WADA Technical Letter – TL23 Growth Promoters

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Written by: Reviewed by:	*WADA* WG on Contaminants WADA Laboratory Expert Advisory Group	Approved by:	*WADA* Executive Committee
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Minimum Reporting Level for Certain Substances Known to be Potential Meat Contaminants

1.0 Introduction

WADA wishes to draw the attention of the Laboratories and *Anti-Doping Organizations* in charge of *Results Management* (the *Results Management* Authority, or RMA) to the following observations and instructions on the reporting of certain *Prohibited Substances*, which seek to address the fact that these substances may be used as growth promoters for livestock in some countries and therefore may be associated with findings resulting from the consumption of contaminated meat.

a) **Clenbuterol** is used in China, Guatemala and Mexico, for cattle, lamb, poultry, and swine.

b) **Ractopamine** is used in many countries for cattle, swine, and large breed turkeys.

c) **Zeranol** is used in many countries for cattle.

d) **Zilpaterol** is used in many countries for cattle.

2.0 Reporting Requirements

All of the scientific evidence indicates that it is highly unlikely that consumption of edible tissue from livestock treated with any of these growth promoters would lead to urinary concentrations greater than (>) 5 ng/mL.

Therefore:

a) The presence in urine of one or more of these substances, namely clenbuterol, ractopamine, zeranol and zilpaterol, at an estimated concentration greater than (>) a *Minimum Reporting Level* (*MRL*) of 5 ng/mL shall be reported as an *Adverse Analytical Finding* (*AAF*).

b) The presence in urine of one or more of these substances, namely clenbuterol, ractopamine, zeranol and zilpaterol, at an estimated concentration at or below (≤) the *MRL* of 5 ng/mL [1] shall be reported as an *Atypical Finding* (*ATF*), triggering a mandatory investigation by the RMA to determine whether evidence exists that establishes that the consumption of contaminated meat is more likely than not the explanation for the *ATF*. If such evidence exists, the RMA will take no further action in respect of the *ATF.* If such evidence does not exist, the RMA will progress the finding as an *AAF.*

[Comment: Depending on the circumstances, the consumption of meat containing clenbuterol or ractopamine or zeranol or zilpaterol may lead to very low concentrations of that substance in the urine of the consumer of the meat. Therefore, the presence in urine of clenbuterol or ractopamine or zilpaterol or zeranol at a concentration of 5 ng/mL or less shall be reported as an ATF, even though the likelihood of contaminated meat consumption as the cause decreases the closer the urinary concentration gets to that limit. Upon receipt of the ATF, the RMA shall conduct a mandatory investigation to determine whether there is sufficient evidence to support contaminated meat

consumption as the more likely than not explanation [1].]

c) To estimate the concentration of the relevant target Analytes in the "A" *Sample*, the Confirmation Procedure shall follow the requirements for Non-Threshold Substances with an *MRL* established in the effective TD MRPL [1].

2.1 Application of *Minimum Reporting Levels* (*MRL*)

2.1.1 Clenbuterol and zilpaterol:

The *MRL* is applied to the unmodified, free form parent compound only, without considering contributions from any *Metabolite (i.e.,* The Laboratories shall not target any phase-I or phase-II *Metabolite)*.

2.1.2 Ractopamine:

The *MRL* is applied to the total content of ractopamine, including the unmodified ractopamine free form parent compound and the phase-II glucuro- and sulfoconjugated *Metabolites* expressed as ractopamine parent compound equivalent (as determined either after deconjugation or through the direct detection of the conjugated phase-II *Metabolites*).

2.1.3 Zeranol:

The *MRL* is applied to:

a) The total content of zeranol, including the unmodified zeranol free form parent compound and the phase-II glucuroconjugated *Metabolite* expressed as zeranol parent compound equivalent (as determined either after deconjugation or through the direct detection of the conjugated phase-II *Metabolites*), and

b) The total content of zeranol phase-I *Metabolites* (zearalanone and taleranol), including the unmodified phase-I *Metabolites* and their respective phase-II glucuroconjugates, expressed as phase-I *Metabolite* equivalent (as determined either after deconjugation or through the direct detection of the conjugated phase-II *Metabolites*).

However, the *MRL* is independently applied to each target Analyte (*i.e.,* total content of either zeranol, zearalanone or taleranol) and shall not be applied to the sum of the estimated concentrations of these different molecular species. For zeranol findings related to possible mycotoxin origin, refer also to TL04 [2].

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[1] A Stakeholder Notice detailing the mandatory investigative process has been published on 01 June 2021 (https://www.wada-ama.org/en/resources/stakeholder-notice-regarding-potential-meat-contamination-cases).

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3.0 References

[1] *WADA Technical Document* TD MRPL: Minimum Required Performance Levels and Applicable *Minimum Reporting Levels* for Non-Threshold Substances Analyzed by Chromatographic-Mass Spectrometric Analytical Methods.

[2] *WADA* Technical Letter TL04 – Analysis and Reporting of Zeranol.

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