

Amendment to Final Report for Study 275.30

Study No.: 275.30

Amendment No.: 1

Effective Date: 11 February 2011

Study Title: Provide data on various arsenic species present in broilers treated with roxarsone: Comparison with untreated birds.

Change(s): (1, 2, 3, etc.)

1. Corrected formatting on lines 123-124.
2. Corrected formatting on lines 140-141.
3. Corrected formatting on lines 153-160.
4. