MAURICE M. SUH
DANIEL L. WEISS
GIBSON, DUNN & CRUTCHER LLP
333 S. Grand Avenue, Suite 5115
Los Angeles, CA 90071-3197
Telephone: (213) 229-7000
Facsimile: (213) 229-7520
MSuh@gibsondunn.com
DWeiss@gibsondunn.com

HOWARD L. JACOBS
LAW OFFICES OF HOWARD L. JACOBS
2815 Townsgate Road, Suite 200
Westlake Village, CA 91361
Telephone: (805) 418-9892
Facsimile: (805) 418-9899

Attorneys for Floyd Landis

IN THE COURT OF ARBITRATION FOR SPORT

IN THE MATTER OF FLOYD LANDIS,

CAS 2007/A/1394

FLOYD LANDIS V. UNITED STATES ANTI-DOPING AGENCY

DECLARATION OF KEITH GOODMAN

I, Keith Goodman, declare and state as follows:

1. I am over the age of 18 and have personal knowledge of the following facts and, if called as a witness, could and would competently testify to them.

2. I have a Ph.D. in nutritional biochemistry with a minor in analytical chemistry with specific expertise in isotope ratio mass spectrometry. I manage the day-to-day operations of a pharmaceutical research laboratory. The details of my professional career are further described in my CV, which is attached to this declaration as Exhibit 1. However, by way of summary, my experience in the field of analytical chemistry, and specifically, isotope ratio mass spectrometry is as follows:

a. I am currently a Senior Director of Analytical Chemistry at Xanthus Pharmaceuticals in Cambridge, MA and manage a state-of-the-art pharmaceutical research laboratory. In this capacity, I have (1) designed and executed *in vitro* (with purified cell fractions) and *in vivo* (animal) metabolism experiments to evaluate pharmacokinetics (metabolism and exposure) of drugs and (2) developed assays using high performance liquid chromatography (HPLC) and liquid chromatography tandem mass spectrometry (LC MS/MS) to analyze samples from *in vivo* and *in vitro* experiments.

b. I have previously managed a stable isotope laboratory for Boyce Thompson Institute for Plant Research, in Ithaca, NY.

c. I am familiar with and have used several different types of isotope ratio instruments and other analytical instruments, including the API 4000 tandem mass spectrometer coupled to an Agilent HPLC system used for structural confirmation and quantitative analysis, a Waters HPLC system, an Agilent MSD GC MS for structural

confirmation and quantitative analysis, a Finnigan MAT 252 with GC combustion interface for isotope ratio analysis of mixtures of volatile organic molecules, a Finnigan Delta S with a Gilson autosampler for gas and headspace gas analysis and a tube cracker interface for isotope analysis of samples prepared offline, a VG Optima with GC Isochrom II interface (for online combustion of volatile organics), a Carlo Erba elemental analyser for bulk analysis of solids and liquids, a Finnigan MAT Delta Plus with a Conflo II interfaced to a Carlo Erba NC2500 elemental analyzer, the Europa Geo 20-20 dual-inlet gas isotope ratio mass spectrometer with an ANCA-SL elemental analyzer and an ANCA-TG for trace gas measurements, and a Finnigan BreathMAT IRMS for isotopic analysis of breath CO_2.

d. I have served as an expert witness/consultant to the US Track and Field Association in 1999 following an alleged testosterone doping violation. The T/E ratio was borderline elevated at T/E 7.4 (the threshold was 7 at the time) so the IRMS test was used as final confirmation. The subsequent IRMS data was interpreted as positive. I then audited the preparation and CIR re-analysis of the athlete's "B" sample at Dr. Schantzer's laboratory in Cologne. Over the following few weeks, I worked with the lawyers to assemble the findings for the International Association of Athletics Federations (IAAF) arbitration in Monaco.

e. I have years of hands on experience with the gas chromatography combustion isotope ratio mass spectrometry (GC-C-IRMS) and have authored several papers that deal with the analytical performance and limitations of these systems. These include issues of peak overlap and resolution, which are critical in obtaining reliable isotope ratio measurements.

f. I am very familiar with the analytical parameters known as retention time and relative retention time from my work in managing and operating analytical and stable isotope laboratories and because they are crucial to accurate results in chromatography and specifically, isotope ratio calculation.

g. I am very familiar with issues involving the quality of chromatograms and matrix interference, including co-eluting contaminant peaks, inadequate peak detection and integration algorithms. I am very familiar with the impact these issues may have in the case of biologically derived samples (i.e. urine, plasma, or tissues).

3. The use of Gas Chromatography Combustion Carbon Isotope Ratio Mass Spectrometry is a well-established method for determining the isotopic value of target substances. In order to achieve accurate results, the GC-C-IRMS method requires, among other things, (1) proper identification of the target substances, (2) proper quality control measures, (3) good chromatography (specifically, purified material) and (4) adherence to good laboratory procedures.

