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UNITED STATES ANTI-DOPING AGENCY
INDEPENDENT ANTI-DOPING REVIEW BOARD

In The Matter Of
FLOYD LANDIS

—

SUBMISSION TO USADA INDEPENDENT ANTI-DOPING REVIEW BOARD

I. INTRODUCTION

This matter arises from the alleged positive drug test of Floyd Landis at the Tour de France on July 20, 2006. Mr. Landis allegedly tested positive for exogenous testosterone. Floyd Landis vehemently denies the allegations being made in this case.¹

This submission is made without access to complete documentation, and without access to any documents that would be required in any longitudinal study of

¹ While USADA may have redacted the name “Floyd Landis” in the documents provided to this Review Board, Landis will not participate in the charade that this is a confidential proceeding for two primary reasons: (1) given the improper leak and press statements by the UCI, the entire free world is aware that Floyd Landis, the 2006 Tour de France Champion, provided the only positive urine sample that is being pursued through disciplinary proceedings as a result of the 2006 Tour de France; and (2) the August 30, 2006 cover letter from USADA to the Review Board, which states “Re: UCI File No. 29/06, Tour de France, July 20, 2006,” destroys any confidentiality in this specific proceeding given point (1) above.

testosterone/epitestosterone values. This submission should not be considered in any respect to be a complete recitation of the defenses that may be offered by or on behalf of Floyd Landis, and Floyd Landis specifically reserves the right to make any submission to any adjudication body in connection with these false charges. That being said, it is submitted that the documentation that has been provided to date does not meet the requisite positivity criteria as established by the World Anti-Doping Agency (“WADA”). Specifically, the following will be established:

1. The carbon isotope results do not satisfy the WADA positivity criteria, in that:
 - a. Only one of four metabolites tested clearly exceeds the 3‰ threshold provided by WADA;
 - b. The measurement value that is the best indicator of exogenous testosterone usage in urine proves that Floyd Landis did not use testosterone; and
 - c. All of the 5 α -Androstanediol ¹³C-values reported by LNDD are inaccurate.
2. Absent a positive CIR result, there is no case to answer under the WADA TECHNICAL DOCUMENT TD2004EAAS.

As such, there is no case to answer, and the proceedings should be dismissed by this Anti-Doping Review Board (“ADRB”).

II. SUMMARY OF CARBON ISOTOPE RATIO RESULTS

USADA brings this case primarily based upon the carbon isotope ratio results (“CIR”)², which USADA alleges provides evidence of the use of exogenous testosterone. A good summary of the CIR theory is provided at Maitre et al., Urinary Analysis of Four Testosterone Metabolites and Pregandiol by Gas Chromatography-Combustion-Isotope Ratio Mass Spectrometry After Oral Administration of Testosterone, 28 Journal of Analytical Toxicology (Sept. 2004) [attached hereto as Exhibit 1]:

“IRMS allows measurements of slight differences in the carbon isotope ratio (¹³C/¹²C) of the exogenous and endogenous testosterone. Synthetic testosterone is produced from precursors derived from plants with low ¹³C content, whereas the ¹³C and ¹²C content in the natural endogenous form depends on the isotopic carbon composition of the food diet and is influenced by additional effects of human biological processing.”

Carbon isotope ratios are expressed in terms of delta units per mil. Maitre went on to describe this calculation as follows:

The symbol δ is the standard notation for expressing carbon isotope ratios. It is defined as parts per thousand deviation of isotopic compositions from that of Pee Dee Belemnite (PDB), and is calculated according to:

$$\delta^{13}\text{C}/\text{‰} = \frac{(^{13}\text{C}/^{12}\text{C}) \text{ sample} - (^{13}\text{C}/^{12}\text{C}) \text{ standard}}{(^{13}\text{C}/^{12}\text{C}) \text{ standard}}$$

Once the $\delta^{13}\text{C}/\text{‰}$ value for the testosterone metabolites is calculated, the positivity criteria mandated by WADA requires that this value be compared between metabolites that are believed to be affected by exogenous testosterone use and those metabolites that are not so affected. See WADA Technical Document TD2004EAAS (attached hereto as Exhibit 2), p.3:

“3. Isotope ratio mass spectrometry:

² This CIR method is also referred to as Isotope Ratio Mass Spectrometry, or “IRMS.”

