

BEFORE THE AMERICAN ARBITRATION ASSOCIATION
North American Court of Arbitration for Sport Panel

United States Anti-Doping Agency,

Claimant,

V.

Floyd Landis,

Respondent.

RESPONDENT FLOYD LANDIS'
SUPPLEMENTAL PRE-TRIAL BRIEF

AAA No. 30 190 00847 06

I.

INTRODUCTION

In an apparent concession that LNDD's GC/MS test method is unreliable, USADA has staked this case upon the accuracy of LNDD's IRMS results. *See* Pre-Trial Response Brief, at 2 ("Given that LNDD's analytic finding is based upon the IRMS results . . . "). In so doing, USADA continually asserts that its GC-IRMS method and results are perfect. *See* Pre-Hearing Brief, at para. 63 ("Nothing . . . casts the slightest doubt on the reliability of LNDD's IRMS results.") Now that the EDF analysis has been completed, it is clear that nothing could be further from the truth.¹ As detailed in the many pages of

¹ Because the ruling on the admissibility of the retesting results has not yet issued, those issues will not be addressed here. However, the retesting results also support

[Footnote continued on next page]

USADA's briefs, the operation of the GC-C-IRMS instrument is a complicated task, requiring precision in each step of its operation. *See* Pre-Hearing Brief, at p. 16 - 49. This precision is necessary because the instrument is designed to accurately quantify not just tiny amounts of material, but ratios of those materials. From the EDF analysis, two critical defects are confirmed that are central to LNDD's ability to accurately run its Isoprime instrument and analyze its results.

- In violation of ISL 5.4.4.2.1 and 5.4.4.2.2, the chromatography that LNDD relies upon to calculate its per mil values for 5 α Androstanediol ("5 Alpha"), 5 β Androstanediol ("5 Beta"), Androsterone ("Andro") and Etiocholanolone ("Etio"), as well as its internal standard, 5 α AndrostenolAC ("5 Alpha AC") and blanc urines is completely unreliable and unfit for IRMS analysis. LNDD's chromatograms show co-eluting peaks, disappearing peaks, high sloping baselines, and other matrix interferences that violate ISL standards and have resulted in the inconsistent and incorrect results seen here. The impact of those failures were confirmed by the results of the analysis of the EDFs, as expected. In particular, the impact of the poor chromatography is demonstrated by the fact that when the EDFs are rerun, the values are simply all over the place.

[Footnote continued from previous page]

the conclusion that LNDD performed its IRMS analysis in an entirely unreliable fashion.

- In violation of ISL 5.4.4.4.1.4., LNDD manually applied background subtraction in its peak integration process without documenting its method. The use of "manual background subtraction" means that an LNDD technician – not the OS2 program – has chosen where each peak associated with a target isotope (5 Alpha, 5 Beta, Andro, Etio, Pregnandiol and 11Ketoetio) begins and ends. Picking where the peak begins and ends is tantamount to determining the final value. In so doing, LNDD failed to create an audit trail and document its methodology as required by the ISL. Indeed, but for the demand to reprocess the EDFs, LNDD's "manual" reprocessing of the chromatographic data would have remained a secret.

These two issues are determinative as to the accuracy and reliability of the IRMS data. The poor chromatography and manual "reprocessing" are both violations of the ISL that materially affect the IRMS results. Moreover, because of the EDFs, it is now clear that the impact of both is not speculative. LNDD's IRMS "results" now jump around and the same metabolite values differ as much as 3 per mil, depending on which method or software is being used.

In conjunction with the issues raised in Mr. Landis' opening brief, this case should not proceed due to the utter lack of reliability of LNDD's method and results.

II.

FACTUAL SUMMARY

The analysis of the Electronic Data Files ("EDFs") proceeded according to the following schedule. On Thursday, April 26, 2007 at 12:30 PM, Dr. Simon Davis and Dr.

Will Price arrived at LNDD to witness and assist in the extraction of EDFs related to the IRMS analysis of samples provided by Mr. Landis while competing in the 2006 Tour de France. Analysis of the EDFs allows an expert in Isotope Mass Spectrometry to determine if the data was processed correctly. In this particular case, as to Sample 995474, it allowed an expert to examine whether there are flaws in the software and methods used on the O/S 2 Optima software that make the results unreliable.

At or around 1:00 PM, USADA representatives Dr. Bowers and Dr. Jeanine Jumeau, along with Dr. Botrè and Drs. Davis and Dr. Price arrived and were admitted into LNDD. At that point, everyone was escorted to a conference room. There, in the conference room, Dr. Buisson, the LNDD head of IRMS, informed the group that:

1. The EDFs from Isoprime1 (the instrument used to test Sample 995474) had already been copied to an archive CD; and
2. The original information on the Isoprime1 hard-drive had been erased.

At this point Dr. Davis asked to inspect Isoprime1. This request was refused with the explanation from Dr. Buisson that the data files are removed during backup, so there would be nothing left to inspect.

Dr. Davis next inquired about the linearity data from Isoprime1. USADA representative Dr. Bowers argued that he did not interpret the Panel's order to include EDFs relating to linearity, but instead it was restricted exclusively to the run that included Sample 995474.

Dr. Davis next requested that Dr. Botrè also collect the EDFs from the 10 "retesting" samples. Specifically, he asked that Dr. Botrè collect:

1. the sample files; and
2. the linearity files; and
3. the log files.

Dr. Bowers again argued that the Panel's order was restricted exclusively to the run that included Sample 995474 and that no data on the "retesting" samples should be provided.