4. I have reviewed the document package in this case and related documents, the transcript of the hearing of *United States Anti-Doping Agency v. Floyd Landis*, held on May 13 – 23, 2007 and the resulting Award of the Majority and the Dissent, the exhibits in that case and the pleadings and briefs in this appeal and the underlying case. These documents all reference the testing conducted at the Laboratorie National de Depistage et Dopage ("LNDD") in France.

5. I am being paid $2,000 plus travel expenses, which are nominal, for my participation in this case. This is far below what I normally would charge for this kind of case and the time I have spent reviewing these materials and testifying. I am participating in this

appeal proceeding at this drastically reduced rate because I believe that to uphold an anti-doping sanction on the evidence in this case is morally and ethically wrong.

6. After a review of the files and records and laboratory documents in this case, I have concluded that the GC-C-IRMS test results allegedly supporting an adverse analytic finding against Floyd Landis in the above-captioned case, including the GC-C-IRMS results for Stage 17 and other stages from the 2006 Tour de France, are inaccurate and unreliable and of no scientific worth.

THE CARBON ISOTOPE RATIO TEST

7. The purpose of the CIR test is to determine whether synthetic (exogeneous) testosterone is present in the urine sample. The test works by detecting the ratio of Carbon 13 to Carbon 12 present in testosterone. All testosterone (natural and synthetic) is composed of carbon. However, synthetic testosterone, made from soy plants, has far less Carbon-13 then the testosterone produced naturally in the human body. By comparing the ratios of Carbon-13 to Carbon-12 in the urine sample, scientists, theoretically, are able to determine whether synthetic (exogenuous) testosterone has been ingested.

8. The CIR test measures the isotopic ratios in four metabolites of testosterone. Metabolites are derived form testosterone once it is processed in the body. The CIR test detects the following metabolites: Androsterone ("Andro"), Etiocholanolone ("Etio"), 5a-Androstanediol ("5 Alpha") and 5B-Androstanediol ("5-Beta"). The Carbon-13 to Carbon-12 ratios in the metabolites will be the same as what was present in testosterone before the body broke it down.

9. Several factors, such as diet, can make the levels of Carbon-13 in the metabolites naturally low. To account for these variations, the CIR test compares the Carbon-13 to Carbon-

12 ratio of the metabolites to the same ratio of an endogenous reference compound ("ERC"). An ERC is a compound produced naturally by the body and is not affected by the introduction of synthetic (exogenuous) testosterone.

10. To accurately measure the ratio of Carbon-13 to Carbon-12 for each metabolite, the test must first be able to clearly identify each metabolite in the urine sample. The test does this by running the sample through a Gas Chromotgraph / Mass Spectrometer. The Gas Chromotograph passes the metabolites through columns coated with various hydrocarbon coatings. Each metabolite will pass through the column at a different rate, depending on how it interacts with the hydrocarbon stationary phase. These times are called retention times, or the time it takes for the compounds to exit the Gas Chromatograph column. Once they emerge through the tubes, the metabolites are ionized, and the mass spectrometer measures each metabolite's mass-to-charge ratio. The scientist can then assign each specific metabolite a retention time for passing through a Gas Chromotograph.

11. To measure the Carbon-13 to Carbon-12 ratio, the scientist will introduce the metabolite into a Gas Chromotograph followed by an Isotope Ratio Mass Spectrometer ("IRMS"). Instead of measuring the mass-to-charge ratio like the Mass Spectrometer, the IRMS measures the ratio of carbon isotopes in CO2 derived form the combusted sample. The IRMS is very simple. It essentially combusts (with heat and oxygen) the components of a sample after they pass through the Gas Chromotograph. The metabolites (more precisely the Carbon-13 and Carbon-12 in each metabolite) react with oxygen to form carbon dioxide (CO2). The insturment measures the ratio of Carbon-13 to Carbon-12 in the CO2 produced by each metabolite.

12. Theoretically, a laboratory can identify each metabolite that produced a certain Carbon-13 to Carbon-12 ratio in the IRMS by comparing it to the results of the Gas

Chromotograph and Mass Spectrometer (GC-MS) test. The GC-MS test used mass-to-charge to identify each metabolite with a known retention time. Since the GC-IRMS test also passes the metabolites through a Gas Chromtograph, each substance in the sample should have a retention time similar to the GC-MS test (although many variables may cause a change in a metabolite's retention time as discussed below). Therefore, by using retention time, the scientist can assign the Carbon-13 to Carbon-12 CIR ratio to a specific metabolite that was initially identified using GC/MS.

13. After the scientist assigns the Carbon-13 to Carbon-12 ratio to each metabolite, the scientist subtracts that value from the naturally occurring ratios of Carbon-13 to Carbon 12 measured in the ERC. That value (called the delta-delta value) is compared to the criteria (a delta-delta threshold) set out by WADA. If the delta-delta value for a certain metabolite is greater than the threshold set forth by WADA, the scientist can determine theoretically, for purposes of a doping violation, whether the sample contained synthetic testosterone.

