any explanation and supporting information from the *Athlete,* which should be received within the specified deadline, the *Athlete* Passport Management Unit shall forward it to the Expert Panel for review with any additional information that the Expert Panel considers necessary to render its opinion in coordination with both the

Passport Custodian and the *Athlete* Passport Management Unit, and update their recommendation in *ADAMS* as "Athlete's explanation provided to Expert panel". At this stage, the review is no longer anonymous. The Expert Panel shall promptly reassess or reassert the case and reach one of the following conclusions:

a) Unanimous opinion of "Likely doping" by the Experts based on the information in the Passport and any explanation provided by the *Athlete*; or
b) Based on the available information, the Experts are unable to reach a unanimous opinion of "Likely doping" set forth above.

[Comment to Article C.6.1: Such a reassessment shall also take place when the Athlete does not provide any explanation.]

C.6.2 If the Expert Panel expresses the opinion set forth in section C.6.1(a), then the *Athlete* Passport Management Unit shall promptly update their recommendation in *ADAMS* as "APF confirmed" and inform the Passport Custodian, who shall charge the *Athlete* in accordance with Article 7 above and continue with *Results Management* in accordance with this *International Standard*.

C.6.3 If the Expert Panel expresses the opinion set forth in section C.6.1(b), the Expert Panel shall promptly update their respective opinions in ADAMS and the *Athlete* Passport Management Unit shall update the *Athlete* Passport Management Unit Report, accordingly, and recommend the Passport Custodian to pursue additional *Testing* and/or gather intelligence on the *Athlete* (refer to Information Gathering and Intelligence Sharing Guidelines), as appropriate. The Passport Custodian shall notify the *Athlete* and *WADA* of the outcome of the review.

C.7 Passport Re-setting

C.7.1 In the event the *Athlete* has been found to have committed an anti-doping rule violation based on the Passport, the *Athlete's* Passport shall be reset by the Passport Custodian at the start of the relevant period of *Ineligibility* and a new Biological Passport ID shall be assigned in *ADAMS*. This maintains the *Athlete's* anonymity for potential *Athlete* Passport Management Unit and Expert Panel reviews conducted in the future.

C.7.2 When an *Athlete* is found to have committed an anti-doping rule violation on any basis other than the *Athlete Biological Passport*, the Passport will remain in effect, except in those cases where the *Prohibited Substance* or *Prohibited Method* may have altered Passport *Markers* (e.g. for an *AAF* reported for anabolic androgenic steroids, which may affect the *Markers* of the steroid profile, or for the *Use* of Agents Affecting Erythropoiesis or blood transfusions, which would alter the haematological *Markers*). The Passport Custodian shall consult with their *Athlete* Passport Management Unit following an *Adverse Analytical Finding* to determine whether a Passport reset is warranted. In such instances, the *Athlete's* profile(s) would be reset from the time of the beginning of the sanction.

3.8. Athlete Passport Management Unit Requirements and Procedures

WADA Technical Document – TD2023APMU

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1.0 Introduction

This *Technical Document* (*TD*) has been established to harmonize effective management of *Athlete* Passports by providing specific requirements that an *Athlete* Passport Management Unit (APMU) shall meet in order to be a *WADA*-approved APMU**.**

2.0 APMU Roles and Responsibilities

2.1 The APMU is the dedicated unit that is responsible for the timely management of Passports in the *Anti-Doping Administration and Management System* (*ADAMS)* on behalf of the Passport Custodian. Passport management by the APMU involves:

- Performing Passport assessments to make timely *Target Testing* recommendations to the Passport Custodian via the APMU Report in *ADAMS* when appropriate; and
- Managing the review of atypical Passports according to Annex C of the *International Standard* for *Results Management* (ISRM) [1], including, but not limited to, the following:
  - Issuing and updating APMU Reports in *ADAMS*,
  - In case of an *Atypical Passport Finding* (*ATPF)*, or when a review is otherwise justified, assigning and liaising with the Expert panel as required,
  - Compiling all necessary information to establish an *Athlete* Biological Passport (*ABP*) Documentation Package, and
  - Declaring *Adverse Passport Findings* (*APFs*) to the Passport Custodian and *WADA*.

2.2 The APMU shall assess and manage Passport *Sample* validity in *ADAMS*, in consultation with the Experts or Laboratories when necessary, per Article 8.2 of this *TD*.

2.3 The APMU shall provide support to the Passport Custodian in defining priorities in order to optimize the efficiency of their *ABP* program. These priorities may include, but are not limited to, cost efficiency, special analyses, Test Distribution Plans (TDP), and *Target Testing*.

3.0 APMU Hosting

3.1 An APMU shall be hosted by a Laboratory.

[Comment: Hosting in this context is defined as the provision of facilities and resources for the efficient functioning of the APMU.]

3.2 APMU hosting by a Laboratory does not preclude the use of qualified APMU managers employed by *ADOs* or other Laboratories.

3.3 Passport management shall be carried out in *ADAMS* using dedicated APMU accounts associated with the host Laboratory regardless of the physical location of the APMU manager(s).

3.4 The host Laboratory shall implement procedures to maintain the operational independence of the APMU, including the appointment of dedicated personnel with a specified time commitment to the APMU and a separate allocation in the budget so that the APMU can continue to function should the *WADA* accreditation of the Laboratory be suspended (see Article 7.1.5 of this *TD*).

4.0 APMU Personnel

4.1 The host Laboratory shall have a *Person* qualified to function as the designated head of the APMU by assuming professional, organizational, educational, and administrative responsibility of the APMU. The APMU Director is responsible for ensuring the APMU operates in compliance with this *TD* and applicable *International Standards*. In particular, the APMU Director assumes the responsibility of signing and delivering all *APFs* to the Passport Custodian and *WADA*.

[Comment: The head of the APMU is termed "Director" herein, however use of this title is not a requirement and can be adjusted according to the needs of the organization.]

4.1.1 The APMU Director's qualifications shall ensure that this individual is competent and capable of leading the APMU operations, including:

- A doctoral degree (or equivalent) in one of the natural sciences or medicine, or in the absence of a doctoral degree, a master's degree (or equivalent) with extensive and appropriate anti-doping science experience and training (*i.e.,* minimum of five (5) years);
- Management experience;
- Ability to oversee compliance with quality management practices; and
- Good command of at least one of *WADA*'s two official languages, English and French.

It is acknowledged that the APMU Director plays an essential role in the APMU operations and that *WADA* APMU approval is delivered based upon appointment of a proper candidate. *WADA* reserves the right to review the credentials of such appointment in accordance with the above qualifications.

4.1.2 The APMU Director is responsible for maintaining documentation for each personnel employed by, or under contract to, the APMU. Such documentation shall contain copies of the curriculum

vitae or qualification form, a job description, and records of initial and ongoing training related to anti-doping.

4.1.3 Any personnel changes to the position of APMU Director shall be communicated to *WADA* no later than one (1) month prior to the date the APMU Director is scheduled to vacate the position. A succession plan shall be submitted to *WADA*.

4.1.4 The APMU Director is notably responsible for monitoring the quality of Passport management and ensuring that other APMU personnel have the experience and training necessary to perform their duties.

