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Written by:	WADA Science	Approved by:	WADA Executive Committee
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## MECLOFENOXATE

### 1.0 Introduction

WADA wishes to draw the attention of the Laboratories to the following observations and instructions on the analysis and reporting of **Meclofenoxate Metabolite 4-Chlorophenoxyacetic acid (4-CPA)**.

Meclofenoxate is rapidly degraded to 4-CPA in biological fluids (e.g. human plasma or urine) <sup>[1,2]</sup>. However, 4-CPA is also used as a herbicide and a plant growth regulator in some countries or regions of the world. Therefore, the presence of 4-CPA in urine may originate not only from meclufenoxate administration but also from an oral ingestion of residues of 4-CPA in food <sup>[3]</sup>.

*[Comment: The substances from the chlorinated phenoxy acid herbicides (CPAHs) class, which includes 4-CPA, present similar pharmacokinetics, and after ingested, they are rapidly eliminated unchanged in the urine <sup>[3]</sup>. In workers that regularly spray these herbicides in the plantation fields, the ranging concentration found of CPAHs in urine was 15-800 ng/mL, while for the general population, the presence of CPAHs never exceeds the urinary concentration of 2.5 ng/mL <sup>[4]</sup>.]*

### 2.0 Analysis and Reporting Requirements

Before reporting a result as an *Adverse Analytical Finding (AAF)* for meclufenoxate, Laboratories shall evaluate whether the finding is the result of the consumption of 4-CPA contaminated food.

- Laboratories shall investigate the presence of meclufenoxate when 4-CPA is found in a urine *Sample*;
- Laboratories shall report an *AAF* for meclufenoxate if:
  - Meclofenoxate is found in a urine *Sample* at any concentration, in conjunction with 4-CPA being present at an estimated concentration above (>) the *Minimum Reporting Level (MRL)* for stimulants; or
  - In the absence of meclufenoxate, when the estimated 4-CPA urinary concentration is higher than (>) 1 µg/mL.

*[Comment: Due to the instability of meclufenoxate in urine, its identification in the “B” sample is not necessary. Therefore, the “B” Confirmation Procedure may only confirm the presence of 4-CPA (in compliance with the TD IDCR <sup>[5]</sup>) for the AAF to be valid.]*

### 3.0 References

- [1] Yoshioka S., Yukio A., and Mitsuru U. Kinetics of hydrolysis of meclufenoxate hydrochloride in human plasma. *J Pharm Pharmacol.* **39**(3): 215, 1987.
- [2] Guddat, S., et al. Detection of meclufenoxate and its degradation products Dimethylaminoethanol and p-chloro-phenoxyacetic acid. In *Recent Advances in Doping Analysis (14)*, Schanzer W, Geyer H, Gotzmann A, Mareck-Engelke U (eds). Sport und Buch Strauß: Köln, 2006; 399.

## WADA Technical Letter – TL01

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- [3] Arnold E.K., and Beasley, V.R. The pharmacokinetics of chlorinated phenoxy acid herbicides: a literature review. *Vet Hum Toxicol.* **31**(2): 121, 1989.
- [4] Aprea C., Sciarra G., and Bozzi N. Analytical methods for the determination of urinary 2, 4-dichlorophenoxyacetic acid and 2-methyl-4-chlorophenoxyacetic acid in occupationally exposed subjects and in the general population. *J Anal Toxicol.* **21**(4): 262, 1997.
- [5] *WADA Technical Document* TD IDCR: Minimum Criteria for Chromatographic-Mass Spectrometric Confirmation of the Identity of Analytes for *Doping Control* Purposes.

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