LNDD'S ALLEGED QUALITY CONTROLS ARE OF NO VALUE

14. As the director of a laboratory, I am keenly aware of the importance of quality controls in connection with accurate CIR test results. If performed properly, quality control measures ensure precise, accurate and reliable testing and thereby provides the necessary assurances that the GC/C/IRMS instrument is functioning properly and accurately.

I have reviewed ISL 5.4.7.3 (Assuring the Quality of Test Results). ISL 5.4.7.3 states:

> Analytical performance should be monitored by operating quality control schemes appropriate to the type and frequency of testing performed by the Laboratory. The range of quality control activities includes:
>
> - Positive and negative controls analyzed in the same analytical run as the Presumptive Adverse Analytical Finding Sample.

As explained more fully below, I believe that LNDD violated ISL 5.4.7.3 because it had no meaningful positive and negative controls. Further, and independent of ISL 5.4.7.3, I conclude that the measures described by LNDD as "quality controls" provide no assurance of accuracy, do not function as true quality controls and provide no assurance that the GC-C-IRMS results are accurate and reliable, especially for the Stage 17 Sample. I believe that the quality control measures provide no benefit to USADA in its attempt to prove that it has presented evidence of a doping violation to the "comfortable satisfaction" of the hearing body.

15. In the Appellee Response Brief, USADA suggests that the quality controls of LNDD in this case provide the necessary assurances of accuracy, Appellee Response Brief, at 29-35. This is wrong. After reviewing the quality controls as described in the Appellee Response Brief, and the relevant documents, I conclude that the quality controls in this case provide no assurance that the GC-C-IRMS results are accurate and reliable, especially for the Stage 17 Sample. I believe that the quality control measures provide no benefit to USADA in its attempt to prove that it has presented evidence of a doping violation to the "comfortable satisfaction" of the hearing body. As I will describe further, the failure of the quality control measures in this case is particularly troubling in connection with the other laboratory failures in this case, including (1) failed identification, (2) poor chromatography, (3) manual processing errors, (4) deleted data and (5) other ISL rule violations.

16. USADA has consistently identified four quality control measures. These are (1) internal standard 5 alpha-androstanol acetate, (2) negative control "blank urine," (3) positive control "mix cal acetate" and (4) an instrument performance check. Appellee Response Brief, at *id.*, USADA's Pre-Hearing Brief ¶¶ 53-58, Ex. B to USADA's Response to Second Request for

Production of Documents ¶ 4 at 8. None of these measures provide any quality control assurance.

The Internal Standard: 5 Alpha-Androstanol AC

17. The use of the internal standard 5 alpha-androstanol acetate ("5 Alpha AC") provided no quality control assurance and it is a mistake to rely upon it for any purpose related to assuring the Panel that the results were accurate or reliable. Indeed, the contrary is true. 5 Alpha AC was added to the Mix Cal Acetate, as well as to every Sample Fraction ("F1, F2, F3") and Blank Urine Fraction (Blank Urine 1, Blank Urine 2, Blank Urine 3; hereinafter "BLU 1, BLU2, BLU3") with a known isotopic value.

18. The purpose of including 5 Alpha AC in the Mix Cal Acetate is to verify the accuracy of the GC-C-IRMS instrument.

19. If LNDD's testing process was accurate and reliable, LNDD should have identified 5 Alpha AC at a theoretic delta value of -30.46, within a measurement of error as stated by LNDD of ±0.5 delta units. *See* Ex. 24, USADA0175.

20. The Internal Standard 5 Alpha AC, a reference standard with a certified isotopic value, provided no quality assurance because LNDD could not determine its isotopic value within its declared acceptable range of error in four instances during the testing of Sample 995474. The exhibit prepared by Dr. Meier-Augenstein demonstrates that 5 Alpha AC was measured outside of its acceptable isotopic values. *See* Meier-Augenstein Presentation at Slides 52, 54; Closing Presentation at Slides 39, 40, 134, 136. The fact that LNDD failed to properly determine the isotopic values of 5 Alpha AC – the internal standard – within its measurement of uncertainty is strong evidence that LNDD's IRMS testing was variable and unreliable , because it can not even properly identify isotopic ratio in a pure solvent, which should be routine.

(Maurice, measurement variability is precision not accuracy. I tried to maintain proper scientific definitions while keeping your point largely in tact)

21. In the context of this case, it does not matter that there were some instances in which some of the Internal Standard 5 Alpha ACs were within the stated measurement of error of 0.5 delta units of the delta value of -30.46. In my opinion, it was out of this stated measure far too many times – four times out of 12 in the testing of Sample 995474 to give me any assurance that the instrument was operating properly.