4.2 The APMU shall use qualified scientific personnel to serve as APMU manager(s) to manage the Passport review process and *Sample* validity, and to provide *Target Testing* and Analytical *Testing* recommendations through APMU Reports in *ADAMS*. APMU manager(s) shall be employed by the host Laboratory or be under contract by an *ADO* or another Laboratory. The APMU should have at least one APMU manager per module of the *ABP,* where one manager may supervise multiple modules based on their qualifications.

[Comment: The designation of "manager" is used herein, however use of this title is not a requirement and can be adjusted according to the needs of the organization. The APMU Director can also serve in the role of APMU manager as required. Where the APMU manager is employed by an ADO, it is assumed that this individual will have access to the identity and other privileged or confidential information about the Athlete, past Testing and/or Results Management and investigations history. This additional information shall not be shared by the APMU manager in the APMU Report but is recognized to be important to contribute to effective Target Testing.]

4.2.1 APMU manager(s) shall have qualifications in one or more modules of the ABP. The qualifications are at minimum:

- Bachelor's degree (or equivalent) in one of the natural or health sciences. Documented experience of three (3) years or more in anti-doping or similar scientific training is equivalent to a Bachelor's degree for this position; and
- Adequate training in one or more modules of the *ABP*, capacity to understand and evaluate analytical results and the physiological response to the *Use* of *Prohibited Substances* and *Prohibited Methods*, as well as criteria relevant for *Target Testing*.

4.2.2 Where the APMU manager has strong qualifications in Laboratory steroid analysis, steroid doping and metabolism and/or clinical endocrinology, and is not employed by the Passport Custodian, the APMU manager can act as a first Expert for the Steroidal Module of the *ABP*.

4.3 The APMU should have administrative personnel to coordinate with the Passport Custodian to compile the necessary documentation required for the *ABP* Documentation Packages, manage communication with various stakeholders and assist with the organization of APMU-related documentation.

5.0 APMU Confidentiality and Security

5.1 All APMU related activities shall be carried out in accordance with the confidentiality requirements of the *Code* and *International Standards*.

5.2 While APMU activities are typically carried out using Passport data associated with a unique ID, and while APMU staff generally do not have access to data that would enable them to identify *Athletes* in *ADAMS*, APMUs may access Personal Information where additional information is needed to assess a Passport (e.g., when assessing a Passport that has generated an *ATPF*). In such contexts, Personal Information shall only be processed for the purposes set out in this *TD*, and shall be handled by the APMU in accordance with the *International Standard* for the Protection of Privacy and Personal Information (ISPPPI) [2] and applicable laws.

5.3 Without limiting the above, the APMU shall adhere to those information retention times set forth in Annex A of the ISPPPI. In consultation with the Passport Custodian, the APMU shall develop specific plans and procedures to ensure the secure retention and eventual destruction of Personal Information.

5.4 The APMU shall develop, maintain, implement and ensure ongoing compliance with a written information security program that includes physical, organizational, technical, environmental and operational safeguards appropriate to the sensitivity of the information in its custody or to which it has access. Such program shall be based on a threat and risk assessment by expert(s) in the relevant field, and shall ensure the confidentiality of its procedures and security of its information systems regardless of the physical location of the APMU personnel at the time of Passport management, such as when the APMU manager is physically located in an *ADO*, another Laboratory or when travelling.

6.0 *ABP* Expert Panel

6.1 The APMU shall engage the services of qualified Experts for the review of Passports in accordance with Annex C of the ISRM [1]

6.2 The APMU should inform *WADA* about any changes in their pool of Experts.

6.3 The APMU shall establish, in consultation with the Passport Custodian, a list of Experts who are qualified to comprise an Expert panel for the review of Passports.

- For the Hematological Module, the Expert panel should consist of at least three (3) Experts who have qualifications in one or more of the fields of clinical and laboratory hematology, sports medicine and exercise physiology, as they apply to blood doping.
- For the Steroidal Module, the Expert panel should be composed of at least three (3) Experts with qualifications in the fields of Laboratory steroid analysis, steroid doping, and/or clinical endocrinology, as it applies to steroid *Marker* metabolism.

- For the Endocrine Module, the Expert panel should be composed of at least three (3) Experts with qualifications in the fields of endocrine biomarker analysis, doping with growth hormone and related compounds, and/or clinical endocrinology, as it applies to growth hormone *Marker* metabolism.

For each module, an Expert panel should consist of Experts with complementary knowledge such that all relevant fields are represented.

All three (3) Experts forming an Expert panel assigned to review a particular Passport shall not be of one and the same nationality and no two (2) Experts shall have a primary affiliation with the same organization, institution or company, including, but not limited to, universities, hospitals and research institutes.

Where applicable, at least one Expert on the Expert panel should currently serve or have previously served as an Expert and reviewed Passports for a *WADA*-approved APMU.

6.4 The APMU shall ensure that each Expert:

- Has access to relevant *ABP* Expert education resources provided by *WADA*;
- Has an Expert account in *ADAMS* for the anonymous review of Passports assigned by the APMU;
- Is independent of the Passport Custodian and has no conflicts of interest in reviewing Passports, as documented in a conflict-of-interest declaration; and
- Has signed the *WADA ABP* Expert Code of Conduct Declaration.

[Comment: An APMU manager may also concurrently serve as an Expert for other APMUs, provided all requirements of Article 6.0 of this TD are met.]

7.0 Process and Requirements for *WADA* APMU Approval

Passports shall only be managed by APMUs that have been approved by *WADA*.Applying for *WADA* APMU Approval

7.1.1 Expression of Interest

The candidate APMU shall officially contact *WADA* in writing to express its interest in the *WADA* APMU approval process.

7.1.2 Preliminary Discussion with *WADA*

The purpose of this discussion is to clarify issues with regard to the approval process and to obtain information about different aspects of the APMU relevant to the approval process. Such a discussion could be conducted prior to or during the approval process.

7.1.3 Description of the Candidate APMU

The candidate APMU shall then complete a detailed application form provided by *WADA* and submit it to *WADA* no later than eight (8) weeks following receipt. The application form includes, but is not limited to, the following:

- List of staff, their qualifications and intended role within the APMU;
- Description of the APMU information security program (see Article 5.4 of this *TD*), including a description of the physical, organizational, technical, environmental and operational security measures implemented to protect records and computer systems;
- List of external Experts, their contact information, their qualifications and signed *ABP* Expert Code of Conduct Declaration;
- Business Plan for the APMU and letters of support from *ADOs* that demonstrate a commitment to manage, according to Article 2.0 of this *TD*, a minimum of 100 active hematological Passports and 500 active steroidal Passports from *Signatories* annually, within one year of receiving approval. An eligible Business Plan shall demonstrate a commitment to provide at least 200 APMU Reports for hematological Passports and 500 APMU Reports for steroidal Passports per year.

  [Comment: A Passport is considered active when at least one Sample collection is planned during the first year of operation of the APMU. There is no minimum number of active endocrine Passports required for the business plan.]

7.1.4 Liability Insurance Coverage

The APMU shall provide documentation to *WADA* that professional liability risk insurance coverage or equivalent has been obtained which covers the APMU to an amount of no less than (≥) 2 million USD annually, and should ensure that the Expert panel has suitable professional liability risk insurance or equivalent coverage.