To resolve these issues, Dr. Botrè placed a telephone call to Panel Member McLaren to seek instruction. Mr. McLaren was unable to contact Panel Member Campbell but was able to contact Panel Chair Brunet. The decision of the Panel was that:

1. Dr. Botrè would take with him copies of all requested data – this data included the EDFs for the samples, controls and linearity runs for Sample 995474, the EDFs related to the retesting and the log files related to the retesting; and
2. no samples would be reprocessed on this day; and
3. the decision as to what, if anything, would be done with the data collected would await later review.

At this time, on or about 2:30 PM, Dr. Buisson and Ms. Mongongu (one of two LNDD IRMS chemists involved in this case) left the conference room to gather the "master" CDs onto which the data had been copied.

At or around 3:00 PM, Dr. Buisson returned to the conference room and announced that one of the linearity files had been "lost." No explanation as to how the file was lost was given.

During the copying of the EDFs for Sample 995474, it was noted that the date stamp on the CD containing the "A" sample run for Sample 995474 was January 30,

2007, while the date on the CD for the "B" sample run for Sample 995474 was April 26, 2007 at 9:47 AM – approximately three hours before Dr Botrè and the other experts were expected to arrive. The date stamp, which includes the date and time of the last file write for any individual file, is part of the detailed directory listing for any folder on a Windows or O/S 2 based personal computer.

In contrast to the Isoprime1 machine used to analyze Sample 995474, the hard drive for the Isoprime2 machine used to analyze the "retesting" samples was reported to be intact and installed in the Isoprime that analyzed the retesting samples. Therefore, the experts were able to observe the transfer of the electronic data files generated during the retesting from the local hard drive to a network folder then to a CD. At or around 3:35 PM, after the 995474 copy CD was created, the experts were escorted to the Isoprime room for the copying of the files related to the "retesting" samples. Dr. Davis instructed Dr. Buisson as to which files to copy. Dr. Buisson created a separate folder on the desktop and copied the data files Dr. Davis requested into this folder.

Upon the completion of the copying of the data files, Dr. Davis instructed Dr. Buisson to copy the log files. Dr. Bowers objected. Dr. Buisson questioned Dr. Davis as to what information was in the log files. Dr. Davis informed her and Dr. Bowers restated his new objection. Dr. Davis asked Dr. Botrè to insist that the log files were copied. Dr. Botrè decided to have them copied, but placed them on a separate CD from the other EDFs.

At this point, using a different network computer, CDs were created – one containing the log files and a separate CD containing the data files.

The experts were then escorted back to the conference room. There, Dr. Davis inspected the three CDs and printed a “file detail” list. The file detail list is the detailed directory listing of a folder that contains, among other things, the date and time stamps. During that time, Dr. Buisson returned to the room and announced that the “retesting” CD contained an unintended file. It included a “Cal Acetate” file that Dr. Buisson asserted “didn’t work.” She then requested the return of the CD and offered to make another CD without that file. Dr. Botrè decided that this would not be necessary. Next, Dr. Davis asked to inspect the Master CDs again. This inspection was allowed. Upon his completion of the inspection of the Master CDs relating to sample 995474, Dr. Davis was asked by Bowers to join a conference call with USADA retained expert Dr. Thomas Brenna for the purpose of discussing the data reprocessing procedure. The call ended shortly after it started. At this point, the experts left LNDD.

On May 4, 2007, Drs. Botrè, Brenna, Davis and Jumeau arrived at LNDD for the reprocessing of the previously copied data. Prior to the reprocessing, the persons present discussed whether to reprocess only the Stage 17 samples or to additionally reprocess the retesting samples. Additionally, the issue of access to log files was again addressed. Attempts to reach the panel members by phone failed; as such this discussion was tabled. The group, along with Drs. Ceaurriz and Buisson and IRMS chemists Mongongu and Frelat, proceeded to the IRMS room for the reprocessing. There it was decided that because Dr. Botrè was not familiar with the operation of the Optima software, that the LNDD operator originally responsible for processing the result would operate the reprocessing. Dr. Botrè requested the reprocessing on the Isoprime1 as a means of

verifying that the files in his possession were the same file printed in the LNDD Documentation Package. LNDD staff did not know how to transfer data from a CD onto the computer operating the Isoprime1; however, Dr. Davis was able to assist in the process. Dr. Botrè assumed that if the results were identical to the results originally reported that this would be good evidence that the EDFs were also identical to the ones that produced those results. However, LNDD technicians admitted to using “manual” background subtraction on all samples coming off the Isoprime1. Each operator uses her “judgment and experience” to manually select background points as well as peak start and end. As such, LNDD was unable to reproduce the original results, despite 22 attempts to do so. Because of this situation, it was agreed that three outputs would be produced and printed for each sample:

1. automatic background subtraction; and
2. manual processing – using the same operator exercising her judgment as she did during the process of creating the original data printed in the LNDD Documentation Package; and
3. no background subtraction

The reprocessing of the files started at 3:45 PM and continued until 7:00 PM, whereupon it was halted for the night. All agreed to continue on the following day at 9AM.

On May 5, 2007 at 9:15 AM a preliminary meeting was held. It was agreed that the Stage 17 reprocessing would be finished and then the outstanding issues would be resolved.

Upon completion of the reprocessing of the B sample files, the stability runs from the A and the B were reprocessed. Once completed, two of the three linearity runs – the ones conducted on June 26th and July 31st of 2006 – were reprocessed. The September 25, 2006 linearity run was not reprocessed because LNDD destroyed the EDF without having backed it up and as a result it was not available for reprocessing.

At 11:20 a.m., reprocessing of the Stage 17 samples using Masslynx (the software used on the computer controlling LNDD's Isoprime2) commenced. LNDD staff did not know how to convert the Optima data into data readable by Masslynx; however, Dr. Davis was able to assist in the process. All files were then processed on Masslynx. It was agreed that only one Masslynx result would be output and printed – the result from the routine processing parameters of the laboratory.