22. I further comment that the statement by the AAA Panel in Paragraph 195 regarding the internal standard is nonsensical. In that paragraph, the AAA Panel stated that the internal standard's sole purpose was use as a chromatographic standard and therefore it was somehow unnecessary for LNDD to properly calculate the isotopic value of the internal standard. This makes no sense at all. If the internal standard is run, for whatever stated reason, LNDD should be able to properly calculate its isotopic value within the applicable measure of uncertainty. Inability to do so – especially as often as occurred here – indicates something was very wrong with the GC/C/IRMS instrument or the CIR test as performed by LNDD. In addition, the fact that LNDD has a specification for delta value precision suggests that it is certainly intended to be used as an isotopic standard.

23. Furthermore, and even contradicting the AAA Panel and its reasoning, on direct examination, USADA's own expert, Dr. Brenna, testified that: "It also has standards that have been – a standard that has been added to every sample that elutes early, and that standard is further checked to determine that the instrument is running properly during analysis of every particular sample." Tr. of Proceeding at 237.

Blank Urines Sample

24. Blank Urine Samples, or "negative controls," are designed to provide assurance that the CIR test is not determining a false positive. The Blank Urine Samples in this case as used by LNDD do not provide any such quality control assurance. As previously described, the internal standard 5 Alpha AC was determined to be outside of the measurement of uncertainty for the Sample B F3 fraction – the same fraction USADA relied upon to establish the AAF for Stage 17.

25. Furthermore, when the Blank Urine Samples were reprocessed on May 4 – 5, 2007 pursuant to this Panel's discovery order, the results provided no assurance that the GC/C/IRMS instrument was operating with sufficient accuracy and reliability such that the Blank Urine Samples were of any value. The reprocessing involved running the same data files for Sample 995474 pursuant to four different processing results: (1) the GC-C-IRMS' automatic feature, (2) reprocessing using the same "manual" technique, (3) reprocessing with zero background subtraction and (4) reprocessing according to Masslynx. The reprocessing yielded different results, and sometimes dramatically different results, for each of the target metabolites of testosterone in Sample 995474, for both Sample A and Sample B. *See* Exhibit GDC 01350, Closing Presentation Slide 113.

26. Upon reprocessing, the B Sample 5 alpha, when measured with automatic processing, went from -1.6 delta-delta to -3.45 delta-delta, and the A Sample 5 alpha went from -1.59 delta-delta to -3.65 delta-delta. The delta-delta variances between manual processing and automatic processing are too great (more than a 2 per mil difference) to provide any assurance that the blank urine provided effective quality control. The variation in analysis of biological samples in this case yields errors that are too extreme to be reliable for doping analysis. This is

especially important given that these blank urine fractions are the same fractions USADA relied upon to establish the AAF.

27. I have read the AAA Panel's opinion with respect to blank urine, in Paragraphs 202 to 205, and disagree with that analysis in its entirety. Whether or not the inconsistent figures are directly related to 5 alpha is not the point – the point is whether the blank urine variances are so great as to render it useless as a quality control. In my opinion, the failure of LNDD to be able to reproduce the results in the Blank Urine Samples using the same method in fact renders it a useless quality control.

28. Second, I note that Dr. Brenna in fact expressed concern over the reprocessing results. Dr. Brenna testified that he would have been concerned with the results of the manual reprocessing in the fractions themselves, at Tr. of Proceedings at 892-93.

Mix Cal Acetate Cannot Serve as a Positive Control

29. The purpose of a Positive Control is to ensure that the CIR test does not arrive at a false negative and does so, theoretically, by challenging the CIR test with a known positive. The Mix Cal Acetate mixture in this case as used by LNDD does not constitute effective positive control or quality control in this case. Mix Cal Acetate consists of four (4) steroid standards: (1) the internal standard 5 Alpha AC, (2) Etiocholanolone AC, (3) 5 Beta Androstandiol Di-AC and (4) 11 keto-etiocholanolone AC. Each of these acetate standards has an established isotopic value.

30. Mix Cal Acetate cannot serve as a positive control in this case because of several independent reasons. First, the Mix Cal Acetate solution is a non-complex matrix, unlike urine. Mix Cal Acetate preparation is a "clean matrix." As such, it contains only 5 Alpha AC, Etiocholanolone AC, 5 Beta Androstanediol diAC, 11-keto-etio AC in a solvent. A solvent is

chemically pure. In short, there are no other unidentified substances in the Mix Cal Acetate that could create the interference that is routinely seen in the actual sample chromatograms in this case. In contrast, urine is an exceptionally complex matrix that varies from person to person and under conditions of extreme exercise, which means that it contains a number of unidentified compounds that can create matrix interference. As a result, the chromatograms for the Mix Cal Acetate show no matrix interference, and the test results of the Mix Cal Acetate provide no assurance that LNDD can accurately identify or determine the isotopic values of the compounds in urine (a highly complex matrix). This is particularly true here, where the chromatography in the actual blanks and fractions is poor. *See* Ex. 24, USADA0173; Ex. 25, USADA0349. Indeed, USADA has argued that the addition of this matrix interference in the biological samples is why the internal standard cannot be quantified accurately in the blank and sample fractions. Appellee's Brief at 62. In making this conclusion, I agree with Dr. Meier-Augenstein's testimony that conducting a chromatographic analysis of the Mix Cal Acetate is like "shooting fish in a barrel," unlike the related analysis of human samples. Tr. of R. at 1452:8-13.