7.1.5 Operational Independence

The APMU shall ensure a degree of operational independence from the host Laboratory such that the APMU can continue to fulfil its responsibilities in compliance with this *TD* should the *WADA* accreditation of the Laboratory be suspended, where the reason for the Suspension does not have an impact on the function of the APMU. Operational independence implies that the APMU shall have a separate allocation in the budget and sufficient technical and human resources to permit the APMU to manage its own affairs without hindrance or interference by host Laboratories.

7.1.6 Compliance with the *WADA* APMU Code of Ethics

The candidate APMU shall implement and comply with the provisions in the *WADA* APMU Code of Ethics. The APMU shall provide the APMU Code of Ethics to APMU personnel and ensure their understanding and compliance with all aspects. The candidate APMU shall provide to *WADA* a letter of compliance with the APMU Code of Ethics, signed by the APMU director.

7.1.7 *WADA* Recommendation for Approval

After receipt of the application form, *WADA* will complete and submit a report to the candidate APMU. The report will include a recommendation concerning approval of the candidate APMU. In the case where the recommendation is that the APMU should not be approved, the report

will identify improvements required in order to be re-considered for designation as a *WADA*-approved APMU. In the case where the recommendation is that the APMU should be approved, the report and recommendation will be submitted to the *WADA* Executive Committee for approval.

7.1.8 Issuing Approval Letter and Publishing APMU List on *WADA's* Website

A letter signed by a duly authorized representative of *WADA* shall be issued in recognition of approval of an APMU, specifying the name of the APMU Approval may be granted with retroactive effect. An updated list of approved APMUs shall be published by *WADA* on *WADA*'s website.

7.2 Maintaining *WADA* Approval

An APMU shall continue to function if the Laboratory's accreditation is suspended, provided that the APMU continues to meet other criteria for approval, and that any non-conformities related to the Suspension of the Laboratory's accreditation do not have an impact on the APMU. The APMU's approval shall be revoked if the *WADA* accreditation of the associated Laboratory is revoked.

[Comment: Suspension or Revocation of APMU approval shall not be considered in decisions on Suspension or Revocation of Laboratory accreditation unless the APMU non-compliance has a clear impact on the function of the Laboratory.]

7.2.1 Minimum Number of Passports and APMU Reports

In order to maintain proficiency, *WADA*-approved APMUs are required to review a minimum number of Passports and provide APMU Reports for Passports of *Signatory* Passport Custodians. *WADA* shall monitor the total number of Passports under the responsibility of the APMU and the number of APMU Reports issued by the APMU. If the annual number falls below 100 active hematological Passports, 500 active steroidal Passports, 200 hematological APMU Reports or 500 steroidal APMU Reports, *WADA* APMU approval may be suspended or revoked.

[Comment: For the purposes of WADA APMU monitoring, a Passport is considered active when at least one Sample is collected during the previous twelve months period at the time of the assessment. There is no minimum number of active endocrine Passports or APMU Reports required to maintain APMU approval.]

7.2.2 Documenting Compliance with the *WADA* APMU Code of Ethics

The APMU shall annually provide to *WADA* a letter of compliance with the provisions of the APMU Code of Ethics, signed by the APMU Director. All APMU personnel shall sign the *WADA* APMU Code of Ethics on a yearly basis and the signed documents shall be kept as part of their personnel file. The APMU may be asked to provide documentation demonstrating compliance with the provisions of the APMU Code of Ethics.

7.2.3 Documenting Sharing of Knowledge

The APMU shall proactively share knowledge with other *WADA*-approved APMUs. The APMU should participate at least once annually in a *WADA* Working Group or an anti-doping symposium or conference. The APMU shall supply an annual report on sharing of knowledge with *WADA*. A description of this sharing of knowledge is provided in the *WADA* APMU Code of Ethics.

7.2.4 Maintaining Professional Liability Insurance Coverage

The APMU shall maintain an ongoing professional liability risk insurance coverage or equivalent which covers the APMU to an amount of no less than (≥) 2 million USD annually, and should ensure that the Expert panel has suitable professional liability risk insurance or equivalent coverage. Proof of the corresponding coverage shall be provided to *WADA* upon request.

7.2.5 APMU Compliance Monitoring by *WADA*

WADA shall monitor the compliance of APMUs against the requirements listed in applicable *International Standards* and *TDs*. In addition, *WADA* shall also conduct periodic audits of APMU compliance to assess the overall performance of each APMU and to decide its approval status.

7.2.6 APMU Assessment by *WADA*

WADA reserves the right to conduct document-based audits as well as inspect and assess the APMU through on-site or remote assessments at any time, at *WADA*'s expense. The notice of an on-site assessment will be made in writing to the APMU Director. In exceptional circumstances, the on-site assessment may be unannounced.

7.2.7 Suspension or Revocation of Approval

Suspension or Revocation of APMU approval may occur whenever the APMU fails to comply with applicable *International Standards* and/or *TDs*, or where such measure is otherwise required in order to protect the interests of the anti-doping community.

Without limitation, the following nonconformities in the routine operations of an APMU may be considered in support of Suspension:

- Failure to comply with any of the requirements listed in applicable *International Standards* and/or *TDs*;
- Failure to cooperate with *WADA* or the relevant *Testing* Authority in providing documentation;
- Noncompliance(s) with the APMU Code of Ethics;
- Major changes in key staff without proper and timely notification to *WADA*;
- Failure to cooperate in any *WADA* inquiry in relation to the activities of the APMU;

- Noncompliance(s) identified from APMU assessment(s); or
- Loss of resources jeopardizing the quality and/or viability of the APMU.

Noncompliance(s) in APMU performance will be assessed by *WADA* on a case-by-case basis considering the severity and consequences to the anti-doping system. Evidence of serious or multiple noncompliance(s) will be reported by *WADA* to an external assessment panel, who will make a recommendation to *WADA* regarding the approval status of the APMU and the required corrective actions and associated deadlines. *WADA* reserves the right to provisionally suspend an APMU's approval pending a full investigation. Such a decision may be taken by the Chair of *WADA's* Executive Committee.

The period and terms of Suspension shall be proportionate to the seriousness of the noncompliance(s) and the need to ensure reliable management of *Athlete* Passports. A period of Suspension shall be of a duration to be decided by *WADA* and up to a maximum of six (6) months, during which time any nonconformity(ies) must be corrected and such correction documented and reported to *WADA*. If the nonconformity(ies) is/are not corrected during the initial Suspension period, the Suspension shall either be further extended or the APMU approval revoked. The Suspension period may be extended up to a maximum of an additional six (6) months, based on justifiable delays in implementing the satisfactory corrective actions. If the APMU has provided evidence determined to be satisfactory by *WADA* that the noncompliance(s) are corrected, the APMU's approval shall be re-instated. If the APMU has not provided evidence determined to be satisfactory by *WADA* at the end of the extended Suspension period, not to exceed twelve (12) months, the APMU's approval shall be revoked.

During the period of Suspension of the APMU, the management of all *Athlete* Passports shall be transferred by the Passport Custodian to another *WADA*-approved APMU after signing an agreement with this other APMU.

