IFHA REFERENCE LABORATORY

WHITE MANUAL

Version 5
August 2017

1. IFHA Reference Laboratory White Manual

This White Manual sets out the process which the International Federation of Horseracing Authorities (IFHA) has established for reviewing applications for laboratories wishing to be appointed as an IFHA Reference Laboratory and for the maintenance, suspension or revocation of an appointment.

2. Preamble

Objectives of the IFHA Reference Laboratory Programme

At present each racing jurisdiction has access to one or more analytical laboratories as the key infrastructure in their anti-doping controls. However, these laboratories vary in many ways, including but not limited to: scale of the laboratory, funding, equipment, staff expertise, volume of testing, number of operating years, and their capability to detect the use of prohibited substances as defined by the IFHA, especially the Major Doping Agents (MDA).

The central purpose of the IFHA Reference Laboratory programme is to foster an environment in which all races that are significant to the IFHA rankings of horses, races and jockeys are supported by analytical laboratories which the IFHA has reviewed and have been assessed by it to have certain characteristics considered important by the IFHA. These characteristics include but are not limited to the scale of operations, resourcing (floor space, equipment, staffing, funding), research activity and capability to detect the use of prohibited substances including in particular the MDA.

It should be noted that it is not intended that all racing analytical laboratories would become IFHA Reference Laboratories, and the fact that a racing analytical laboratory has not been appointed as an IFHA Reference Laboratory is in no way a reflection on the general competency of that organisation.

Pre-existing landscape

It may be noted that there is an existing framework within which racing analytical laboratories operate.

Broadly described these are the elements of this framework:

(i) Laboratory accreditation

A number of jurisdictions have relied on national or recognised accreditation bodies. These bodies assess the facility's performance based on the relevant international standard. For racing analytical laboratories this is, in most cases, ISO/IEC 17025. The review process examines a range of matters including: the qualifications, training, knowledge and experience of staff; correct equipment that is properly calibrated and maintained; adequate quality assurance procedures; appropriate testing procedures and so on. However, the scope of accreditation and the performance specification are not standardised

for horseracing laboratories, and these can be defined by the applicant laboratory.

The International Standards Organisation (ISO) is a non-governmental international organisation which develops market relevant International Standards which are voluntary and consensus-based. The ISO has published ISO/IEC 17025 "*General Requirements for the Competence of Testing and Calibration Laboratories*". This standard specifies the general requirements for the competence to carry out tests and/or calibration. It covers testing and calibration performed using standard methods, non-standard methods and laboratory-developed methods. The standard is intended for use by laboratories in developing their management system for quality, administrative and technical operations. Laboratory customers, regulatory authorities and accreditation bodies may also use it in confirming or recognising the competence of laboratories.

(ii) ILAC – G7

International Laboratory Accreditation Cooperation (ILAC) is the international authority on laboratory and inspection body accreditation, with a membership consisting of accreditation bodies and stakeholder organisations throughout the world. Its core purpose is to promote international acceptance of the equivalence of calibration, test and inspection reports produced by accredited facilities.

ILAC has published ILAC – G7 "*Accreditation Requirements and Operating Criteria for Horseracing Laboratories*". The purpose of ILAC – G7 is to **amplify** the general requirements laid down in ISO/IEC 17025 as they apply to the particular circumstances of horseracing laboratories. Specifically, ILAC – G7 consists of three parts:

Part A provides interpretation of some of the requirements of ISO/IEC 17025 for horseracing laboratories. It consists of a compilation of test-method-related requirements for horseracing laboratories that accreditation bodies have put forward.

Part B contains recommendations for establishing the presence of prohibited substances that have been agreed within the horseracing industry.

Part C contains the following recommendations: (i) compliance with an appropriate performance specification as required by the relevant authority; and (ii) adoption of harmonised definitions for terms commonly used by racing chemists.

(iii) Association of Official Racing Chemists

The Association of Official Racing Chemists (AORC) consists of individuals, not laboratories. It has almost 200 members concerned with the detection of drugs in racing animals.

The AORC has developed a series of guidelines and recommendations for use by racing chemists:

- AORC Guidelines for the Minimum Criteria for Identification by Chromatography and Mass Spectrometry;
- AORC Guidelines for Referee Analysis;
- AORC Proficiency Testing Urine Drug List and the AORC Proficiency Testing Plasma Drug List (current versions);
- AORC Guidelines for Controlling the Application of Screening Limits; and
- A Glossary of Terms Commonly Used in Racing Chemistry.