31. Second, the Mix Cal Acetate cannot serve as a positive control because it did not go through the LNDD sample preparation process. In order to be a true positive control, the Mix Cal Acetate must go through the sample preparation process in order to render accurate results of a known positive substance.

32. Third, Mix Cal Acetate does not contain three of the six target analytes necessary to quantify isotopic value in this case. In order to properly serve as a positive control, it would be necessary to have all six target analytes. These are: (1) 5 alpha androstandiol, (2) 5 beta androstandiol, (3) androsterone, (4) etiocholanalone, (5) pregnandiol and (6) 11 ketoetiocholanalone. Instead, the Mix Cal Acetate is missing 5 Alpha, Pdiol and Andro.

Without these, the isotopic value of the target analytes can not be determined, especially in the F3 fraction. Without these three key target analytes, only one of the three delta-delta values, Etio – 11-ketoetio, can be determined. Etio – 11-ketoetio, for both the A Sample and the B Sample, was never an issue in this case because the delta-delta values were -2.58 and -2.02, respectively.

33. Fourth, to be an effective positive control, the isotopic values of the target analytes must be what you would expect in a positive sample. More simply, the isotopic values of andro, etio, 5 alpha and 5 beta should be in the approximate range of negative 28 delta units and the isotopic values of pregnandiol and 11 keto-etio should be in the range of negative 23 delta units.

34. In making this conclusion, I disagree with the AAA Award at paragraphs 209 to 211, which suggests that "the situation of a 'dirty' matrix can only work effectively as a positive control when detecting an exogenous substance. Testosterone is not such a substance." AAA Award ¶ 209-11. This makes no sense. In the detection of testosterone in a doping case, testosterone is derivatized prior to analysis, thereby, making it an exogenous substance. Further, the contention that steroids from different origins would be mixed and therefore render a positive control unusable is nonsensical because that is what occurs, theoretically, if a person were to take testosterone – the endogenous testosterone in the body is mixed with the administered testosterone. In order to make a true positive control, the laboratory could spike urine with known amounts of synthetic metabolites to create a positive control. If for some reason, they find this method unsatisfactory, they could conduct an in vivo administration of testosterone in humans or animals and collect the urine. Another method would be to remove the testosterone from urine and then replace the components with a desired isotope ratio. Synthetic urine, or urine from individuals with lower levels of testosterone could also be used. Indeed, there is

absolutely no concern with mixing the endogenous testosterone metabolites with synthetic testosterone – because when creating a true positive control, the laboratory is capable of stripping urine of its endogenous steroids (ie., removing naturally occurring testosterone from the urine). Even after the urine is stripped, it is still a complex matrix, unlike the solvent mixture that is Cal Mix Acetate. In fact, LNDD knows how to do this. The positive controls in the T/E test show that LNDD is fully capable of creating positive controls in a urine matrix when testing for endogenous substances. This is true because LNDD's T/E positive controls were in fact stripped of endogenous testosterone metabolites.

LNDD's Instrument Checks Provided No Quality Control Assurance

35. As for quality control, I would also point out that LNDD has set for itself a very low acceptance standard for its quality control methods. In SOP ECC-10, LNDD sets forth its acceptance standard for Cal Mix IRMS. In ECC-10, LNDD sets a standard deviation of only 3 of 4 alkanes to be within LNDD's stated +/- 0.5 delta units. These four alkanes (decane, undecane, dodecane and methyldeconate) are in a pure matrix and thus extraordinarily easy to measure. This is inexplicable. If LNDD cannot measure all four of these alkanes within its own determined measurement of uncertainty, then its ability to properly measure the isotopic value of a substance in a dirty matrix with high background and interference from neighboring peaks is nil. In 1995, I measured a similar standard and made replicate injections of two different concentrations over a 4 day period achieving 1SD<0.2 per mil variation for 118 injections. Also, for the work I presented, isotope ratios were calculated using default parameters for vendor-supplied software, not manual integration. LNDD's acceptable error is more than twice what I was able to achieve for almost 40 times the number of injections over a significantly longer timeframe. *See* Goodman 1988: "Hardware Modifications to an Isotope Ratio Mass

Spectrometer Continuous-Flow Interface Yielding Improved Signal, Resolution, and Maintenance", K.J. Goodman, Analytical Chemistry, 70, 833-837, 1998.

36. The same is true for the Mix Cal Acetate. There, LNDD again states that only 3 of 4 of its steroid acetates must be within its stated error of +/- 0.5 delta units. Again, this is inexplicable. Inability to measure all four steroid acetates in a pure matrix within its stated measurement of uncertainty would lead me to believe that LNDD was incapable of properly measuring the isotopic value of a substance in a dirty matrix with high background and interference from neighboring peaks.