The *WADA* Executive Committee shall revoke the approval of any APMU if it determines that Revocation is necessary to ensure reliable management of *Athlete* Passports. Revocation may be based on, but not limited to, the following noncompliance(s) in the routine operations of an APMU:

- Repeated suspensions of *WADA* APMU approval;
- Systematic failure to comply with applicable *International Standards* and/or *TDs*;
- Failure to correct a lack of compliance with any of the requirements listed in applicable *International Standards* and/or *TDs* during a Suspension period;
- A serious or repeated violation of the APMU Code of Ethics;
- Repeated and/or continuous failure to cooperate in any *WADA* inquiry in relation to the activities of the APMU;
- Serious noncompliance(s) identified from APMU assessment(s); or
- Loss of resources jeopardizing the quality and/or viability of the APMU.

7.2.8 Appeals

WADA's decision to suspend or revoke an APMU's approval may be appealed in writing by the APMU before *CAS* within twenty-one (21) days of the date of receipt of notification.

8.0 Passport Management and Administration

The APMU shall manage all Passports under the custody of the Passport Custodian.

8.1 Passport Review Process

The APMU shall carry out the Passport review process as described in Annex C of the ISRM [1].

8.1.1 When assessing a newly matched *Sample* in a Passport:

- The APMU shall assess the validity of individual *Samples* contained within the Passport in *ADAMS* and address any observed irregularities according to Article 8.2 of this *TD* by updating the APMU Report;
- The APMU shall review any new *Samples* within the updated Passport and provide *Target Testing*, *Sample* analysis or other recommendations via the APMU Report as required;
- Where required for its analysis, the APMU may request further information from the Passport Custodian including, but not limited to, circumstances and details of *Sample* collection, transport, and analysis, redacted *Athlete Competition* schedule, travel history, *Athlete* performance, redacted *Athlete* medical information, information on an *Adverse Analytical Finding (AAF)* that is potentially relevant in the context of the Passport, or altitude/whereabouts information which may help them interpret the new *Sample*;
- Where the Passport includes elements justifying a review or upon request by the Passport Custodian, the APMU shall send the Passport for review in *ADAMS* by an Expert.

  [Comment: One of the benefits of the ABP is the ability to focus resources on atypical results requiring attention. As such, it is not mandatory for an APMU to review all newly matched Samples under their responsibility that do not generate a specific notification requiring mandatory follow-up. Nevertheless, at the discretion of the Passport Custodian, an APMU may be requested to review normal Passports.]

8.1.2 When assessing a Passport that generated an *ATPF*:

- All ATPFs shall be reviewed by a Laboratory-based APMU manager;

  [Comment: ATPFs are generated by the following primary Markers: hemoglobin (HGB) and the OFF-Score for the Hematological Module; the testosterone to epitestosterone ratio (T/E) in urine, and testosterone (T) and/or the testosterone to androstenedione ratio (T/A4) in blood for the Steroidal Module; and the GH-2000 score for the Endocrine Module.]

- The APMU shall review any previous APMU Reports associated with the Passport;

- The APMU shall assess the validity of individual *Samples* contained within the Passport in *ADAMS,* address any irregularities according to Article 8.2 of this *TD* and update the APMU Report accordingly;
- The APMU shall evaluate the need for urgent *Target Testing* of the *Athlete* and communicate *Testing* recommendations to the Passport Custodian via the APMU Report as required;
- The APMU shall assess the need for additional analysis of existing *Samples* by specific methods (*e.g.,* Agents Affecting Erythropoiesis, Gas Chromatography / Combustion / Isotope Ratio Mass Spectrometry [GC/C/IRMS], Steroid Esters, hGH Isoform Differential Immunoassay, etc.) and communicate these to the Passport Custodian via the APMU Report as required. The APMU may also recommend specific *Sample(s)* to be placed in long-term storage.
- If an Expert has previously recommended that follow-up *Testing* include a minimum number of *Samples* before further review of an *Athlete*'s Passport data, the APMU may delay sending the Passport for Expert review until the planned number of *Samples* have been collected and analyzed;
- If, after managing the *Sample* validity, the Passport remains atypical, the APMU shall, without delay, send the Passport for review in *ADAMS* by an Expert according to Article C.2.2 of the ISRM [1]. In the event of an Expert opinion of:
  - "Likely Doping": the APMU shall update the APMU Report indicating "Likely Doping", specifying any detailed analysis or *Testing* recommendations from the Expert (if provided), and continue the Passport review process according to Article C.3 of the ISRM [1];
  - "Suspicious": the APMU shall update the APMU Report indicating "Suspicious", highlighting the main atypical features, and outline a *Target Testing* strategy (if necessary) based on the Expert recommendations, or recommend further analysis (*e.g.,* GC/C/IRMS);
  - "Normal": the APMU shall update the APMU Report indicating "Normal", summarizing the review by the Expert and outlining any *Testing* recommendations provided by the Expert;
  - "Likely Medical Condition": the APMU shall update the APMU Report indicating "Likely Medical Condition" with submission to additional Experts if recommended in the Expert evaluation and should inform the *Athlete* via the Passport Custodian. If the first Expert is not a medical doctor, the Passport should be sent to a medical doctor from the Expert panel prior to contacting the Passport Custodian.

    [Comment: the APMU recommendation in ADAMS should mirror the Expert's opinion(s) and any changes in the status of the APMU recommendation should be based on a change in Expert opinion(s) upon further review of the Passport.]

8.1.3 When assessing a urine *Sample* that generated an *Atypical Passport Finding* - Confirmation Procedure Request (*ATPF*-CPR; see TD EAAS [3]) for the steroidal Passport:

- The APMU shall assess the validity of the *Sample* generating the Confirmation Procedure (CP) request in *ADAMS,* address any irregularities according to Article 8.2 of this *TD* and update the APMU Report accordingly;
- When the *ATPF*-CPR has been triggered for a *Sample* where the presence of ethanol or other factors impacting the steroid profile have been reported, the APMU shall evaluate the need to perform CP(s) and update the APMU Report accordingly within seven (7) days. Justification not to proceed with CP(s) may include:
  - the presence of ethanol glucuronide (EtG) in a *Sample* from an *Athlete* with previous similar findings in their Passport with negative GC/C/IRMS results (indicating a pattern of alcohol abuse); or
  - communication of the existence of other *AAFs* reported for the *Sample* to the APMU by the Passport Custodian or *Testing* Authority, as applicable, which would likely lead to a maximum sanction; or
  - communication of the existence of a *Therapeutic Use Exemption (TUE)* for the *Athlete* to the APMU by the Passport Custodian or *Testing* Authority, as applicable.

  [Comment: As stated in the TD EAAS, in such cases, the Passport Custodian, or Testing Authority as applicable, shall advise the Laboratory, in writing and within fifteen (15) days following reception of the ATPF-CPR notification, whether or not to proceed with CP(s) of the Sample's steroid profile.]
- In cases when an *ATPF*-CPR is generated for two (2) or more *Samples*, which are linked to a single *Sample* Collection Session from the same *Athlete*, the APMU should advise the Passport Custodian, and *Testing* Authority as applicable, to prioritize the confirmation of the *Sample* with the highest concentration of *Markers* of the steroid profile. In such cases, the Passport Custodian, or *Testing* Authority as applicable, shall advise the Laboratory, in writing and within fifteen (15) days following reception of the *ATPF*-CPR notification, whether or not to proceed with CP(s) of the *Sample*'s steroid profile.