When a parameter of the steroid profile indicates a need to further study, its ¹³C/¹²C value expressed in delta units per mil (δ‰) or that of its metabolites will be measured and compared to that of urinary reference steroids within the sample not affected by administration. Depending upon the nature of the endogenous steroid suspected to have been administered, the metabolites analysed could be ... androsterone, etiocholanolone, the androstanediols ... while the urinary reference steroid usually analysed by the Laboratories is one of, pregnanediol ... or 11-ketoetiocholanolone.”

Here, the French Lab (LNDD) that analyzed the Landis “A” and “B” samples tested for and calculated the δ‰ values for the following testosterone metabolites that are affected by exogenous testosterone administration: androsterone, etiocholanolone, and the androstanediols (5α-Androstanediol³ and 5β-Androstanediol⁴). LNDD also tested for and calculated the δ ‰ values for the following testosterone metabolites that are not affected by exogenous testosterone administration: pregnanediol (specifically, 5β-pregnanediol⁵) and 11-ketoetiocholanolone⁶. Without conceding the accuracy of the data, LNDD calculated the following values, expressed as corrected and uncorrected values:

For the “A” sample [see Document package, p. USADA 0185]:

	True Value	Corrected Value
Androsterone	-27.71	-25.05
Etiocholanolone	-26.43	-23.63
5αAdiol	-32.12	-27.72
5βAdiol	-28.82	-23.73
11Ketoetio	-24.10	-21.06

³ Also referred to as 5αAdiol.

⁴ Also referred to as 5βAdiol.

⁵ Also referred to as 5βPdiol.

⁶ Also referred to as 11-Ketoetio.

5βPdiol	-26.61	-21.58
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For the “B” sample [see Document package, p. USADA 0351]:

	True Value	Corrected Value
Androsterone	-27.93	-25.29
Etiocholanolone	-26.58	-23.80
5αAdiol	-31.88	-27.43
5βAdiol	-28.79	-23.69
11Ketoetio	-24.75	-21.78
5βPdiol	-26.16	-21.05

The final step in the analysis of the positivity criteria is stated in WADA

Technical Document TD2004EAAS (attached hereto as Exhibit 2), p.3, as follows:

“The results will be reported as consistent with the administration of a steroid when the ¹³C/¹²C value measured for the **metabolite(s)** differs significantly i.e. by 3 delta units or more from that of the urinary reference steroid chosen. In some *Samples*, the measure of the ¹³C/¹²C value of the urinary reference steroid(s) may not be possible due to their low concentration. The results of such analysis will be reported as “inconclusive” unless the ratio measured for the metabolite(s) is below -28‰ based on non-derivatized steroid.”

In this case, LNDD calculated this difference for all four testosterone metabolites tested. In so doing, LNDD compared the measures of androsterone and etiocholanolone to the urinary reference steroid 11-Ketoetio; and compared the measures of 5αAdiol and 5βAdiol to the urinary reference steroid 5βPdiol. For reasons that are not stated, LNDD only calculated these measured differences based on corrected values (for sake of

completeness, the measured differences for the true values are provided here as well).

The measured differences are as follows:

For the “A” sample [See Document Package, pp. USADA 0185-0186]⁷:

	True Measurement	Corrected Measurement
Etiocholanolone – 11Ketoetio	-2.33‰	-2.58‰
Androsterone – 11Ketoetio	-3.61‰	-3.99‰
5βAdiol - 5βPdiol	-2.21‰	-2.15‰
5αAdiol - 5βPdiol	-5.51‰	-6.14‰

For the “B” sample [See Document Package, pp. USADA 0351-0352]⁸:

	True Measurement	Corrected Measurement
Etiocholanolone – 11Ketoetio	-1.83‰	-2.02‰
Androsterone – 11Ketoetio	-3.18‰	-3.51‰
5βAdiol - 5βPdiol	-2.63‰	-2.65‰
5αAdiol - 5βPdiol	-5.72‰	-6.39 ‰

III. THE CARBON ISOTOPE RESULTS DO NOT SATISFY THE WADA POSITIVITY CRITERIA

A. THE WADA POSITIVITY CRITERIA MUST BE READ AS

REQUIRING THAT THE ¹³C/¹²C δ VALUE MEASURED FOR ALL METABOLITES

⁷ According to the LNDD documents themselves, these figures have a huge measure of uncertainty of ±0.8‰.

