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Written by:	WADA Laboratory Expert Group	Approved by:	WADA Executive Committee
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MINIMUM REQUIRED PERFORMANCE LEVELS FOR DETECTION AND IDENTIFICATION OF NON-THRESHOLD SUBSTANCES

In order to ensure that all *WADA*-accredited Laboratories can report the presence of *Prohibited Substances*, their *Metabolite(s)* or their *Marker(s)* in a uniform way, a minimum routine detection and identification capability for testing methods has been established. It is recognized that some Laboratories will be able to identify a wider range or lower concentrations of *Prohibited Substances* than other Laboratories. While such individual capabilities are encouraged in order to improve the overall system, it is also recognized that there are Minimum Required Performance Levels (MRPL) at which all Laboratories shall operate.

1. Minimum Required Performance Levels (MRPL)

The MRPL is an analytical parameter of technical performance with which the Laboratories shall comply when testing for the presence of a particular *Prohibited Substance*, its *Metabolite(s)* or *Marker(s).* The MRPL is the concentration of a *Prohibited Substance* or *Metabolite* of a *Prohibited Substance* or *Marker* of a *Prohibited Substance* or *Method* that Laboratories shall be able to routinely detect and identify.

- The MRPL is not a threshold (T) nor is it a Limit of Detection (LOD). *Adverse Analytical Findings* may result from concentrations below the established MRPL values;
- MRPL values are relevant for the detection and identification of Non-Threshold Substances; they do not apply to Threshold Substances, which are covered in other Technical Documents (e.g. TDDL[1], TD19NA[2]);
- MRPL values are established taking into account the metabolism, stability, pharmacokinetics and pharmacodynamics of the *Prohibited Substance*. Thus, substances with a long-term doping effect (e.g. anabolic steroids) will have lower MRPL values than substances which are taken for an immediate ergogenic effect (e.g. stimulants);
- The MRPL is established for the *Prohibited Substance* itself and/or its *Metabolite(s)* or *Marker (s)* or degradation product(s) depending on the extent of their metabolism and/or stability in the *Sample* matrix.

[1] *WADA* Technical Document TDDL: Decision Limits for the Confirmatory Quantification of Threshold Substances.

[2] *WADA* Technical Document TD19NA: Harmonization of Analysis and Reporting of 19-Norsteroids Related to Nandrolone.
http://www.wada-ama.org/en/Science-Medicine/Anti-Doping-Laboratories/Technical-Documents/

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Table 1. MRPLs for detection of Non-Threshold *Prohibited Substances* in human urine

Prohibited Class	Specific Examples / Exceptions	MRPL[a]
S1.1a Exogenous anabolic Androgenic Steroids (AAS)		5 ng/mL
	Dehydrochlormethyltestosterone	2 ng/mL
	Metandienone	2 ng/mL
	Methyltestosterone	2 ng/mL
	Stanozolol	2 ng/mL
S1.2 Other Anabolic Agents	Clenbuterol	0.2 ng/mL
S3. Beta-2 Agonists[b]		20 ng/mL
S4. Hormone Antagonists and Modulators	Aromatase inhibitors, SERMs and other anti-estrogenic substances	20 ng/mL
	Formestane[c]	50 ng/mL
S5. Diuretics and other Masking Agents		200 ng/mL
S6. Stimulants		100 ng/mL
	Octopamine	1000 ng/mL
S7. Narcotics		50 ng/mL
	Buprenorphine	5 ng/mL
	Fentanyl (and derivatives)	2 ng/mL
S8. Cannabimimetics		1 ng/mL
S9. Glucocorticosteroids		30 ng/mL
	Budesonide (6β-hydroxy-budesonide)[d]	30 ng/mL
P2. Beta-Blockers		100 ng/mL

[a] In each case, the MRPL applies to the parent compound or appropriate *Metabolite(s)* or *Marker(s)* depending on each substance's biotransformation pathways, excretion profile and/or stability in the *Sample* matrix.

[b] Salbutamol and Formoterol are considered Threshold Substances; therefore their determination and reporting is covered in the Technical Document on Decision Limits (TDDL)[1].

[c] GC-C-IRMS analysis shall be conducted before reporting an *Adverse Analytical Finding* for *Samples* containing formestane between 50 ng/mL and 150 ng/mL (after adjustment for the specific gravity of the *Sample* when SG > 1.020). Refer to the Technical Document on GC-C-IRMS [3].

[d] For detection of budesonide administration *via* systemic routes, Laboratories shall target the detection of the 6β-hydroxy-budesonide metabolite.

[3] *WADA* Technical Document TDIRMS: Detection of synthetic forms of Endogenous Anabolic Androgenic Steroids by GC-C-IRMS.

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2. Limit of Detection (LOD) of the Initial Testing Procedure

The Laboratory's method validation of the Initial Testing Procedure shall include the estimation of the LOD for each Non-Threshold Substance or its representative *Metabolite(s)* or *Marker(s)* using the relevant reference material, when available. It is not necessary to estimate the LOD for all potential *Metabolites* of a given Non-Threshold Substance. The estimated LOD shall be not higher than 50% of the MRPL. In the absence of a suitable reference material for a specific Non-Threshold Substance or its representative *Metabolite(s)* or *Marker(s)*, the LOD will be assumed to be similar to that of a related *Prohibited Substance* of the same class.

When detecting Non-Threshold Substances using chromatography and mass spectrometry methods, the LOD is expressed as the minimum concentration of the analyte that can be detected with reasonable certainty in urine. The estimation of the LOD is based on the *Signal-to-Noise (S/N)* ratio, which may be obtained by comparing measured signals from samples with known low concentrations of analyte with those of blank samples. A *S/N* ratio of 3 is generally considered acceptable. However, other widely recognised procedures may be applied.

3. Confirmation Procedure

The Laboratory shall document that the Confirmation Procedures for Non-Threshold Substances allow the identification of every Non-Threshold Substance or its representative *Metabolite(s)* or *Marker(s)* (in compliance with the Technical Document on Identification Criteria for Qualitative Assays, TD IDCR[4]) at the MRPL.

4. Reporting of Non-Threshold Substances

A confirmed identification of a Non-Threshold Substance at any concentration shall be reported as an *Adverse Analytical Finding*, with the following exceptions:

- Non-Threshold Substances in classes S6, S7, S8, S9 and P2, which are prohibited *In-Competition* only, should not be reported below 50% of the MRPL.
- Glucocorticosteroids should not be reported below the MRPL.
- The detection of hydromorphone in urine constitutes an *Adverse Analytical Finding* unless it is determined to be the result of the administration of a permitted substance such as hydrocodone.

  Also, Laboratories should not report hydromorphone at levels below the MRPL when the finding could be the result of a minor biotransformation of morphine, which is also detected at much higher concentrations in the *Sample.*

[4] *WADA* Technical Document TDIDCR: Identification Criteria for Qualitative Assays incorporating Column Chromatography and Mass Spectrometry.
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5. References

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1. WADA Technical Document TDDL: Decision Limits for the Confirmatory Quantification of Threshold Substances.
2. WADA Technical Document TD19NA: Harmonization of Analysis and Reporting of 19-Norsteroids Related to Nandrolone.
3. WADA Technical Document TDIRMS: Detection of synthetic forms of Endogenous Anabolic Androgenic Steroids by GC-C-IRMS.
4. WADA Technical Document TDIDCR: Identification Criteria for Qualitative Assays incorporating Column Chromatography and Mass Spectrometry.