8.1.4 When assessing a Suspicious Steroid Profile Confirmation Procedure Request (SSP-CPR):

The APMU will receive an SSP-CPR notification through *ADAMS* when there is no existing urine steroidal Passport for the *Athlete* in *ADAMS* (*i.e.* this is the first *Sample* in the *Athlete's* steroidal Passport), and the *Sample's* "steroid profile" meets any of the following criteria:

a) T/E ratio > 4.0;

b) Concentration of T or E (adjusted for the SG) > 200 ng/mL in males or > 50 ng/mL in females;

c) Concentration of A or Etio (adjusted for the SG) > 10,000 ng/mL;

d) Concentration of 5αAdiol (adjusted for the SG) > 250 ng/mL in males or > 150 ng/mL in females.

Upon receipt of an SSP-CPR notification:

- The APMU shall assess the validity of the *Sample* generating the CP request in *ADAMS,* address any irregularities according to Article 8.2 of this *TD* and update the APMU Report accordingly.
- The APMU shall evaluate the need to perform CP(s) and update the APMU Report accordingly within seven (7) days of receipt of the SSP-CPR notification. The Passport Custodian, or *Testing* Authority as applicable, shall advise the Laboratory, in writing and within fifteen (15) days following reception of the SSP-CPR notification, whether the Laboratory shall proceed with CP(s).

  [Comment: In the absence of an ATPF-CPR or SSP-CPR, the APMU may also make a recommendation for CPs of the steroid profile, based on assessment by the APMU.]

8.1.5 Expert Review of Normal Passports

The APMU should provide the Experts from time to time with Passports for review, even when the values are within normal ranges and presenting no suspicious elements, as this will ensure that Experts are provided a balanced perspective on the *Athletes'* Passports.

8.2 Management of *Sample* Validity

8.2.1 The APMU shall assess and manage the validity of urine, blood (serum) and blood *ABP* (whole blood) *Samples* in *ADAMS* according to applicable *International Standards* and TDs, including the ISRM [1], TD EAAS [3] *International Standard* for Laboratories (ISL) [4], and the *International Standard* for *Testing* and *Investigations* (ISTI) [5].

8.2.2 Any changes in *Sample* validity made by the APMU shall be noted in applicable fields in *ADAMS* and in the APMU Report.

8.2.3 Where multiple *Samples* were provided by an *Athlete* during a single *Sample* Collection Session and are present in a Passport, the APMU shall invalidate all but one *Sample* based on assessment by the APMU.

8.2.4 Where multiple *Samples* were provided by an *Athlete* on the same day from different *Sample* Collection Sessions and are present in a Passport, the APMU may invalidate all but one *Sample* after assessment by the APMU in consultation with the Passport Custodian, as required

8.2.5 For urine *Samples* where a substance(s) that may alter the steroid profile is detected by the Laboratory (e.g., alcohol), the APMU may invalidate the *Sample* when it is considered to affect the sensitivity of the Adaptive Model to detect changes in future *Samples*.

8.2.6 For blood *ABP Samples* of suspicious profiles where the Blood Stability Score (BSS) could not be calculated, the APMU shall assess the collection-to-analysis time (CAT), any available temperature logger data, and the potential degradation of blood *Markers*, including scattergrams, in order to evaluate *Sample* validity, liaising with (an) Expert(s) as required.

8.3 The APMU Report

The APMU Report is a central element in the administrative sequence of the *ABP* that shall be entered and maintained by the APMU in *ADAMS.* The APMU Report provides an up-to-date overview of the current status of an *Athlete's* Passport together with recommendations, as appropriate, for efficient follow-up by the Passport Custodian. The APMU Report serves to update the Passport Custodian*, WADA* and other *ADOs* with whom the Passport is shared. In addition, it provides a record of events associated with a Passport in *ADAMS*.

The APMU Report may include, without limitations:

- Assessments of *Sample* validity by the APMU and/or Experts;
- Recommendations for complementary Analytical *Testing* (*e.g.,* Agents Affecting Erythropoiesis, HIF stabilizers, Homologous Blood Transfusion, confirmation of steroid profile, GC/C/IRMS, long-term steroid *Metabolites*, IGF-I analogs, Steroid Esters, hGH Isoform Differential Immunoassay etc.) on *Samples* collected;
- Recommendations for further Analytical *Testing* on *Samples* collected previously;
- Recommendations for long-term storage of *Samples* for Further Analysis;
- *Target Testing* recommendations based on available data and Experts' recommendations; and
- A summary of any recent Expert reviews.

8.3.1 APMU Reports shall be written in English and should not contain any information that could identify the *Athlete*.

8.3.2 The APMU Report shall not contain any reference to an *AAF* that may be known to the APMU, with the exception of when the *AAF* is used by the APMU as a reason not to perform CP(s) following an *ATPF*-CPR or SSP-CPR for the steroid profile (see Articles 8.1.3 and 8.1.4 of this *TD*). If the APMU assessment leads to an Expert review, the APMU may, however, separately inform the Expert(s) of the existence of the *AAF*. Depending on the result of the Expert review, the APMU shall further inform the *Results Management* Authority managing the *AAF* of the result of the Expert review, via the Passport Custodian, if that information is potentially relevant in the context of the *Results Management* based on the *AAF*.

[Comment: While Passport sharing is strongly encouraged to enhance ADO efficiencies and program effectiveness through exchange of information and mutual recognition of program outcomes, this must be carried out within the framework of the ISPPPI [2] and Article 14.1.4 of the Code [6]. The information regarding an AAF shall therefore not be recorded in the APMU Report and shall not be disclosed unnecessarily. Only those individuals and/or organizations involved in the applicable Results Management process should be privy to this information.]

8.3.3 *Target Testing* recommendations shall be included in the APMU Report with a sufficient level of detail for the Passport Custodian to conduct effective, timely and appropriate *Testing*.

8.4 Investigating Urine Exchange

When a urine *Sample* steroid profile is not consistent with other *Sample*(s) from the *Athlete's* *Passport*, urine exchange with the urine of another individual may be suspected and confirmed using DNA analysis across multiple *Samples*. This process is managed and reported according to the following steps:

- When evaluating a newly matched urine *Sample*, where other *Samples* exist in the *Athlete*'s Passport, the APMU shall evaluate the likelihood that all *Samples* are from the same individual. If a *Sample* shows inconsistency compared to others in the Passport (*e.g.* differences in *Marker* levels), the APMU shall update the APMU Report indicating "Suspicion of Urine Exchange";
- If the APMU suspects urine exchange, an investigation shall be launched by the Passport Custodian, with support from the APMU, using a combination of actions such as *Sample* storage, confirmation of the steroid profiles of relevant *Samples*, collection of additional *Samples*, and/or DNA analysis, as applicable.