(iv) Article 6 of IFHA International Agreement on Breeding, Racing and Wagering

Article 6 of the International Agreement on Breeding, Racing and Wagering (IABRW) stipulates that the aim of signatory countries is that their laboratories should:

- be accredited according to ISO/IEC 17025, and to the supplementary document ILAC-G7;
- conform with the Guide for establishing the presence of prohibited substances (Part B of ILAC-G7);
- meet the Performance specification of the International Federation of Horseracing Authorities;
- take part in inter-laboratory comparisons;
- control the detection of legitimate therapeutic substances through the application of internationally harmonised screening limits which have been recommended by the IFHA's Advisory Council on Equine Prohibited Substances and Practices and selectively adopted by the relevant signatory countries; and
- control the detection of certain environmental substances through the application of internationally harmonised residue limits which have been recommended by the IFHA's Advisory Council on Equine Prohibited Substances and Practices and selectively adopted by the relevant signatory countries.

3. Reference Laboratory Appointment Committee

a. The Reference Laboratory Appointment Committee (RLAC) is an agency of IFHA.

b. The IFHA Executive Director shall be the Chairman of the RLAC and other members may be appointed by the Executive Council from time to time.

c. The purpose of the RLAC is to decide on the appointment, suspension and revocation of appointment as an IFHA Reference Laboratory.

d. In considering an application for appointment or determining whether to suspend or revoke an appointment the RLAC may inform itself by any means it considers useful.

e. Amongst other things the RLAC may appoint assessors to carry out "on site" assessment, review documentation, and may arrange Proficiency Testing (PT) to be conducted.

f. The RLAC administers a PT Scheme and a Negative Samples Exchange Program for the IFHA Reference Laboratories.

4. Reference Laboratory Technical Committee

a. The Reference Laboratory Technical Committee (RLTC) is an agency of the IFHA.

b. Members of the RLTC may be appointed by the Executive Council on the advice of the RLAC from time to time.

c. The purposes of the RLTC are to:

- Train assessors appointed by the RLAC
- Act as a source of advice to assessors on individual assessments
- Act as a source of advice to the RLAC on individual assessments
- Act as a source of advice to the RLAC on revisions to the White Manual
- Carry out such other functions as the RLAC or the Executive Council may give to it from time to time

5. Process and Requirements for IFHA Reference Laboratory Appointment

This section describes the specific requirements that a laboratory shall fulfill in the process of applying for, obtaining, and maintaining appointment as an IFHA Reference Laboratory.

5.1 Applying for IFHA Reference Laboratory appointment

The application to be appointed as an IFHA Reference Laboratory must have received the support of and be presented by a racing authority, regional association, or national association that is a member of the IFHA.

5.1.1 Submit application

The laboratory shall complete an application form approved by the RLAC (Annexure A).

Note: The RLAC may require an update of this information during the process of assessment.

All documentation must be delivered to the RLAC in order for the applicant to be considered for appointment. An attachments checklist (Annexure B) may be used to assist the submission of relevant documentation. The completed application shall be signed by the Head of the Laboratory.

5.1.2 Assessment fees & charges

The application shall be accompanied by the administrative fee set by the RLAC. If the preliminary assessment by the RLAC is satisfactory, the applicant will be considered as a candidate laboratory, which will then be responsible for meeting the costs of proficiency testing and on-site assessment.

5.1.3 Initial assessment

The RLAC will carry out an initial assessment of the application. If the RLAC is satisfied on the basis of the documentation provided, that the candidate may satisfy the threshold criteria for appointment then proficiency testing will be arranged and an assessment team (comprising one or more assessors) will be appointed to carry out an on-site inspection. If the RLAC determines on the basis of the documentation provided that the applicant has not met the threshold criteria, then it may at its absolute discretion reject the application.

5.1.4 Proficiency Testing (PT)

A set of approximately 5 PT samples consisting of equine urine, plasma and hair will be prepared and dispatched to the candidate laboratory. Each PT sample will contain one unknown substance at or above the concentration as outlined in Annexure C.

The candidate laboratory shall successfully identify, and if relevant quantify, the substances detected. It shall provide a report within 3 weeks from receipt of the PT samples.

All analytical data must be kept by the candidate laboratory, to be reviewed by the assessor and possibly by the RLAC.