After this was accomplished, it was agreed to forgo reprocessing of the retesting data. As a result, the only outstanding issue was the printout of the log files. Dr. Botrè called each of the panel members, again without success.

At or around 3:30 PM, Mr. McLaren returned Dr. Botrè's call and ordered that the log files for April 17-22, 2007 be printed and provided to both party's experts.

III.

ARGUMENT

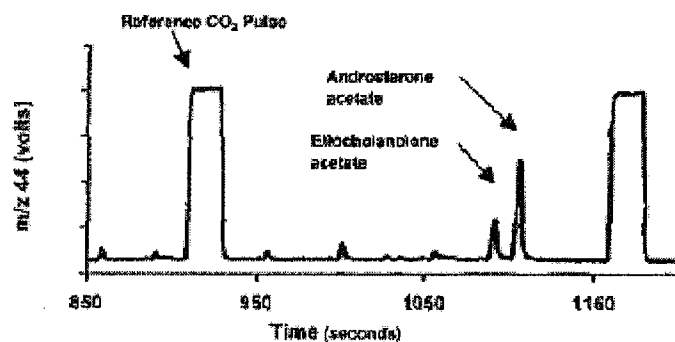
A. LNDD's Poor Chromatographic Technique and Protocols Extends To, and Infects, LNDD's GC-IRMS Results

The accuracy of the GC-IRMS test results depends upon the ability of LNDD to generate accurate chromatograms, from which the critical IRMS values are derived. It is

a bedrock principle that the generation of accurate chromatograms, with well-separated peaks and good symmetry, is critical to accurate IRMS results. See L. Bowers, R. Hildebrand & E. Symanski, "Application of Gas Chromatography-Combustion-Isotope Ratio Mass Spectrometry to Doping Control," 2nd Annual USADA Symposium on Anti-Doping Science.

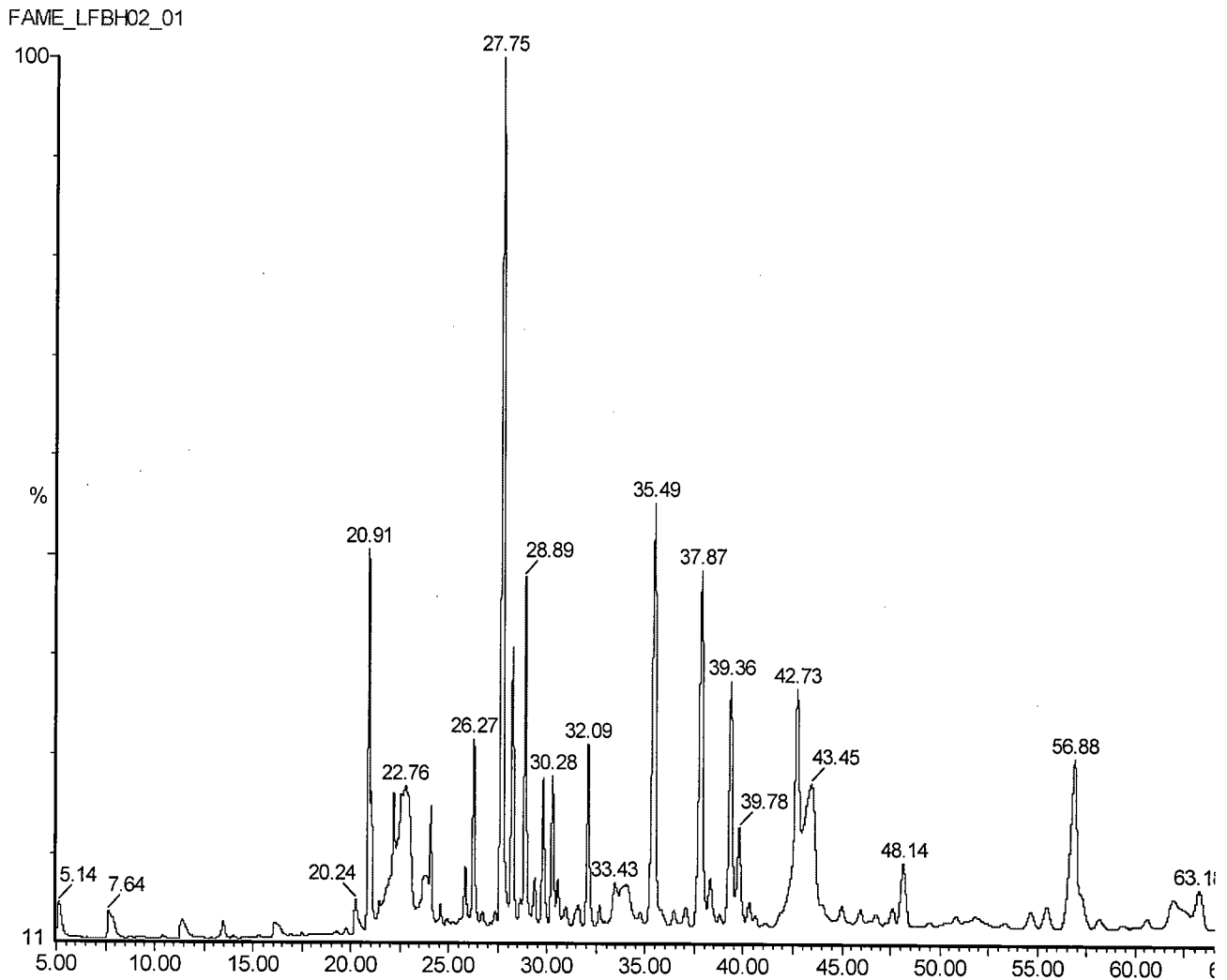
The accurate production of chromatograms is directly tied to ensuring that target compounds are not confused with other, unrelated substances. The importance of accurate chromatography is embodied in ISL sections 5.4.4.2.1 – 5.4.4.2.2, which require, for both threshold and non-threshold substances, that the confirmation method avoids interference in the detection of Prohibited Substances (or their metabolites) by components of the urine sample matrix. These interferences – also known as matrix interferences – destroy the accuracy of both the identification and quantification of prohibited substances or their metabolites. The reason that matrix interferences create this inaccuracy is because the size and shape of chromatograms are affected when the target substances are confused with other substances. When these target substances are confused, the chromatograms take on additional area and height that gives a false reading as to the identification and amount of the target compound. That is exactly what happened here.