8.4.1 The outcomes of this investigation may indicate:

a) Confirmation by DNA analysis that all *Samples* belong to the same *Athlete*. In this case, the APMU shall update the APMU Report accordingly.

b) Multiple DNA profiles are present: where at least two (2) different DNA profiles are identified across different *Samples*, where each urine *Sample* corresponds to a single DNA profile, however the DNA profile corresponding to the *Athlete* under investigation is not known. A strategy shall be undertaken in order to obtain additional *Samples* and the APMU shall update the APMU Report accordingly indicating "Multiple DNA Profiles Identified".

c) Confirmed urine exchange: where at least two (2) different DNA profiles have been identified, where each urine *Sample* corresponds to a single DNA profile, and the DNA profile belonging to the *Athlete* is confirmed with a reasonable degree of certainty (*e.g.* using multiple *Samples*, different *Sample* types, different *Sample* Collection Personnel). In such cases, the APMU shall update the APMU Report, indicating "Urine Exchange Confirmed".

d) Mixed *Sample*s: where multiple DNA profiles are found within individual *Samples*. In such cases, the APMU shall liaise with the Passport Custodian, or *Testing* Authority as applicable, regarding the *Sample* in question to explore whether the Laboratory should consider further investigations towards declaring an *AAF* for *Sample Tampering* or *Attempted Tampering*.

[Comment: Where Tampering or *Attempted Tampering of a Sample can be established by the analyzing Laboratory based on evidence from that Sample alone (e.g., substitution with another fluid, mixing of urines, addition of proteases to the Sample), the Laboratory can report the finding as an AAF or Atypical Finding for Tampering or Attempted Tampering (see Article 4.0 of the TD EAAS [3]). In contrast, when urine exchange can be established based on steroid profile and/or DNA evidence across multiple Samples, the APMU shall report the finding of confirmed urine exchange to the Passport Custodian, who shall proceed with Results Management according to Code Article 2.2 [6]]*

8.5 Analysis of Steroid Esters

When blood *Samples* demonstrate atypical or suspicious steroid *Markers*, or have been collected during the same *Sample* Collection Session as urine *Samples* identified with an atypical or suspicious "steroid profile", the APMU, in consultation with the Passport Custodian, should consider requesting analysis to detect the presence of Steroid Ester(s) in the associated blood *Samples*.

The detection of Steroid Ester(s) in blood also constitutes an unequivocal demonstration of the exogenous origin of the steroid(s). On the other hand, the absence of detectable Steroid Ester(s) in blood shall not invalidate an *AAF* based on the GC/C/IRMS analysis in urine.

8.6 Compiling the *ABP* Documentation Package

8.6.1 The APMU shall be responsible for compiling the *ABP* Documentation Package using the template provided by *WADA*. The Passport Custodian shall collect information and bear the cost of compiling *ABP* Documentation Packages unless it has established an agreement to share the costs with relevant *Testing* Authorities.

8.6.2 Upon request by the APMU and as needed to compile the *ABP* Documentation Package, the Passport Custodian shall provide a detailed *Athlete Competition* and altitude schedule, relevant information from *DCFs*, temperature logger and Chain of Custody documentation to the APMU.

8.6.3 The APMU shall confer with the Expert panel to determine the scope of such compilation, including the recommended elements and the number of tests that need to be included. It is only mandatory to have a full *ABP* Laboratory Documentation Package for those *Samples* that are deemed essential by the Expert panel *(*see TD LDOC [7]*)*. Other relevant *Samples*, for example those that confirm the baseline levels of a *Marker*, only require an *ABP* Laboratory Certificate of Analysis *(*see TD LDOC [7]). If the Passport Custodian is not the *Testing* Authority of the test requiring Laboratory documentation, the Passport Custodian shall coordinate with the *Testing* Authority to obtain such documentation.

[Comment: Where a Laboratory Documentation Package for specific analysis (GC/C/IRMS, ERA or hGH) is requested during the compilation of an ABP Documentation Package, a request should be addressed to the Laboratory as per specific Annexes of the TD LDOC.]

8.6.4 The following key information shall be included in an *ABP* Documentation Package regardless of the module (Hematological, Steroidal, or Endocrine):

- For the *Athlete*: age (excluding the date of birth), gender, and sport/discipline;
- For all *Samples*: date and time of collection, *ADAMS* ordinal number in the Passport, *Sample* code, *Marker* values and graphical results obtained by the Adaptive Model;
- For *Samples* selected by the APMU and Expert panel:
  - *ABP* Laboratory Documentation Package(s) and/or *ABP* Certificate(s) of Analysis from the relevant Laboratory(-ies) and/or *ABP* Laboratory(-ies) (see TD LDOC [7]); and

- The Passport Custodian shall provide Chain of Custody documentation, DCF information and a detailed *Competition* calendar covering the period defined by the selected *Samples*; and

For the Hematological Module, the following additional information shall be provided for the *Samples* selected by the APMU and Expert panel:

- Temperature profile during the transportation of the blood *ABP Sample* and, when available, the BSS; and
- Responses provided by the *Athlete* on the *ABP* Supplementary Report Form during the *Sample* Collection Session.

For the Steroidal Module, the following additional information shall be provided for the *Samples* selected by the APMU and Expert panel:

- Urine *Samples*
  - pH;
  - Specific gravity (SG);
  - Laboratory documentation, including screening and confirmed values (where applicable) of steroid concentrations and ratios (see TD LDOC [7] and TD EAAS [3]);
  - GC/C/IRMS results, where applicable;
  - Indication of ethanol consumption: urinary concentrations of ethanol and/or ethanol *Metabolite*(s);
  - Indication of microbial growth (see TD EAAS [3]); and
  - Information on the presence or absence of substances that may alter the steroid profile (see TD EAAS [3]).
- Blood *Samples*
  - Laboratory documentation, including screening and confirmed concentrations (where applicable) of steroid *Markers* (see TD LDOC [7])*;*

For the Endocrine Module, the following additional information shall be provided for the tests selected by the APMU and Expert panel:

- Laboratory documentation, including screening and confirmed concentrations (where applicable) of *Markers* of the Endocrine Module (see TD LDOC [7])*;*

9.0 References

[1] The World Anti-Doping *Code International Standard* for *Results Management*.

[2] The World Anti-Doping *Code International Standard for the Protection of Privacy and Personal Information*.

[3] *WADA Technical Document* TD EAAS: Measurement and Reporting of Endogenous Anabolic Androgenic Steroid (EAAS) *Markers* of the Urinary Steroid Profile.

[4] The World Anti-Doping *Code International Standard for Laboratories*.

[5] The World Anti-Doping *Code International Standard* for *Testing* and Investigations.

[6] The World Anti-Doping *Code.*

[7] *WADA Technical Document* TD LDOC: Laboratory Documentation Packages.

[Comment: Current versions of WADA ISL and Technical Documents may be found at https://www.wada-ama.org/en/anti-doping-partners/laboratories]

Part 4: Collaboration Agreement Template

A non-mandatory collaboration agreement template is contained herein to facilitate the exchange of relevant information and mutual recognition of *ABP* program outcomes between *ADOs* that share *Testing* jurisdiction over a single *Athlete* (e.g., *National Anti-Doping Organization* and *International Federation*). *Anti-Doping Organizations* will need to review and modify this template as necessary to ensure it complies with applicable laws.