5.1.5 Site visit

The RLAC-appointed assessor(s) will carry out an on-site assessment after the reported results of the PT samples have been agreed by the RLAC as being satisfactory (i.e., all unknown substances identified and no false positive reported).

An appeal against the results of the proficiency testing shall be dealt with according to the procedures set out in Sections 2.4 and 4.10 of the AORC Proficiency Testing SOP, with the RLAC Chairman acting as the PT Program Coordinator, the RLAC acting as the PT Committee. The IFHA Executive Council will be informed of the appeal, investigation outcome, decision and recommendation. Any appeal against the results of the proficiency testing that cannot be resolved between the appellant and the RLAC may be referred to the IFHA Executive Council.

5.1.6 Report

Within approximately one month after the site visit, the assessment team will submit a confidential report to the RLAC. In preparing the report, the assessor(s) may have regard to the matters set out in Annexure D and to any other matters which in his, her or their judgment are relevant. The assessment team may make a recommendation on whether an appointment should be made or, if this is not the case, may identify deficiencies to be corrected or needed improvements in order to be considered for appointment.

The RLAC may at its absolute discretion copy the assessment team's confidential report or provide a summary of the report to the candidate laboratory.

5.1.7 RLAC's decision

A decision by the RLAC to reject a candidate laboratory's application is subject to review by the IFHA Executive Council on an application by the head of the candidate laboratory.

If RLAC determines that the candidate laboratory has failed its application, it cannot re-apply for appointment within 12 months from the date of notification.

5.1.8 Issue and publication of award of appointment

A document signed by the President of the IFHA or his nominated delegate shall be issued in recognition of appointment. A list of IFHA Reference Laboratories will be available on the IFHA's website.

5.2 Maintaining appointment as an IFHA Reference Laboratory

The IFHA Reference Laboratories shall successfully participate in the RLAC PT Scheme and the Negative Sample Exchange Program. In the normal course, an on-site reassessment will take place every 3 to 4 years. However, the RLAC reserves the right to assess and inspect an IFHA Reference Laboratory at any time. The notice of the assessment/inspection will be made in writing to the Head of the IFHA Reference Laboratory.

An IFHA Reference Laboratory shall continually comply with the criteria set out in Annexure A. The RLAC may at its absolute discretion request documentation from an IFHA Reference Laboratory relevant to the criteria set out in Annexure A.

Failure of an IFHA Reference Laboratory to provide timely information requested by the specified date shall be considered a refusal to cooperate and may result in suspension or revocation of appointment.

5.3 Suspension of appointment

Whenever the RLAC has substantive reason to believe that suspension of appointment may be required and that immediate action is necessary the RLAC may immediately suspend a laboratory's appointment.

The period and terms of suspension shall be proportionate to the seriousness of the non-compliance(s) or lack of performance. A period of suspension shall be up to 12 months, during which time any non-compliance or identified deficiency must be corrected, documented and reported to the RLAC at least six (6) weeks before the end of the suspension period. Delay in submitting the proper corrective and preventive action reports may lead to an extension of the suspension period. If any non- compliance or identified deficiency is not corrected during the suspension period, the Reference Laboratory appointment will be revoked, unless a one-time only extension of the suspension period, not to exceed two (2) months, is granted by the RLAC.

A decision by the RLAC to suspend an appointment is reviewable by the IFHA Executive Council on application by the relevant laboratory within 5 working days of being notified .

5.4 Revocation of appointment

The RLAC may revoke the appointment of a laboratory. A decision by the RLAC to revoke an appointment is reviewable by the IFHA Executive Council on application by the relevant laboratory within 5 working days of being notified .

If a laboratory, whose appointment has been revoked, should seek a new appointment at a time agreed by the RLAC, it shall begin the process as a new applicant laboratory as described in Section 5.1.

5.5 Notification

5.5.1 Written notice

When a laboratory's appointment is suspended or revoked, the RLAC shall immediately serve the laboratory with written notice of the suspension or revocation. This notice shall state the following:

1) The reason for suspension or revocation;

2) The terms of the suspension or revocation; and

3) The period of suspension.

5.5.2 Effective date

Subject to any application to the IFHA Executive Council for review of the RLAC decision, a suspension is immediately effective. A revocation is effective sixty (60) calendar days after the date of the written notice or, if a review is requested, upon the Executive Council's decision to uphold the proposed revocation. A Reference Laboratory that has received notice that its appointment is in the process of being revoked shall be immediately suspended until the revocation is made final or is rescinded by the IFHA Executive Council.