⁸ According to the LNDD documents themselves, these figures have a huge measure of uncertainty of ±0.8‰.

TESTED DIFFERS SIGNIFICANTLY, WHICH CRITERIA IS NOT MET IN THIS CASE

The WADA Positivity criteria, as mentioned above, requires a showing that “¹³C/¹²C value measured for the **metabolite(s)** differs significantly i.e. by 3 delta units or more from that of the urinary reference steroid chosen.” This requirement must be read as requiring that **all metabolites tested** differ significantly as described, i.e. by 3 delta units or more from the urinary reference standard chosen. Such a reading was confirmed in 2006 by the WADA-accredited laboratory in Lausanne:

“According to the technical document of the WADA Laboratory Committee, an athlete would be reported as consistent with the administration of a steroid when the ¹³C/¹²C-value measured for the **metabolites** differs significantly, i.e. by 3.0‰ or more from that of the urinary reference steroid chosen.” Baume et al., Use of Isotope Ratio Mass Spectrometry to Detect Doping with Oral Testosterone Undecanoate: Inter-Individual Variability of ¹³C/¹²C Ratio, Steroids 2006, at p. 6 [attached hereto as Exhibit 3]

In this case, it is clear that the Landis sample does not meet this positivity criteria, as only one of four metabolites tested clearly exceeds the 3‰ example provided by WADA (a second metabolite, measured at -3.51‰ ±0.8‰ on the “B” sample, cannot be said to exceed this threshold). For these reasons, the CIR results do not support a finding of exogenous testosterone use.

Landis submits that this criteria must be read as requiring that all metabolites tested exceed this threshold to declare the CIR test as positive. However, at worst, this criteria is vague and ambiguous, as the drafters – WADA – used the incredibly poor and imprecise description “¹³C/¹²C value measured for the **metabolite(s)**.”⁹

It is well settled law that ambiguities in a document or contract must be construed

⁹ Which description was clarified by Baume, supra, as requiring all tested metabolites to be positive under this criteria.

against the drafter of the document. See, e.g., 2 Restatement Contracts, 2d, § 206, p 105 [“In choosing among the reasonable meanings of a promise or agreement or a term thereof, that meaning is generally preferred which operates against the party who supplies the words or from whom a writing otherwise proceeds.”]; United States v. Seckinger, 397 U.S. 203, 216 (1970) [“our interpretation adheres to the principle that, as between two reasonable and practical constructions of an ambiguous contractual provision, such as the two proffered by the Government, the provision should be construed less favorably to that party which selected the contractual language. This principle is appropriately accorded considerable emphasis in this case because of the Government’s vast economic resources and stronger bargaining position in contract negotiations.”]¹⁰; USA Shooting & Q./International Shooting Union (UIT) (CAS 94/129) [““The fight against doping is arduous, and it may require strict rules. But the rule-makers and the rule-appliers must begin by being strict with themselves. Regulations that may affect the careers of dedicated athletes must be predictable ... They should not be the product of an obscure process of accretion.”]; USOC et al. v. IOC et al. (CAS 2004/A/725) [“The rationale for requiring clarity of rules extends beyond enabling athletes in given cases to determine their conduct in such cases by reference to understandable rules. As argued by Appellants at the hearing, clarity and predictability are required so that the entire sport community are informed of the normative system in which they live, work and compete, which requires at the very least that they be able to understand the meaning of rules and the circumstances in which those rules apply.”].

¹⁰ The only basis for the application of the UCI anti-doping regulations, and the WADA Technical Document that WADA and the UCI will assert is incorporated as binding in this case, is the contractual relationship between the parties. The analogy of the Government’s vast economic resources and stronger bargaining power is particularly apt in the context of athletes vs. anti-doping authorities.