Collaboration Agreement

Between

[•]

(hereinafter referred to as "[A]" or as a "Party")

and

[•]

(hereinafter referred to as "[B]" or as a "Party"; and collectively with [A], the "Parties")

WHEREAS the principle of the *ABP* is to have a single Passport for each *Athlete*, managed by a single *Anti-Doping Organization (ADO)* referred to as the Passport Custodian;

WHEREAS [A] is an *[ADO]* that has *Testing* jurisdiction over certain *Athletes* and wishes to perform Passport *Testing* in respect of such *Athletes*;

WHEREAS [B] is an [*ADO*] that also has *Testing* jurisdiction over those same *Athletes* and also wishes to perform Passport *Testing* in respect of such *Athletes*;

WHEREAS [A] and [B] wish to establish a framework to govern the exchange of ABP-Related Information (as defined below) and the mutual recognition of *Athlete Biological Passport (ABP)* program outcomes between [A] and [B] to enhance the efficiency and effectiveness of their respective *ABP* programs.

THEREFORE, it is agreed upon between the Parties:

Clause 1 - Definitions

Capitalized and italicized terms used in this Agreement shall have the meanings ascribed to them under the World Anti-Doping Code ("*Code*") while capitalized and underlined terms shall have the meanings ascribed thereto in an *International Standard*, both as amended from time to time. [For ease of reference, relevant definitions have been reproduced in Schedule 1 attached hereto.]

Additional definitions created for the purposes of this Agreement shall be capitalized and have the following meanings:

1.1 "*ABP*-Related Information" means any information related to the administration and management of an *ABP* program, including longitudinal profiles of biological Markers; results of the Adaptive Model on Markers data and other information relevant to the evaluation of Markers; APMU and Expert reviews; and *Doping Control* and *Results Management* information related to a relevant Passport.

1.2 "Agreement" means this Collaboration Agreement, including its preamble.

1.3 "*ABP* Operating Guidelines" means the most recent version of the *ABP* Operating Guidelines adopted by *WADA* and available on *WADA's* website (www.wada-ama.org).

1.4 "Representative" means an employee, officer, Third-Party Agent or other designated adviser or agent of a Party.

Clause 2 – Passport *Testing* and Information Sharing

2.1 Where appropriate and necessary to ensure proper coordination and efficient allocation of Passport *Testing* activities and resources between the Parties, the Parties agree to provide each other with:

(a) a list of *Athletes* (over which [A] and [B] both have *Testing* jurisdiction) within their respective Registered Testing Pool (RTP) or other testing pool (TP) who will be subject to *ABP Testing* in accordance with their test distribution plans (TDP), and to discuss the composition of such TDP with the other Party in advance; and

(b) a list of *Events* where each Party intends to conduct pre-*Competition ABP testing*.

2.2 For the avoidance of doubt, nothing in this Clause 2 shall prevent [A] or [B] from *Testing* any *Athlete* within its *Testing* jurisdiction for the purposes of its *ABP* at any time, irrespective of the *Athlete's* status on [A] or [B]'s TDP.

2.3 [A] shall conduct *Testing* of the *Athletes* in [A]'s TDP, and [B] shall conduct *Testing* of *Athletes* in [B]'s TDP, including by means of *Target Testing*. For such purposes:

(a) Each of [A] and [B] is responsible for ensuring that it has proper *Testing* jurisdiction with regard to any *Testing* activities;

(b) Each of [A] and [B] is responsible for ensuring that *Samples* are collected in compliance with the *Code*, the *International Standards*, and the ABP Operating Guidelines;

(c) Each of [A] and [B] shall each bear its own costs of *Testing* (including the costs of storage, transportation and analysis of Samples); and

(d) The Parties, either directly or through their respective APMUs may share ABP-Related Information with each other as regards the *Target Testing* of *Athletes* in [A]'s TDP or [B]'s TDP, as the case may be.

2.4 Each Party agrees that it shall, at its own cost, exclusively use *ADAMS*, and require its respective APMU to use *ADAMS*, for recording doping control forms and other *ABP*-Related Information relating to any *Athlete* tested as part of a Party's *ABP* program.

2.5 Where an *Athlete* within a Party's testing pool has been tested as part of a Party's *ABP* program, the relevant Party shall upload and record all relevant *ABP*-Related Information on *ADAMS*, or ensure that it is being uploaded and recorded by its APMU, as soon as reasonably practical following the test.

2.6 The Party designated as the Passport Custodian, in accordance with clause 3.1 below, agrees that it shall provide the other Party with read-only access to relevant *Athlete* Passports in *ADAMS*. The Parties acknowledge that they may also set specific sharing rules within *ADAMS* to permit each of them automatic access to Passports of *Athletes* over whom they both have *Testing* jurisdiction.

2.7 The Parties acknowledge and agree that where a Party has granted access to a Passport to the other Party within *ADAMS*, such other Party may share *ABP*-Related Information with its duly authorized Representatives (including its APMU and members of its Expert Panel) strictly for the purposes of its *ABP* program.

2.8 If for whatever reason a Passport or other relevant *ABP*-Related Information cannot be readily accessed by a Party through *ADAMS*, the Passport Custodian shall provide the relevant Passport or other information to the other Party in such other secure manner as the other Party may reasonably request.

Clause 3 – *Passport Results Management* Process

3.1 For each *Athlete* included in both [A] and [B]'s Registered Testing Pool or other relevant testing pool, the Parties shall agree which Party should act as Passport Custodian to maximise the effectiveness and efficiencies of each Party's respective *ABP* program, and to ensure the Passport Custodian is the Party that conducts more frequent *Testing* in respect of a given *Athlete*.

3.2 The *Passport* Custodian is responsible for *Results Management* in accordance with the then-current TD on Result Management Requirements for the *ABP* adopted by *WADA*. For *Athletes* included in both [A] and [B]'s TDP, Passports shall be reviewed after each test by the APMU

of the *Passport* Custodian independently of whether [A] or [B] was the *Testing* Authority that conducted the last Passport test.

3.3 To the extent this information is not available to the other Party via *ADAMS*, The Parties shall immediately notify each other in writing of the referral of any *Athlete*'s Passport for review by the other Party's *ABP* Expert panel in accordance with the *ABP* Operating Guidelines, as well as the outcome of such review. The Parties shall also notify each other upon request of an updated list of the members of their *ABP* Expert panel.

3.4 For the avoidance of doubt, relevant *ABP*-Related Information collected by [A] and [B] should, whenever possible, be consolidated for the purposes of pursuing a potential anti-doping rule violation (ADRV) or other *Results Management* procedure against an *Athlete* in accordance with the *Code* and *International Standards*.

3.5 Where the *Passport* Custodian decides not to proceed with an asserted ADRV in connection with a Passport, such decision will not affect the ability of the other Party or *WADA* to appeal such decision.

Clause 4 –Privacy and Security

4.1 The Parties acknowledge and agree that the sharing of *ABP*-Related Information (including Personal Information) under this Agreement is necessary to allow each Party to effectively and efficiently manage its *ABP* program and otherwise fulfill its obligations under the *Code* and the *International Standards*.