To begin with, it is helpful to view an example of clean peak resolution. The following example is instructive:



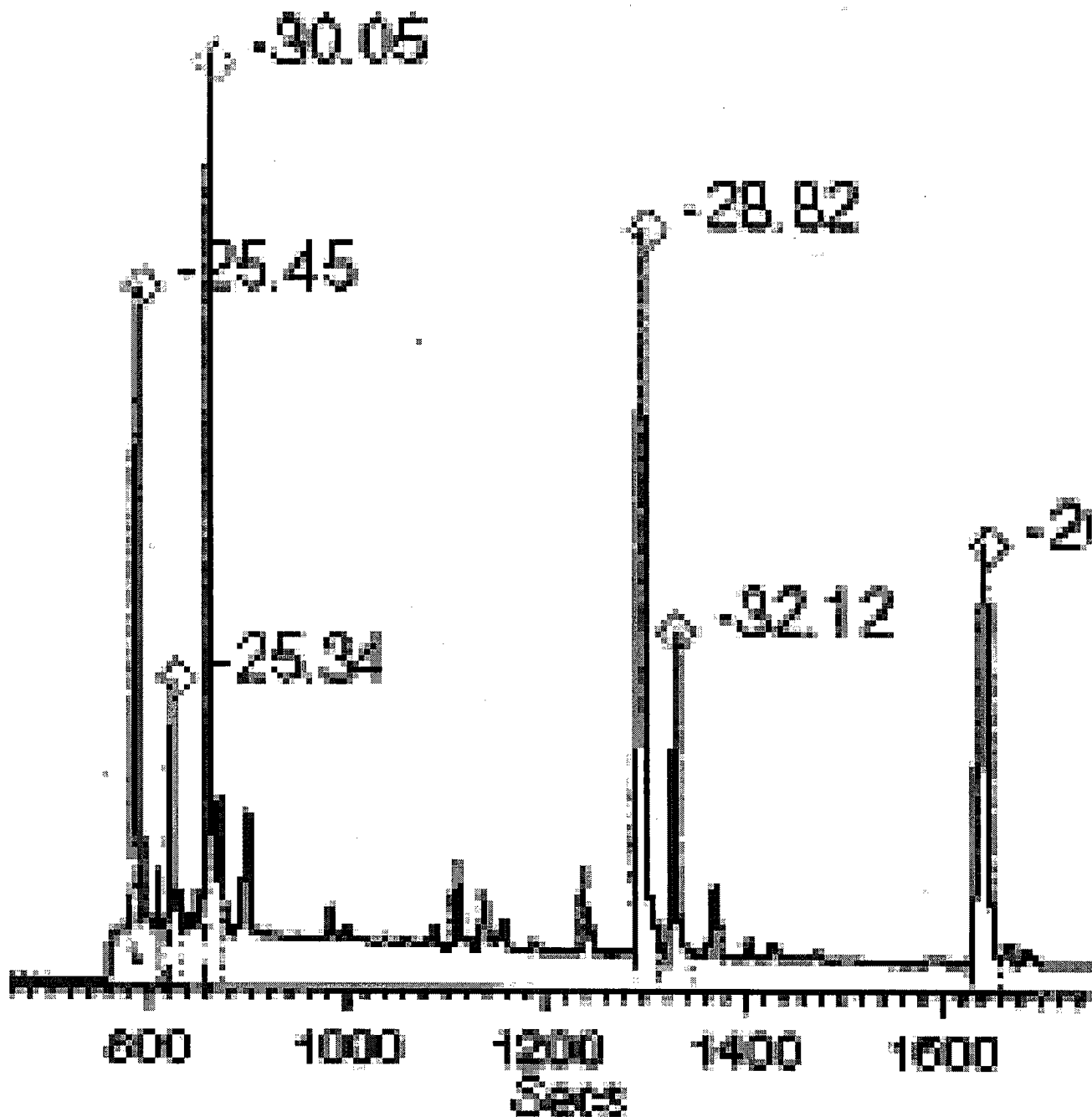
As shown in this figure, the chromatogram has clean, well-defined peaks, that are well-separated. Figure taken from: R. Aguilera *et al.*, Rapid Commun. Mass Spectrom., 14 2294, 2299 (2000).