Therefore, this positivity criteria must be read to mean that the $^{13}\text{C}/^{12}\text{C}$ δ value measured for the all metabolites tested differ significantly (i.e. by 3 delta units or more from that of the urinary reference steroid chosen). In addition to being required by settled law, such a reading of this positivity criteria makes sense: if an athlete were to take synthetic testosterone, and if that synthetic testosterone would cause a significant difference in the measurement of $^{13}\text{C}/^{12}\text{C}$ for one testosterone metabolite when compared to a urinary reference, then one should expect like or similar changes for **all** such metabolites tested. Simply stated, synthetic testosterone should not selectively affect these metabolites.

Furthermore, any notion that WADA intended otherwise, or that the WADA-accredited laboratories clearly understood that this positivity criteria would only require a showing of a single metabolite as exceeding the threshold, is easily dismissed by the following published statement by the WADA-accredited laboratory in Lausanne, which statement shortly post-dates the effective date of the WADA Technical Document TD2004EAAS:

“What are the IRMS criteria to determine endogenous T ingestion, that is, does all the measured T metabolite $\delta^{13}\text{C}$ -values or does only one have to be superior to 4‰.” See Maitre, Urinary Analysis of Four Testosterone Metabolites and Pregandiol by Gas Chromatography-Combustion-Isotope Ratio Mass Spectrometry After Oral Administration of Testosterone, 28 Journal of Analytical Toxicology (Sept. 2004) [attached hereto as Exhibit 1].

If even the WADA-accredited laboratories were asking this question, then WADA can hardly claim that its laboratories understood otherwise. Absent a clarification by WADA, which clarification never occurred, this criteria must therefore be read as requiring that **all** the measured T metabolite $\delta^{13}\text{C}$ -values must show significant differences. Such a

reading is also consistent with the 2006 interpretation of the WADA Technical Document by the WADA-accredited laboratory in Lausanne (See Baume, supra).

In this case, it is clear that the Landis sample does not meet this positivity criteria, as only one of four metabolites tested clearly exceeds the 3‰ example provided by WADA (a second metabolite, measured at $-3.51‰ \pm 0.8‰$ on the “B” sample, cannot be said to exceed this threshold). For these reasons, the CIR results do not support a finding of exogenous testosterone use, and must be considered as negative.

B. THE MEASUREMENT VALUE THAT IS THE BEST INDICATOR OF EXOGENOUS TESTOSTERONE USAGE IN URINE PROVES THAT FLOYD LANDIS DID NOT USE TESTOSTERONE

Additional findings from the CIR results further undermine the erroneous conclusion that those results support a finding of exogenous testosterone use. Published research by WADA-accredited laboratories shows that the measurement 5β Adiol - 5β Pdiol is a better indicator of exogenous testosterone usage than other metabolite measurements, and should allow for longer detection periods of exogenous testosterone than the other metabolites.

See Maitre, Urinary Analysis of Four Testosterone Metabolites and Pregandiol by Gas Chromatography-Combustion-Isotope Ratio Mass Spectrometry After Oral Administration of Testosterone, 28 Journal of Analytical Toxicology (Sept. 2004)

[attached hereto as Exhibit 1]:

“This paper describes the time courses of isotopic ratio values in urine of androsterone (Andro), etiocholanolone (Etio), 5α -androstenediol (5α A), 5β -androstenediol (5β A), and the endogenous reference 5β -pregnanediol (5β P) in the frame of an excretion study following oral ingestion of testosterone initially and 13 h later by a healthy, male Caucasian volunteer ...

“Similarly to the T/E ratio, the $\delta^{13}\text{C}$ -values of the four T metabolites decrease rapidly after T administration with a difference of about 5‰ with respect to the endogenous reference 5 β P ...

“our results suggest that measurements of 5 β -androstanediol δ -values allow the detection of a testosterone ingestion over a longer period than other T metabolites $\delta^{13}\text{C}$ -values.”