ANNEXURE A

IFHA Reference Laboratory Threshold Criteria

	Criteria	Criteria met (Yes/No)	Information
1	Major provider of testing services to racing authority(ies)		List authorities being served:
2	Minimum of 5 years' experience of doping control testing		Years of relevant experience:
3	Analysed at least 20 B-samples in the last 5 years		No. of B-samples analysed:
4	At least two Professional Members of the AORC		Names of AORC Professional or Fellow members:
5	ISO/IEC 17025 accreditation for testing a comprehensive range of drugs in both equine urine and blood, including representatives of all classes in Article 6E of the IABRW of the IFHA.		Provide copies of the scope of accreditation and the last assessment report:
6	Operating in accordance with ILAC-G7 and the guidelines listed therein.		
7	Demonstrated capability to meet the IFHA Performance Specification and the latest version of the AORC PT drug lists in horse urine and horse plasma		Provide a list of Limits of Detection for these substances:
8	♦ No false positive and no more than two (2) false negative results <u>in total</u> in the AORC PT Programme (plasma must be included from 2015) plus, for maintaining appointment, in the RLAC's PT Scheme and Negative Samples Exchange Program in the last three years. ♦ No false positive result from any other PT or samples exchange programmes for at least 3 years.		Provide copies of the reports from all PT and samples exchange programmes participated in the past 3 years:

9	Evidence of contributions to the advancement of racing chemistry: at least 2 peer-reviewed publications on racing chemistry in the past 5 years or at least 2 papers or presentations in the last three ICRAVs.		List relevant publications or presentations:
10	Minimum of 5000 horseracing regulatory samples analysed per year, with no false positive result for the last 3 years.		List the no. of horseracing regulatory samples analysed in the past 3 years, drugs reported, and any false positive reported:
11	Capability to identify the prohibited substances referred to in Annexure C at the required concentrations in the relevant medium.		Provide a list of the Limits of Detection for these substances:
12	Control the detection of legitimate therapeutic substances through the application of IFHA/ARF Screening Limits (or RMTC/ARCI reporting limits).		Provide a list of the Limits of Detection (or Limits of Quantification) and the applicable limits for these substances:
13	Control the detection of environmental substances through the application of residue limits where inadvertent exposure is a relevant risk in the jurisdiction		Provide a list of the Limits of Detection (or Limits of Quantification) and the applicable limits for these substances:

Additional supporting documentation to be provided:

☐ Laboratory organizational chart;
☐ List of technical, administrative, and research staff members and their qualifications;
☐ Schematic representation of the laboratory facilities, including square footage, describing functional areas (e.g., sample reception area, GC-MS and LC-MS instrument rooms, sample storage area, etc.), and identifying secure entrances and exits. Photographs and floor plans may be included.

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Date and Signature of the Head of the Laboratory

ANNEXURE B

IFHA Reference Laboratory Appointment

Attachments Checklist:

Documents to be submitted for:

☐ Initial assessment ☐ Re-assessment

List of attachments:

☐ Laboratory organisation chart

☐ List of technical, administrative, and research staff members and their qualifications

☐ Schematic representation of the laboratory facilities, including square footage, describing functional areas, and identifying secure entrances and exits.

☐ Documents from the major client(s) or racing authority(ies) supporting the applicant laboratory

☐ Scope of accreditation

☐ Last assessment report from the accreditation body

☐ Limits of Detection for the substances in the IFHA Performance Specification and latest version of the AORC PT drug lists

☐ Summary of all Proficiency Test (PT) and negative samples exchange results for the past 3 years

☐ Publications in the past 5 years and/or papers or presentations in the last 3 ICRAV meetings

☐ No. of horseracing regulatory samples tested in the past 3 years and record of any false positive

☐ List of drugs reported in the past 3 years

☐ Number of reference standards and a list of MDAs (shown in Annexure C) available in the applicant laboratory

☐ Test procedures, validation reports and limits of detection for the MDA listed in Annexure C

☐ Limits of Detection (or Limits of Quantification) and the applicable limits for controlling the use of legitimate therapeutic substances and inadvertent exposure to environmental substances

☐ A representative Laboratory Document Package submitted for a positive A-sample

☐ Other documents (please specify)