This stands in sharp contrast to a chromatogram containing overlapping peaks that are not well separated:



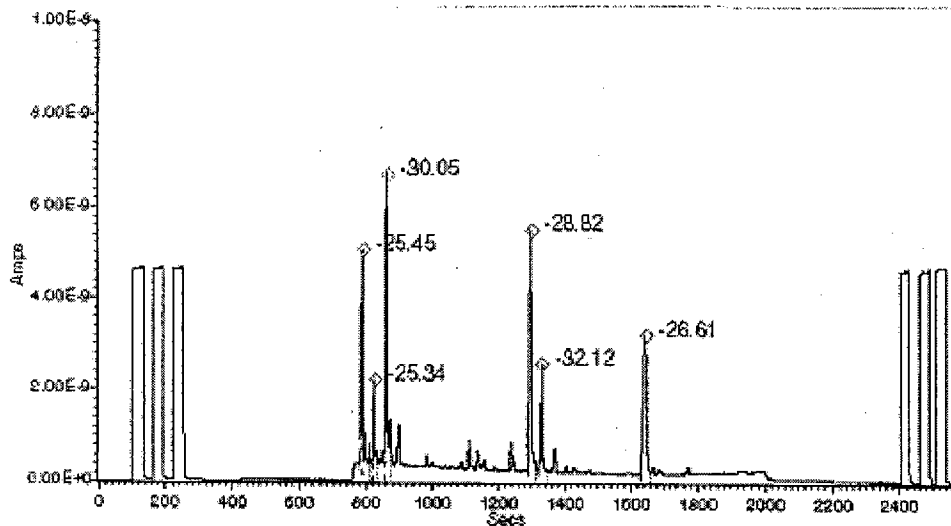
In this chromatogram, the peaks are close together, overlapping and not well-defined. The consequences for the final delta C13 values are tremendous, often resulting in sharply varying values for target analytes.

As will be shown during the arbitration, all of the chromatograms that bear on the alleged adverse analytic findings produced by LNDD show critical problems with overlapping and disappearing peaks, and downward sloping baselines. An example of an overlapping peaks is as follows:



Overlapping peaks create problems because the start and beginning of the two different peaks can be difficult, if not impossible to determine, and therefore, the C13 and C12 values of each peak are not separable, leading to inaccurate results.

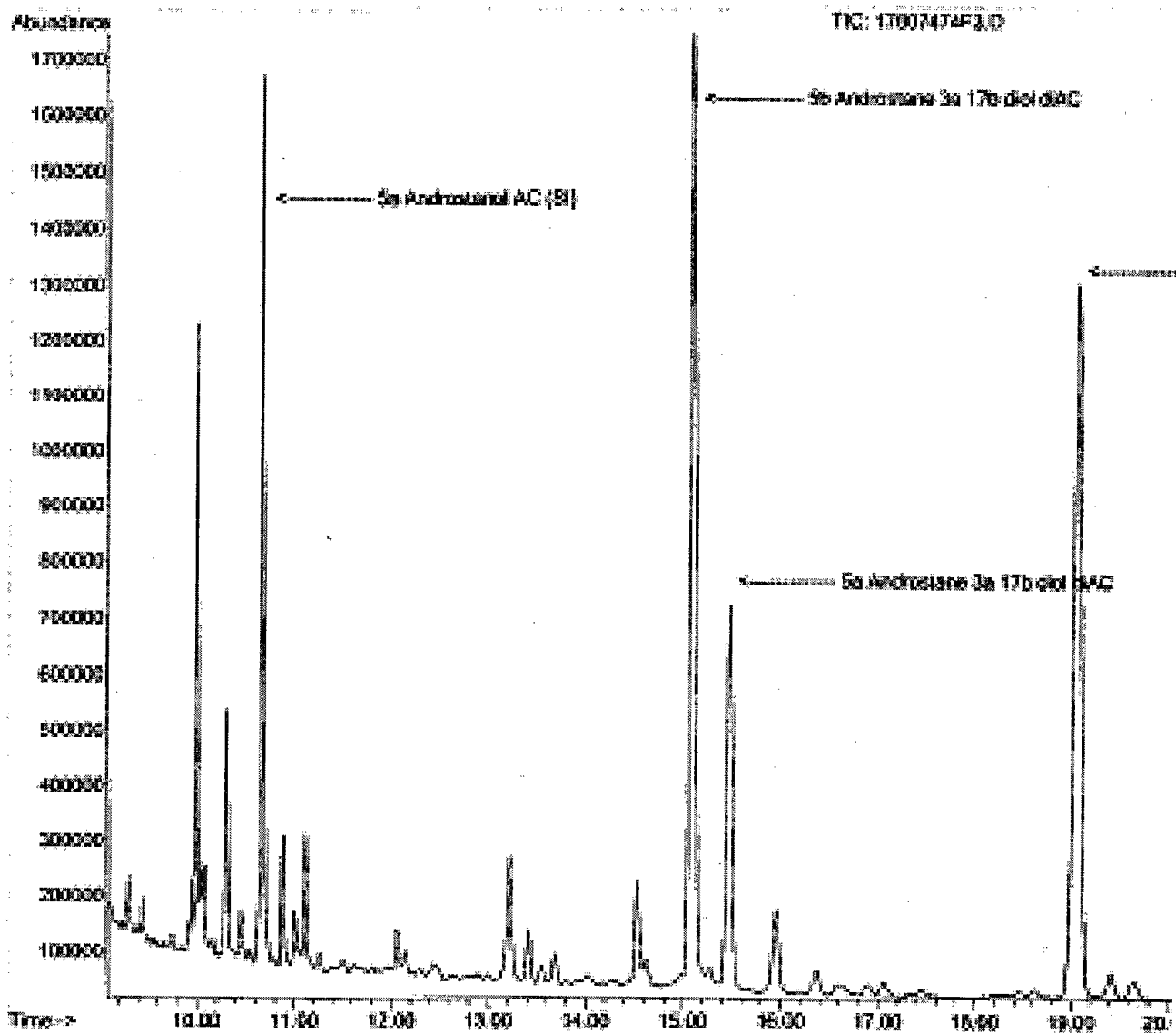
An example of a downward sloping baseline is as follows:



One problem with a downward sloping baseline is the fact that the downward sloping background interferes with the identification of the beginning and end of the peak, again leading to inaccurate results.