37. My opinion that the quality control measures in this case are meaningless is also supported by the way in which they were conducted. I note that USADA emphasizes that there is an IRMS injection sequence – involving the injection of three (3) stability runs, three (3) Mix Cal IRMS runs, Mix Cal Acetate, Blank Urine F3, F3, Blank Urine F1, F1, Blank urine F2, F2, and Mix Cal Acetate.

38. I have read that USADA, in both its AAA panel pre-hearing and reply briefs, emphasized that quality controls were run "immediately before and immediately after" or "minutes before and minutes after" Mr. Landis' A and B Samples. *See* USADA Pre-Hearing Brief ¶ 79 ("The Mix Cal Acetate results from the controls run immediately before and immediately after Respondent's A and B samples . . . ."); USADA Response Brief ¶ 27 ("In its Pre-Hearing Brief, USADA went into considerable detail to explain how the Mix Cal Acetate, Blank Urine and Mix Cal IRMS controls run in the same sequence **minutes before, during, and minutes after Respondent's sample**. . . .) (emphasis added). This is not true.

39. As Dr. Meier-Augenstein made clear in his testimony there was a five hour, fourteen minute gap between the running of the Sample A F2 fraction of Sample 995474, Ex. 24,

USADA0166, and the running of the Mix Cal Acetate. Ex. 24, USADA0183. The summary chart can be seen at Closing Presentation at Slide 42.

40. Dr. Meier-Augenstein also made clear that there was a four hour, forty minute gap between the running of the first Mix Cal Acetate, Ex. 25, USADA0362, and the running of the Sample B F3 Blank Urine of Sample 995474. Ex. 25, USADA0347. The summary chart can be seen at Closing Presentation at Slide 45.

41. I also have seen that in the transcript, LNDD lab personnel, Ms. Mongongu, when pressed to explain these gaps, testified that she forgot to add the Mix Cal Acetate to the A Sample. Tr. of R. at 600:20-601:3. Ms. Mongongu also testified that she could not remember what happened during the gap in the testing of the B Sample. Tr. of R. at 608:5-8. However, Ms. Frelat testified that the gap in the "B" sample occurred because she ran the initial quality controls, i.e., the stability, Mix Cal IRMS and Mix Cal Acetate, approximately four and one-half hours before Mr. Landis' "B" sample was prepared and ready for injection.

42. In totality, these extraordinary gaps and lax procedures give me no assurance in the accuracy or reliability of LNDD's quality control, and its test results in this case generally.

43. Lastly, LNDD's instrument checks provided no quality control assurance. In particular, USADA indicates that the stability runs do not provide any meaningful assurance that the GC-C-IRMS instrument can properly measure the isotopic value of any of the target analytes. The stability runs consist solely of three injections of CO2 gas. The CO2 gas is injected after the combustion phase – so it only tests the mass spectrometer. In effect, the injection of CO2 gas can only ensure that there are no leaks or other gross problems in the mass spectrometer or the general conditions of the system. It cannot ensure that the final isotopic values of GC combustion samples derived from a biological matrix are correct and proper.

IDENTIFICATION

44. One of the most critical components of GC-C-IRMS analysis is the proper identification of testosterone's metabolites. Without the proper identification of these metabolites, the GC-C-IRMS test results are utterly meaningless because there is no assurance that the isotopic values are even related to testosterone. In other words, without proper identification of testosterone's metabolites, the laboratory cannot provide this Panel with any assurance that what is being analyzed is in fact testosterone-derived metabolites. Indeed, ISO/IEC 17025 section 5.4.5.2 states: "The laboratory shall validate non-standard methods, laboratory-designed/developed methods, standard methods used outside their intended scope, and amplifications and modifications of standard methods to confirm that the methods are fit for the intended use. The validation shall be as extensive as is necessary to meet the needs of the given application or field of application. The laboratory shall record the results obtained, the procedure used for the validation, and a statement as to whether the method is fit for the intended use."

45. In my opinion, LNDD failed to properly identify testosterone's metabolites in Sample 995474 such that the test results in this case are unreliable, inaccurate and of no evidentiary value. I find that the procedures used by LNDD are in violation of WADA TD2003IDCR. Further, I find that, even aside from being in violation of WADA TD2003IDCR, the procedures used by LNDD are far outside good laboratory procedure and are utterly unreliable. Lastly, I conclude that LNDD's and USADA's statements about the identification of testosterone metabolites in this case are inexplicable and nonsensical. In order to fully explain this conclusion, I will begin with an explanation of IRMS testing.

46. I have read the statements by USADA from the AAA's Pre-Trial Hearing Brief and the statements in USADA's Appellee Response Brief regarding retention time and relative

retention time and I find USADA's statements logically inconsistent. Moreover, I find that the statements in USADA's Appellee Response Brief of the manner in which identification was conducted are scientifically invalid, inaccurate, unreliable and further, at odds with previous statements made by USADA and LNDD technicians about how identification of testosterone metabolites is conducted at LNDD. In addition, the methodology used is not in accordance with competent laboratory practice as described in ISO/IEC 17025 section 5.4.5.2 provided below. Non-standard methods need to be evaluated and verified in a systematic manner prior to employing them on real samples. It is not appropriate to invent and apply methodology on-the-fly.