4.2 The Parties agree and acknowledge that each Party is responsible for complying with applicable data protection, privacy and data security laws as well as the *Code* and the *International Standards* with respect to any *ABP*-Related Information exchanged pursuant to this Agreement.

4.3 Without limiting the generality of the foregoing, each Party shall:

(a) ensure that it has a valid legal authority or basis to share *ABP*-Related Information with, or receive such information from, the other Party in connection with this Agreement, as the case may be;

(b) treat any *ABP*-Related Information that it receives from the other Party as confidential information at all times and only Process such information for the anti-doping purposes set out in this Agreement and in accordance with the *International Standard* for the Protection of Privacy and Personal Information (ISPPPI);

(c) protect any *ABP*-Related Information that it receives from the other Party by applying all necessary and appropriate security safeguards, including physical, organizational, technical, environmental and other measures to prevent against a Security Breach;

(d) only grant access and access privileges to any *ABP*-Related Information that it receives from the other Party to its duly authorized Representatives (including its APMU and members of its Expert panel) on a need-to-know basis;

(e) subject to clause 4.3(d) above, not disclose any *ABP*-Related Information that it receives from the other Party to any other *Person* without the express prior written consent of the other Party, unless the disclosure is otherwise required by law;

(f) ensure any *Person* (including any duly authorized Representative) with access to *ABP*-Related Information is informed of the confidential nature of such information, of the limited purposes for which it can be used, and has entered into a written agreement to preserve such confidentiality; and

(g) notify the other Party promptly of any Security Breach affecting any *ABP*-Related Information received under this Agreement and take immediate steps to rectify any such Security Breach.

Clause 5 – Effective Date and Termination

5.1 This Agreement shall become effective as of the date of the latest signature appearing on the signature page below and will remain in effect until terminated, except for clause 4 (Privacy and Security) and sub-clause 5.4 of this Agreement which shall survive termination.

5.2 Either Party may terminate this Agreement for any reason by providing thirty (30) days' written notice to the other Party.

5.3 Either Party may terminate this Agreement immediately if the other Party commits a material breach of any term of this Agreement and (if such breach is remediable) fails to remedy that breach within a period of thirty (30) days after being notified in writing of the breach.

5.4 The Parties agree that after the effective date of termination of this Agreement, and subject to applicable data protection and privacy laws, each Party may continue to use all information provided to it by the other Party pursuant to this Agreement, provided that such information is only used for anti-doping purposes in accordance with the *Code* and the *International Standards* and continues to be maintained in accordance with the privacy and security requirements set out in this Agreement, the ISPPPI and applicable laws.

Clause 6 – Authority

6.1 The Parties hereby represent that they have the full power and authority to enter into and perform this Agreement, and the Parties know of no agreement, promises, or undertakings that would prevent the full execution and performance of this Agreement.

6.2 Notwithstanding the above and for the avoidance of doubt, the Parties acknowledge and agree that nothing in this Agreement affects or modifies their respective rights and obligations, and those of other relevant third parties, under the "Agreement Governing the Use and Sharing of Information in *ADAMS*" that the Parties entered into with *WADA*.

Clause 7 - Indemnity

Each Party (the "Breaching Party") shall indemnify and hold harmless the other Party (the "Non-Breaching Party") against any and all costs, charges, damages, expenses and losses (including costs incurred in recovering same) that are incurred by the Non-Breaching Party as a result of any breach of this Agreement by the Breaching Party up to a maximum of [•].

Clause 8 – Miscellaneous

8.1 This Agreement is intended to be the sole and complete statement of obligation of the Parties as to the subject matter hereof, and supersedes all previous agreements, understandings, negotiations and proposals as to such subject matter.

8.2 The failure of either Party at any time to demand strict performance of the terms of the Agreement shall not be construed as a waiver of the right to demand or receive complete performance of all rights, promises and covenants in this Agreement.

8.3 This Agreement does not establish either Party to be the agent of the other Party or create a joint venture or similar relationship between the Parties and no Party shall have the power to obligate or bind the other Party in any manner whatsoever.

8.4 Neither Party may assign, directly or indirectly, by operation of law, change of control or otherwise, this Agreement or any of its rights and obligations hereunder, without the prior written consent of the other Party, which shall not be unreasonably withheld.

8.5 The Parties agree that any and all amendments to this Agreement must be made in writing and be signed by both Parties.

8.6 If any provision or provisions of this Agreement is be held to be invalid, illegal, or unenforceable, such provision shall be severed from this Agreement to the extent required and the validity, legality, and enforceability of the remaining provisions shall not in any way be affected or impaired thereby.

8.7 A *Person* who is not a party to this Agreement shall not have any rights under or in connection with this Agreement. The rights of the Parties to terminate, rescind or agree any variation, waiver or settlement under this Agreement are not subject to the consent of any *Person* that is not a party to this Agreement.

8.8 Section and other headings in this Agreement are for convenience of reference only and shall not constitute a part of or otherwise affect the meaning or interpretation of this Agreement.

Clause 9 - Notices

9.1 Any notice required to be given under this Agreement shall be in writing and shall be delivered personally, sent by email, fax or sent by commercial courier, to the other Party required to receive the notice at the contact information set out below:

(a) [A]:

For the attention of: [•]
Address: [•]
Email: [•]
Fax number: [•]

(b) [B]:

For the attention of: [•]
Address: [•]
Email: [•]
Fax number: [•]

or at such other address, email or fax as the relevant Party may specify by notice in writing to the other Party.

9.2 Any notice shall be deemed to have been duly given:

(a) if delivered personally, at the time of delivery at the address referred to in Clause 11.1;

(b) if delivered by commercial courier, at the time of signature of the courier's receipt;

(c) if delivered by email, at the date and time indicated on such email; or

(d) if sent by fax, at the time of transmission.

Clause 10 – Applicable Law and Jurisdiction

10.1 This Agreement and any dispute or claim arising out of or in connection with it or its subject matter shall be governed by and construed in accordance with the law of [•].

10.2 The Parties agree that any dispute, arguments or claims arising with respect to or in connection with the execution of this Agreement (as well as any subsequent amendment hereof, including, for example, its structure, validity, effectiveness, interpretation, execution, infringement or termination, and also any non-contractual claim relating hereto) shall be the object of an amicable resolution. In the absence of amicable resolution, the dispute shall be submitted to the exclusive jurisdiction of the Court of Arbitration for Sport (*CAS*) in Lausanne,

Switzerland, and settled definitively in accordance with the Code of Sports-related Arbitration. The panel will consist of one arbitrator. The language of the arbitration will be [•].

Clause 11 - Signatories

The signatories to this Agreement hereby warrant that they have read and agree to the terms, conditions and provisions of this Agreement, including any Appendices, and have full power and authority to sign for and bind their respective organizations.

Clause 12 - Counterparts

This Agreement may be executed in any number of counterparts, each of which shall be deemed an original but all of which shall constitute one and the same instrument.

In the name and on behalf of
[A]

_____

……..[Name, Position]

Date: _____

In the name and on behalf of
[B]

_____

……..[Name, Position]

Date: _____