Prohibited Substances List for IFHA Reference Laboratories

ANNEXURE C
Version 3
Revision date 24 May 2017

Proficiency testing		
Matrix	Analytes	Concentrations
Urine	16β-hydroxy stanozolol (metabolite of stanozolol)	**100 pg/mL**
	5α-estrane-3β,17α-diol (metabolite of nandrolone)	**2 ng/mL**
	Norethandrolone	**2 ng/mL**
	Andarine (S4)	**50 pg/mL**
	Ostarine (S22)	**50 pg/mL**
	Clenbuterol	**100 pg/mL**
	FG4592	**100 pg/mL**
	Cobalt	**100 ng/mL (threshold, quantitative analysis required)**
	4-hydroxy testosterone (metabolite of formestane)	**5 ng/mL**
	6α-hydroxyandrost-4-ene-3,17-dione (metabolite of 6-OXO)	**50 ng/mL**
	Tamoxifen	**1 ng/mL**
	GW1516	**100 pg/mL**
	AICAR	**400 ng/mL**
Plasma	Stanozolol	**50 pg/mL**
	Formestane	**250 pg/mL**
	4-Androstene-3,6,17-trione (6-OXO)	**250 pg/mL**
	GW1516	**100 pg/mL**
	Clenbuterol	**20 pg/mL**
	Cobalt	**25 ng/mL (threshold, quantitative analysis required)**
Hair	Testosterone undecanoate	**10 pg/mg**
	Testosterone decanoate	**10 pg/mg**
	Testosterone propionate	**10 pg/mg**
	Stanozolol	**10 pg/mg**
	Clenbuterol	**10 pg/mg**
	Zilpaterol	**10 pg/mg**
	Boldenone undecylenate	**10 pg/mg**

On site assessment		
Matrix	Analytes	Concentrations
Urine	rHuEPOs (in either urine or plasma)	**100 pg/mL**
	GHRP2	**100 pg/mL**
	GHRP6	**100 pg/mL**
	Terbutaline	**200 pg/mL**
Plasma	Testosterone propionate	**50 pg/mL**
	Testosterone undecanoate	**50 pg/mL**
	Testosterone decanoate	**50 pg/mL**
	Boldenone undecylenate	**50 pg/mL**
	Salbutamol	**100 pg/mL**
	rHuEPOs (in either urine or plasma)	**100 pg/mL**
	Minimum of three different rGHs (e.g., reGH, rpGH, rbGH, roGH, rhGH…)	**50 ng/mL**
	IGF-1	**screening only**
	GHRP2	**100 pg/mL**
	GHRP6	**100 pg/mL**
	TB500 (N-Ac LKKTETQ)	**250 pg/mL**
	Dermorphin	**250 pg/mL**

Note:
(1) This list is not exhaustive. The laboratory should cover other substances under the same class, typified from the analytes in this Prohibited Substances List.
(2) For the purpose of this assessment, please do not report drugs as present if measured concentration reads less than 20% of the targeted concentration stated in this list.

ANNEXURE D

IFHA REFERENCE LABORATORY APPOINTMENT ASSESSMENT GUIDE

1. GENERAL

ISO ACCREDITATION SCOPE

- Last assessment/reassessment results
- Is accreditation for a flexible scope?
- All matrices of horse urine, blood and hair covered by accreditation (could be or not covered by flexibility in some countries).

QUALITY ASSURANCE

- Compliance with ILAC-G7?
- Performance in PT and Samples Exchange programs
- Internal audit records
- Last annual system review record/report

SAMPLES

- How many samples analysed/year
- Substances reported
- Reporting/turnaround time
- Experience in B-sample analyses

EQUIPMENT, METHODOLOGY, AND LAB FLOOR AREA

- Limits of detection, and
- Compliance with IFHA Performance Spec and AORC PT Drug Lists
- Compliance with Annexure C.

STAFF

- Number (FTE), qualifications and experience
- Dedicated to screening, confirmation (including quantification) and research

ACCESS TO REF STDs

- MDA
- Others

RESEARCH

- Staff dedicated to research and method development.
- Brief descriptions of ongoing and recently completed R&D projects
- Recent publications and presentations

2. RESULTS of RLAC's PT

   - Documentation and data provided

3. ON SITE ASSESSMENT (unstable drugs)

   - Procedures in place
   - Vertical audit of a reported case
   - Validation of relevant analytical methods (routine or dedicated analytical line).

4. CONCLUSION