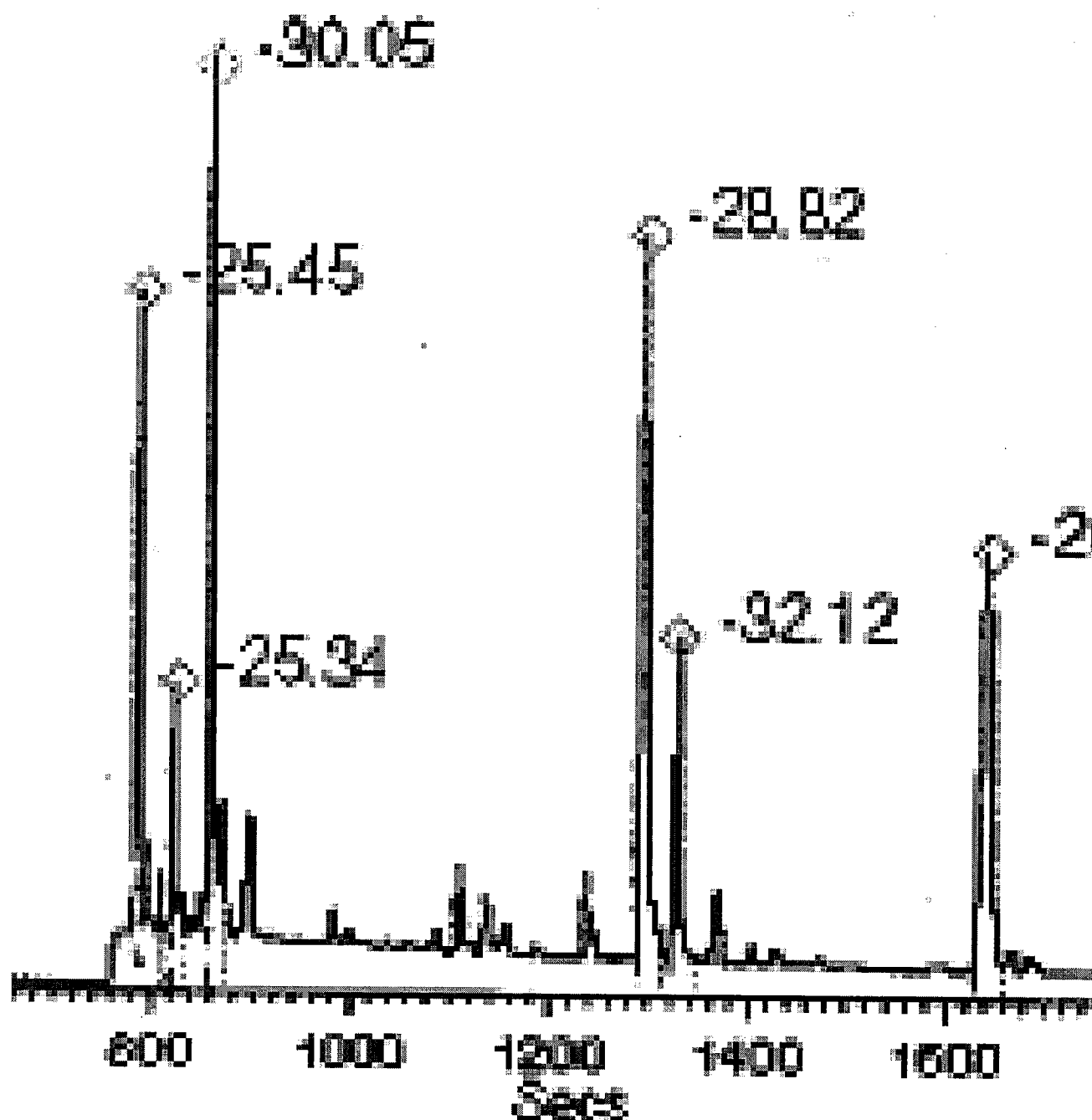
One example of the bad chromatography shown throughout the target samples is set forth below, from Mr. Landis' A Sample confirmation test. This chromatogram contains the 5 Alpha, 5 Beta and 5 Beta Pregnanediol, which was used to calculate to per mil values that reported him as adverse:

File : D:\Mad22\Jul106\2307\17807474F3.D
 Operator : 49
 Acquired : 23 Jul 2006 11:33 using AcqMethod MAN_52.M
 Instrument : MSD22
 Sample Name: 178/07 995474 F3
 Misc Info : 178/07 995474 Fraction 3 data 400pL
 Vial Number: 3



As is clearly shown, there are two additional peaks, one sitting just before the 5 Beta curve and one sitting right after the 5 Beta curve. There are also 8 minor peaks following the 5 Alpha curve. It is unknown (and now unknowable) what those peaks represent, and the relative composition of C13 and C12 in them. In the IRMS run of the

same sample, those two additional peaks (one sitting in front, the other sitting behind, the 5 Beta curve) have now disappeared and are now part of the neighboring peaks.



