

Document Number:	TL24	Version Number:	1.0
Written by:	WADA WG on Contaminants	Approved by:	WADA Executive Committee
Date:	20 May 2021	Effective Date:	1 June 2021

***MINIMUM REPORTING LEVEL FOR CERTAIN DIURETICS THAT ARE KNOWN CONTAMINANTS OF PHARMACEUTICAL PRODUCTS***

## 1.0 Introduction

WADA wishes to draw the attention of the Laboratories and *Anti-Doping Organizations (ADOs)* in charge of *Results Management* (the Results Management Authority, or RMA) to the following observations and instructions on the reporting of certain diuretics (namely, acetazolamide, bumetanide, furosemide, hydrochlorothiazide, torasemide, and triamterene), which are known to be found as contaminants of some legitimate pharmaceutical products.

Diuretics may be abused to mask the presence in urine of other *Prohibited Substances*. However, trace quantities of the six (6) diuretics named above have been found as contaminants in oral pharmaceutical products, including both products available by prescription and products available over the counter. While these products are still compliant with purity levels required by good manufacturing practices, the trace quantities of diuretics found in such products are sufficient to cause an *Adverse Analytical Finding (AAF)*.

At estimated urinary concentrations of 20 ng/mL or less, a diuretic would not be effective to mask the presence of any other *Prohibited Substances* that may be present in the *Sample*. Therefore, the new *Minimum Reporting Level (MRL)* for the six (6) diuretics identified above, set at 20 ng/mL, will minimize the risk of sanctioning *Athletes* who test positive due to the use of contaminated medications, without undermining the fight for clean sport.

## 2.0 Reporting Requirements

- The presence in urine of one or more of these six (6) diuretics, namely acetazolamide, bumetanide, furosemide, hydrochlorothiazide, torasemide, and triamterene, or, when applicable, of their *Metabolite(s)* / degradation product(s) [e.g. chloraminophenamide (ACB), which is a degradation product of hydrochlorothiazide], in each case at an estimated concentration greater than (>) 20 ng/mL, shall be reported as an *Adverse Analytical Finding (AAF)*.
- The presence in urine of one or more of these six (6) diuretics, namely acetazolamide, bumetanide, furosemide, hydrochlorothiazide, torasemide and triamterene, and their *Metabolite(s)* / degradation products, at an estimated concentration at or below ( $\leq$ ) 20 ng/mL, shall be reported as a Negative Finding;
- As the sole exception to this new *MRL* for acetazolamide, bumetanide, furosemide, hydrochlorothiazide, torasemide, and triamterene, where a *Sample* is collected from an *Athlete* participating in a sport or discipline that uses weight classes (see Annex 1), Laboratories shall report the presence of one or more of these six (6) diuretics (or their *Metabolite(s)*/degradation products) at an estimated concentration equal to or below ( $\leq$ ) the *MRL* of 20 ng/mL as an *Atypical Finding (ATF)*, triggering a mandatory investigation by the RMA to determine whether an anti-

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doping rule violation (ADRV) should be asserted.<sup>1</sup>

*[Comment (1): The rationale for this exception is that diuretics may be abused to induce weight loss in sports/disciplines where Athletes need to meet weight criteria. This risk exists both In-Competition and Out-Of-Competition. Therefore, when a Laboratory reports the presence of one or more of the six (6) diuretics identified above (or their Metabolites or degradation products) at an estimated concentration of 20 ng/mL or less in the Sample of an Athlete competing in such a sport or discipline, the RMA shall conduct an investigation to determine whether it is appropriate in all the circumstances to bring proceedings asserting commission of an ADRV.]*

*[Comment (2): As a consequence of this new MRL for these six (6) diuretics, footnotes (e) and (g) of TD2019MRPL, relating to the detection of Threshold Substances (salbutamol, formoterol, cathine, ephedrine, methylephedrine and pseudoephedrine) shall be amended as:*

*e. Salbutamol and formoterol are considered Threshold Substances; therefore, their determination and reporting are covered in the TD DL. When detected in conjunction with a diuretic subject to an MRL (at levels higher than (>) the corresponding MRL of 20 ng/mL), or in the presence of any other diuretic or a masking agent (at any concentration), salbutamol and formoterol shall be reported as an AAF at any concentration.*