Therefore, if an athlete used exogenous testosterone, his measured difference 5 β Adiol - 5 β Pdiol should be greater than his measured difference 5 α Adiol - 5 β Pdiol. In the Landis sample, this is not even close to the case: LNDD reported the following corrected values:

For the “A” sample:

5 β Adiol - 5 β Pdiol: -2.15‰

5 α Adiol - 5 β Pdiol: -6.14‰

For the “B” sample:

5 β Adiol - 5 β Pdiol: -2.65‰

5 α Adiol - 5 β Pdiol: -6.39‰

Had Landis used exogenous testosterone, the Maitre publication indicates that his 5 β Adiol - 5 β Pdiol should be at or greater than -6‰, given the measurement of 5 α Adiol - 5 β Pdiol. At a minimum, one would expect the 5 β Adiol - 5 β Pdiol to exceed the threshold of 3‰, which it does not. The only conclusion that can be drawn from the fact that the 5 β Adiol - 5 β Pdiol measurement is well below the threshold, when the WADA-accredited laboratories state that this measurement is the **best indicator** of exogenous testosterone administration, is that Floyd Landis did not use exogenous testosterone.

C. THE 5 α -ANDROSTANEDIOL ^{13}C -VALUES REPORTED BY LNDD ARE INACCURATE

With the 5 α Adiol - 5 β Pdiol measurement being significantly at odds with all of the other measurements in this case, the Review Board must consider the cause of this disparate measurement, which is inconsistent with every other measurement in the CIR portion of the analysis. It is submitted that the explanation for this erroneous measurement can be found in LNDD's calculation of incorrect values for 5 α Adiol, as evidenced by an examination of the negative control urine $\delta^{13}\text{C}$ -values for that metabolite. Simply put, LNDD's $\delta^{13}\text{C}$ -values for 5 α Adiol for the negative control urine show that their equipment was, for some unexplained reason, measuring excessively low $\delta^{13}\text{C}$ -values for 5 α Adiol.

Published data provides guidance for expected $\delta^{13}\text{C}$ -values for 5 α Adiol for **negative** control urines and for **positive** control urines. See Aguilera et al., Performance Characteristics of a Carbon isotope Ratio Method for detecting Doping with Testosterone Based on Urine Diols: Controls and Athletes with Elevated Testosterone/Epitestosterone Ratios, 47 *Clinical Chemistry* 292, 296 Table 3 (2001) [attached hereto as Exhibit 4], showing that mean $\delta^{13}\text{C}$ -values for 73 negative control urines for 5 α Adiol was -26.35‰, with a maximum of -24.55‰ and a minimum of -27.89‰. See also, Maitre, Urinary Analysis of Four Testosterone Metabolites and Pregandiol by Gas Chromatography-Combustion-Isotope Ratio Mass Spectrometry After Oral Administration of Testosterone, supra, showing that mean $\delta^{13}\text{C}$ -values for negative control urines for 5 α Adiol was -24.3‰ (± 0.4 ‰). In contrast to those figures, LNDD measured $\delta^{13}\text{C}$ -values for negative control urines for 5 α Adiol in the Landis case of -28.40‰ on the "A" sample (See Document package, p. USADA 0185) and -28.31‰ on the "B" sample testing (See Document package, p. USADA 0351). These figures are inconsistent with reported

figures as shown above, and in fact, are more consistent with measurement or calibration error. See, e.g., Maitre, supra, reporting that mean $\delta^{13}\text{C}$ -values for **positive control urines** for $5\alpha\text{Adiol}$ was -28.4‰ ($\pm 0.5\text{‰}$). See also, Shackleton et al., Confirming Testosterone Administration By Isotope Ratio Mass Spectrometric Analysis Of Urinary Androstanediols, 62 *Steroids* 379, 383 (1997) [attached hereto as Exhibit 5] [“In our studies with the Chinese subjects, it can be stated that for the five individuals, none had androstanediol $\delta^{13}\text{C}\text{‰}$ values less than -28.3 during the control period.”]