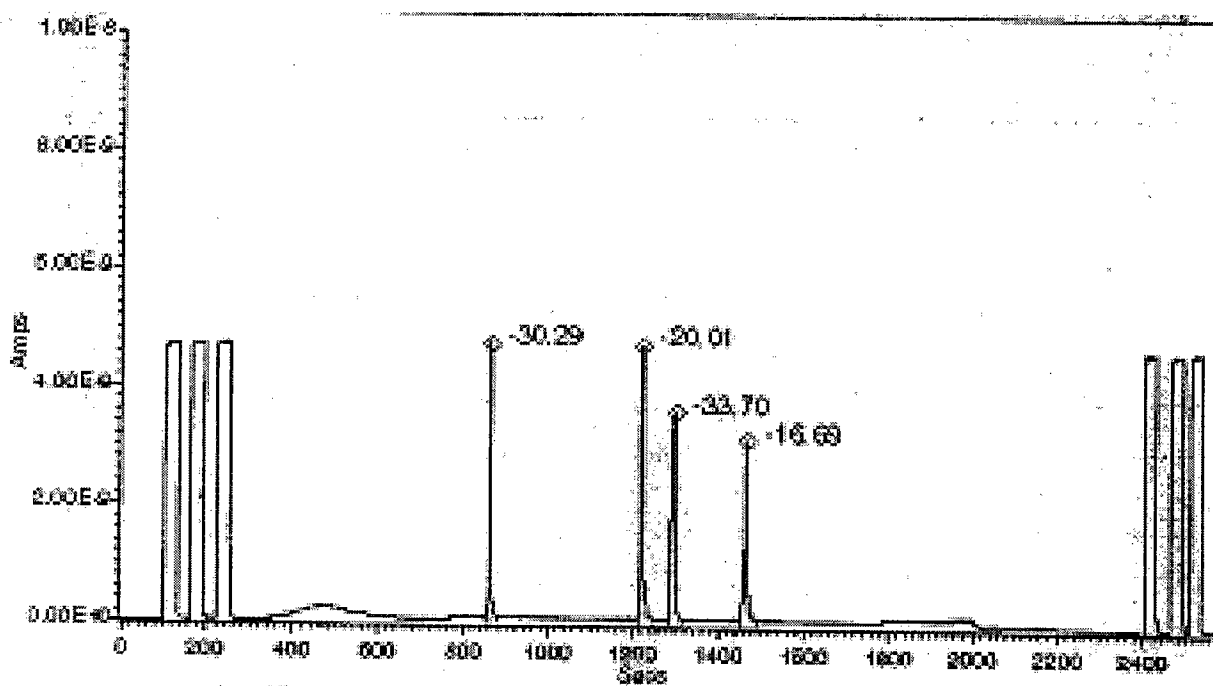
In addition, the 5 Beta tails into the 5 Alpha. Therefore, the reported C13 value for the 5 Alpha does not represent the C13 value for one compound, but rather two or

more compounds. The poor chromatography is further shown by the disappearance of the previous 8 peaks into 4 minor peaks. These problems are repeated over and over in all of the critical chromatograms, as will be shown during the arbitration.

The analysis of the EDFs confirm the existence of the impact of these errors in chromatography. As was made clear during the analysis of the EDFs, LNDD did not use OS2's automatic subtraction program, and instead performed manual subtraction. When the results were rerun, LNDD's technician achieved entirely different results. Because LNDD used a completely manual approach to defining what part of the curve went where, it resulted in a complete lack of reproducibility of results. This is not science, it is guesswork. In other words, the EDF files confirm what Respondent had known: that the chromatograms and the poor techniques used to generate them made for unreliable results, results that cannot be reproduced. Indeed, the chromatograms were so poor and so dependent upon the individual judgment of the particular operator that LNDD's own lab technicians could not consistently reprocess those samples.

B. LNDD's So-Called Quality Assurance Provides No Assurance Whatsoever

USADA repeatedly claims that the fact that the Mix Cal Acetate standards prove the reliability of the results. Again, this is not true. The chromatograms for the Mix Cal Acetates are much cleaner, without the overlapping peaks and downward sloping baselines that are shown in the actual samples. The following example is instructive. This chromatogram is from the Mix Cal Acetate 001A run before Mr. Landis' sample:



The reason that the Mix Cal Acetate chromatography is cleaner, and therefore an accurate quantification of the injected target analytes (5 α Androstanol-AC, Etio-Cholanalone-AC, 5 β Androstanediol-di-AC and 11Keto-Etio-AC), is because the Mix Cal Acetate is a solution containing only those compounds and a solvent. In short, there are no other unidentified substances that could create the interference that is routinely seen in the actual sample chromatograms. In contrast, urine is an exceptionally complex matrix, containing many substances that cause interference, which are clearly seen in Mr. Landis' actual samples. Indeed, the purpose of the lengthy chemical workup phase of the GC-IRMS testing process is to remove the interfering substances from the sample so that target compounds (5 Alpha, 5 Beta, Andro, Etio and Pregandiol and 11Keto-Etio) in the chromatograms are well separated. In short, the Mix Cal Acetates provide absolutely no assurance that the actual samples were analyzed properly, as was clearly demonstrated by the EDF results.

C. LNDD Violated ISL 5.4.4.4.1.4. Through its Background Subtraction

Procedures

As made clear above, a critical component of the GC-IRMS process is the application of subtraction. Background subtraction is the operation by which the background interference in a chromatogram is eliminated so as to result in an accurate picture of the peaks. In other words, through background subtraction, a laboratory will attempt to eliminate the effect of high baselines. This background subtraction operation occurs during the process called "peak integration," which is the process that calculates the area underneath the peak, thereby rendering an accurate result.