47. The theory behind the IRMS test rests on the difference in the isotopic charateristics of carbon of naturally produced (endogenous) or synthetically produced (exogenous) testosterone. Testosterone is composed of Carbon, Oxygen and Hydrogen atoms. However, there are several isotopes of Carbon, including the stable isotopes ^{12}C and ^{13}C. Testosterone and its metabolites are composed of a mixture of ^{13}C and ^{12}C. The ratio of ^{13}C to ^{12}C in any individual will vary based on their source. For example, synthetically produced testosterone where is produced from soy plants, which are relatively low in ^{13}C, also known as ^{13}C depleted, compared to natural testosterone where ^{13}C enrichment is derived from, and varies according to, dietary sources. Thus, a person who uses synthetic testosterone or eats foodstuffs derived from a soy or wheat based diet will have testosterone with fewer ^{13}C atoms. In the context of anti-doping, the IRMS instrument measures the ratio of ^{13}C to ^{12}C, also known as the isotopic ratio or isotopic value, in specific metabolites of testosterone, as explained below.

48. The IRMS test does not measure the isotopic ratio of testosterone – it examines the metabolized products ("metabolites") of testosterone. The IRMS test measures the following

four metabolites of testosterone: Androsterone ("Andro"), Etiocholanolone ("Etio"), 5α-Androstanediol ("5 Alpha") and 5β-Androstanediol ("5 Beta"). The carbon framework of the testosterone metabolites will maintain essentially the same isotopic value as the testosterone from which they originated, according to the limited research conducted in this area mainly on non-atheletes. Therefore, the prevailing theory is that measuring the isotopic ratio of the metabolites is tantamount to measuring the isotopic ratio of testosterone.

49. There are several individual variables that can cause endogenous testosterone and its metabolites to become ^{13}C depleted that are unrelated to using exogenous testosterone, such as diet. To account for these individual variables, the IRMS test compares the $^{13}C/^{12}C$ ratio of a testosterone metabolite to the $^{13}C/^{12}C$ ratio of an endogenous reference compound ("ERC"). Comparing the difference in the $^{13}C/^{12}C$ ratio between a testosterone metabolite and an ERC, <u>if performed properly</u>, indicates the likelihood of testosterone being from an exogenous source.

50. In theory, for any individual at any one time the $^{13}C/^{12}C$ ratio of an ERC should be close to that of a testosterone metabolite. If a person is using exogenous testosterone, however, there will be a detectable and significant difference between the $^{13}C/^{12}C$ ratio in a testosterone metabolite and an ERC. In other words, if a person is taking exogenous testosterone, his or her $^{13}C/^{12}C$ ratio for a testosterone metabolite will be different than the ratio for an ERC.

51. That there is some detectable difference between the $^{13}C/^{12}C$ ratio between the metabolite and the ERC does not result in a positive test, however. Once the $^{13}C/^{12}C$ ratio for the ERC is subtracted from the testosterone metabolite, referred to as the $\delta^{13}C‰$ value or the delta-delta value, it must be compared to the positivity criteria mandated by WADA. The WADA positivity criteria for IRMS is as follows:

> The results will be reported as consistent with the administration of a steroid when the $^{13}C/^{12}C$ 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 $^{13}C/^{12}C$ 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.

See Exhibit WADA0011-0021, at 3.

52. There are several metabolites whose isotopic values are measured by the IRMS instrument (Androsterone, Etiocholanolone, 5α-Androstanediol ("5α-Adiol") and 5β-Androstanediol ("5β-Adiol"), along with the isotopic value of two ERCs (11-Ketoetio and 5β-Pdiol). LNDD in theory identifies and measures all of these metabolites and ERCs. However, the relevant delta-delta numbers are calculated by subtracting the delta value of 11-Ketoetio (ERC) from the delta value of Etiocholanolone and Androsterone (metabolites) and from subtracting the delta value of 5β-Pdiol (ERC) from the delta value of 5β-Adiol and 5α-Adiol (metabolites).

<u>How The Carbon Isotope Ratio ("CIR") Test Operates</u>

53. The IRMS test consists of three main steps: (1) sample preparation, (2) pre-IRMS compound identification by GC/MS and (3) IRMS analysis. Each one of these steps must be performed properly in order to obtain accurate delta-delta values.

54. The IRMS test begins with sample preparation. First, an aliquot is made from the sample; additionally, an aliquot made from blank urine, which is taken from a pool of urine known not to contain synthetic testosterone (it is often the urine pooled from lab technicians). These aliquots are then cleaned through several physical, enzymatic and chemical treatments. The reason for this step is obvious – urine is a waste product, a "dirty" matrix, in which many other substances, in addition to testosterone and its metabolites, will be present. In order to

ensure the accuracy of the IRMS results, the sample must be stripped of those other substances so that it is clear that the laboratory is not measuring/analyzing the wrong substances.