The LNDD readings for $5\alpha\text{Adiol}$ in the negative control urine are so low that they must be inaccurate. In fact, those readings look more like positive control urine values than negative controls. If the negative control urine readings for $5\alpha\text{Adiol}$ are excessively low, it must be the case that the LNDD readings of the Landis sample for $5\alpha\text{Adiol}$ are also excessively low and inaccurate, thus explaining the large difference in the $5\alpha\text{Adiol}$ - $5\beta\text{PdIol}$ measurement. As this measurement in the Landis sample is totally at odds with any of the other measurements as discussed above, it is submitted that the result must stem from laboratory error.

D. SUMMARY

As shown above, the WADA Positivity Criteria or CIR analysis of exogenous testosterone usage has not been met:

1. Whereas the WADA Positivity Criteria requires all four testosterone metabolites to provide clear evidence of testosterone usage, 3 of the 4 metabolites must be considered as negative;

2. The only testosterone metabolite that is even arguably positive under the WADA Positivity Criteria is the result of laboratory error and not the result of testosterone usage; and
3. The one metabolite that has been identified by the WADA-accredited laboratories as the best indicator of exogenous testosterone usage, and the longest-term indicator of exogenous testosterone usage, has been reported as negative.

Any one of these deficiencies would alone be sufficient to render the CIR result negative.

IV. ABSENT A POSITIVE CIR RESULT, THERE IS NO CASE TO ANSWER UNDER THE WADA TECHNICAL DOCUMENT TD2004EAAS

A negative CIR result in most cases mandates a dismissal of doping allegations of exogenous testosterone usage. However, in all cases other than a positive CIR Result, WADA Technical Document TD2004EAAS requires that a longitudinal study be performed. No such longitudinal study has been performed in this case, and no such longitudinal data has been provided to the athlete or to this Review Board. For this reason, there is no case to answer, and the case against Floyd Landis must be dismissed.

Doping charges cannot proceed against an athlete based upon an inconclusive/negative CIR test and a single T/E value. Furthermore, the single T/E analysis in this case is replete with fundamental, gross errors. Examples of these errors include:

1. Mismatched sample code numbers that do not belong to Floyd Landis (see, e.g., Document Package p. USADA 0288, alleged confirmation T/E

data on “B” sample, containing different sample number from that assigned to Floyd Landis; see also Document package USADA 0024, LNDD chain of custody documentation regarding receipt of sample, does not identify any sample numbers matching the code number for the Floyd Landis sample). Clinical laboratories making these types of gross errors could easily find themselves answering to a wrongful death lawsuit. Simply stated, if LNDD cannot get the sample code number correct, how can they be trusted to accurately report quantitative test results?

2. Grossly inconsistent testosterone and epitestosterone samples from sequential tests on the Landis “A” sample:
 - a. See Document Package, pp. USADA 0212 and 0223, testing on Landis sample 995474, vial 10 aliquot (first “A” confirmation analysis), showing testosterone level of 172.23 ng/ml and epitestosterone level of 17.59 ng/ml; and showing corrected values of 127 ng/ml for testosterone and 13 ng/ml for epitestosterone;
 - b. Compare Document package, pp. USADA 0092 and 0101, vial 4 aliquot (second “A” confirmation analysis), showing testosterone level of 61.37 ng/ml and epitestosterone level of 5.20 ng/ml; and showing corrected values of 45.4 ng/ml for testosterone and 3.9 ng/ml for epitestosterone;
 - c. It must be accepted that two test results using the same method on the same urine and tested sequentially should not show three-fold differences in testosterone and epitestosterone. Such differences are

clear evidence of laboratory error, such that none of these results can be accepted as accurate.

“Where doubt has been created with regard to the test procedure, such doubt must go to the benefit of the athlete.” USA Triathlon v. S. Smith (CAS 99/A/241). The LNDD laboratory documents are replete with such gross errors and ineptitude that their results in this case cannot be seriously accepted as accurate. At a minimum, those laboratory errors must go to the benefit of the athlete, and must result in a finding that the T/E results are wholly unreliable.

V. CONCLUSION

For the foregoing reasons, it is submitted that there can be no case to answer, and that the charges against Floyd Landis must be immediately dismissed.

RESPECTFULLY SUBMITTED,

DATED:

LAW OFFICES OF HOWARD L. JACOBS

By: _____
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