The OS2 program had an automatic background subtraction feature. This is shown as follows:

Data Processing Results

Data File Name : DATA.G07
 Folder : 230706
 Sample Name : Mix cal Acetate d01A-100ng inj
 Sample ID :
 Sample Position : 2
 Injection Size : 0.0000
 Sample Type : Sem
 Method : M-AN-41
 Batch Name :
 RunTime User : micromass
 Acquisition Time : 10:53:36 Date : 23/07/06
 Current Time : 11:39:17 Date : 23/07/06

Analysis of Reference Gas Data

Ref Delta 13 = -34.50 Ref Delta 18 = -19.30

Time	Major	Ratio 2/1	Ratio 3/1
122.5	8.609E-9	1.1781E-2	4.2521E-3
182.6	8.616E-9	1.1781E-2	4.2522E-3
242.6	8.618E-9	1.1781E-2	4.2523E-3
2423.4	8.509E-9	1.1781E-2	4.2519E-3
2483.5	8.465E-9	1.1791E-2	4.2516E-3
2533.4	8.526E-9	1.1780E-2	4.2530E-3

Std Dev Of File 1.7125E-7 1.7134E-7

Analysis of Sample Peaks, with Background Subtraction

CO2	Time	Height	Area	2/1	3/1	dC13Pk	dC13Bkd	dC18Pk	dC18
	166.5	4.79E-9	2.0679E-8	1.1921E-2	4.1654E-3	-30.29	-66.47	-39.32	24
	1229.8	4.79E-9	3.7785E-8	1.1938E-2	4.1666E-3	-20.01	-66.70	-39.05	24
	1502.2	3.63E-9	2.8203E-8	1.1782E-2	4.1669E-3	-33.70	-66.54	-39.08	24
	1471.2	3.17E-9	3.2254E-8	1.1976E-2	4.1665E-3	-16.69	-66.30	-39.06	24

This background subtraction feature runs without operator guidance – it simply calculates the appropriate background subtraction based upon an algorithm.

However, during the analysis of the EDF files, it became clear that LNDD did not use the automatic background subtraction feature, but rather, performed the subtraction "manually." This means that the technician had the ability to pick and choose where the peak should start and end. LNDD did this without any audit trail. The reason that having documentation of this "manual subtraction" is critical is that, depending upon where the start and end of the peaks are determined, the actual values of the measured isotopes can

vary tremendously. Indeed, as will be shown during the arbitration, the technician can literally choose the result.

ISL 5.4.4.4.1.4. requires that:

All data entry, recording of reporting processes and all changes to reported data shall be recorded with an audit trail. This shall include the date and time, the information that was changed, and the individual performing the task.

The process of running manual background subtraction is a clear violation of that rule. Furthermore, the impact of that "manual subtraction" is readily apparent from the analysis of EDFs. First, because the subtraction process was done manually, it was not even reproducible—even when more than 20 attempts were tried and rejected—on same machine that ran the original processing, with the same software, and by the original analyst. When LNDD attempted to rerun the sample using the same "manual subtraction" method, it resulted in different values:

This is particularly important because Mr. Landis suspected that this was part of the problem related to the LNDD's IRMS results, which generated a specific document request that called for "All DOCUMENTS that relate to the creation and accuracy of the background subtraction method used by LNDD in the IRMS test." *See Second Request for Production of Documents.* In response, LNDD provided a strikingly misleading response. In response, LNDD stated:

Background Subtraction is embedded in the instrument software, which is proprietary to the instrument manufacturer. LNDD has no separate documentation.

See LNDD Response to Second Request for Production of Documents.

Further, when the automatic background subtraction was used it resulted in different values. Lastly, when compared to Masslynx, again, different values resulted.

The results are listed below:

	-3.14
	-2.65
	-6.95

Sample					
	Original result	Auto	Manual	Zero	MassLynx
A Sample					
E-11K	-2.58	-1.72	-2.32	-1.76	-2.18
A-11K	-3.99	-3.65	-3.14	-2.94	-3.78
5B-P	-2.15	-1.70	-2.65	-2.08	-2.63
5A-P	-6.14	-5.65	-6.95	-5.55	-7.22
B Sample					
E-11K	-2.02	-0.32	-0.35	-1.66	-2.39
A-11K	-3.51	-1.67	-1.61	-2.81	-4.01
5B-P	-2.65	-3.37	-3.05	-2.33	-2.80
5A-P	-6.39	-7.61	-7.19	-5.58	-7.03
Blanks					
	Original result	Auto	Manual	Zero	MassLynx
A Sample					
E-11K	-0.87	-0.51	-0.56	-0.06	0.09
A-11K	-0.48	-0.49	-0.53	-0.02	-0.59
5B-P	-0.55	-0.92	-0.27	-0.47	-1.00
5A-P	-1.59	-3.65	-1.87	-1.46	-2.45
B Sample					
E-11K	-1.08	-1.11	-0.94	-0.25	-0.51
A-11K	-0.08	0.03	0.17	0.83	0.55
5B-P	-0.67	-1.33	-0.69	-0.54	-1.52
5A-P	-1.60	-3.45	-1.89	-1.24	-3.66

It is at this juncture, on the eve of trial, it is learned that there are not one, but four sets of results. This lack of reproducibility and variability conclusively demonstrates a lack of reliability and accuracy in any one figure contained above.

IV.

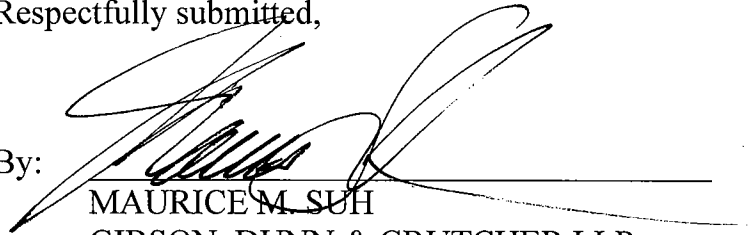
CONCLUSION

For the foregoing reasons, LNDD's GC-IRMS results are unreliable and inaccurate and can not be used to confirm an adverse analytic finding in this case.

DATED: May 7, 2007

Respectfully submitted,

By:



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