55. The aliquots are then separated into three fractions using further physical treatments. The three fractions created are as follows: (1) the F1 fraction, containing 11-Ketoetiocholanolone (11-Keto), (2) the F2 fraction, containing Etiocholanolone (Etio) and Androsterone (Andro) and (3) the F3 fraction, containing 5α-Androstanediol (5α-Adiol), 5ß-Androstanediol (5ß Adiol) and 5ß Pregnanediol (5ß Pdiol). One of the last steps in sample preparation is the addition of an "internal standard." The internal standard, which in this case was 5 Alpha Androstanol Acetate, is a substance with a known isotopic value. Per LNDD, it allegedly serves as a quality control.

The IRMS Test

56. The IRMS test relies on two different instruments - the GC/MS instrument for accurate compound identification in the sample and the GC/C/IRMS instrument for determination of carbon isotope ratio in those compounds identified by GC/MS. Two instruments are needed because neither instrument can perform both the necessary functions to complete the test – identification and measurement. The GC/MS instrument cannot measure natural variation in isotopic values, it can only measure molecular mass; whereas, the GC/C/IRMS instrument can measure natural variation in isotopic values, but combusts all analytes to CO_2 prior to detection so requires independent confirmation of the identity of the molecule. (Maurice, IRMS can measure molecular mass, it measures the mass of CO_2). In some IRMS laboratories, the GC/MS instrument is attached to, and part of, the IRMS instrument. However, at LNDD, two different and non-attached instruments were used.

The GC/MS Analysis: Compound Identification

57. Once the fractions are prepared, the first phase of IRMS testing – compound identification with the GC/MS instrument – begins. The GC/MS instrument is composed of two major components: the gas chromatograph and the mass spectrometer. The gas chromatograph is used to separate molecules by sending these molecules through a column, which is essentially a tube coated with complex hydrocarbons. This coating is called the "stationary phase." Based on the interaction of each individual molecule with the stationary phase, each compound moves through the column at different rates. The amount of time each molecule takes to move through the column is that molecule's retention time. The fastest moving molecules reach the end of the column first, thus corresponding with the first peak in the chromatogram. The next fastest molecule follows and creates another peak in the chromatogram. This process continues until all of the remaining compounds have left the column.

58. Different molecules can have the same retention times, however. Therefore, after each molecule's retention time is measured, they are passed to the mass spectrometer. The molecules are passed through a stream of electrons. Electrons passing near to, or contacting, the analyte result in one or more electrons being dislodged from the molecule in question. This process, known as ionization, results in the molecule becoming "charged". A charged molecule is known as an ion. There are typically a number of different ions created in this process, the parent ion and fragment ions. Parent ions are intact molecules that have simply lost one or more electrons during ionization. Fragment ions are small pieces or "fragments" of the parent ion broken off during the process of ionization. Once ionized, the mass spectrometer measures the abundance of the different ions, also called a response, using each ionized mass-to-charge (m/z) ratio. This is akin to a molecular fingerprint, and is recorded by the mass spectrometer.

59. The GC/MS test produces a series of documents called chromatograms. The chromatogram shows all molecules within a designated m/z ratio. The chromatogram is simply a graph with time on the X-axis and response, or quantity, on the Y-axis. On the chromatogram, there are several peaks, each of which should correspond to a single compound in the sample. In sum, the GC/MS chromatogram identifies compounds by their retention times and m/z ratios.

Step 3: IRMS Analysis

60. After the identification of all of the target metabolites pursuant to the GC/MS analysis, the individual fractions are then injected into the GC/C/IRMS instrument. Once the fraction is injected into the GC/C/IRMS instrument, the compounds in the fraction are separated by gas chromatography. Similar to the GC/MS test, these molecules travel through a column and their retention times are recorded. However, unlike in the GC/MS instrument, after the molecules reach the end of the column, the molecules are combusted CO_2 in the combustion furnace. Only carbon dioxide remains after this step and there is no longer any means to measure the m/z ratio of the intact molecule. , The resulting carbon dioxide is then analyzed by the isotope ratio mass spectrometer, which determines with high precision the carbon isotope ratio of the combusted analyte. This analysis then determines the compound's isotopic value.

61. Although the only matrix containing samples that are injected into the GC/C/IRMS instrument described above is the fractions and blank urine, there are several other non-matrix samples introduced into the IRMS machine during the testing process. These include stability samples, Mix Cal IRMS samples, and Mix Cal Acetate samples and are analyzed as follows: (1) Stability run 1, (2) Stability run 2, (3) Stability run 3, (4) Mix Cal IRMS 003-1, (5) Mix Cal IRMS 003-2, (6) Mix Cal IRMS 003-3, (7) Mix Cal Acetate, (8) Blank Urine fraction