*g. Cathine, ephedrine, methylephedrine and pseudoephedrine are considered Threshold Substances; therefore, their determination and reporting are covered in the TD DL. When detected in conjunction with a diuretic subject to an MRL (at levels higher than (>) the corresponding MRL of 20 ng/mL), or in the presence of any other diuretic or a masking agent (at any concentration), these stimulants shall be reported as an AAF only if present above the MRL established for stimulants (i.e. 50 ng/mL).*

*In addition, Articles 2.1 and 2.2 of TD2021DL shall be amended as follows:*

#### *2.1 Beta-2 Agonists - Formoterol and Salbutamol*

*The confirmation of salbutamol and formoterol requires only the identification of the compound, and not its quantification, if any of these two exogenous Threshold Substances is detected in a Sample in conjunction with either:*

- a prohibited diuretic, which is subject to a Minimum Reporting Level (MRL) and is present in the Sample at levels higher than (>) the MRL, or*
- any other diuretic (not subject to an MRL) or a masking agent, which is present in the Sample at any level.*

*In such cases, the Laboratory shall:*

- Perform the Confirmation Procedure (CP) for the diuretic/masking agent and report the results as an AAF;*
- Perform the (qualitative) CP for the beta-2 agonist and report the results as an AAF if identified at any concentration level in compliance with the TD IDCR, unless there is an approved TUE for the beta-2 agonist (see ISL 2021, Article 5.3.6.2.2).*

#### *2.2 Stimulants - Cathine, Ephedrine, Methylephedrine and Pseudoephedrine*

*The confirmation of these exogenous Threshold Substances requires only the identification of the compound, and not its quantification, if any of these exogenous Threshold Substances is detected in a Sample in conjunction with either:*

- a prohibited diuretic, which is subject to an MRL and is present in the Sample at levels higher than (>) the MRL, or*

<sup>1</sup> A Stakeholder Notice will be published, detailing the mandatory investigative process.

## WADA Technical Letter – TL24

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- any other diuretic (not subject to an MRL) or a masking agent, which is present in the Sample at any level.

*In such cases, the Laboratory shall:*

- Perform the CP for the diuretic/masking agent and report the results as an AAF;
  - Perform the (qualitative) CP for the stimulant and report the results as an AAF if identified, in compliance with the TD IDCR, at an estimated concentration level greater than (>) the applicable MRL for stimulants (as defined in the TD MRPL), unless there is an approved TUE for the stimulant (see ISL 2021, Article 5.3.6.2.2).]
- In each case, when the specific gravity (SG) of the urine *Sample* in question (as measured in the Laboratory) is greater than (>) 1.018, the concentration of the substance estimated in the *Sample* shall be adjusted prior to reporting according to the following equation:

$$\text{(Eq. 2) } \text{Conc}_{\text{adj}} = \frac{(1.020 - 1)}{(\text{SG}_{\text{Sample\_Max}} - 1)} \cdot \text{Conc}_{\text{measured}}$$

*Refer to the effective TD DL for instructions on calculating  $\text{SG}_{\text{Sample\_Max}}$ .*

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## ANNEX 1 Sport/Disciplines with Relevant Weight Classes

- Sports and Disciplines of Olympic and IOC Recognized International Federations, and members of the Alliance of Independent Recognized Members of Sport

SPORT	DISCIPLINE
Arm Wrestling	Arm Wrestling
Bodybuilding	Bodybuilding
Boxing	Boxing
Ju-Jitsu	All
Judo	Judo
Karate	Karate
Kickboxing	All
Muaythai	Muaythai
Powerlifting	All
Sambo	Sambo
Savate	All
Sumo	Sumo
Taekwondo	Sparring
Tug of War	Tug of War
Weightlifting	Weightlifting
Wrestling	All
Wushu	Sanda

- Sports and Disciplines of *Athletes* with an Impairment

### IPC Sports

SPORT	DISCIPLINE
Para-Powerlifting	Para-Powerlifting

### Non-IPC Sports

SPORT	DISCIPLINE
Arm Wrestling	Para-Arm Wrestling
Judo	Para-Judo
Taekwondo	Para-Taekwondo-Kyorugi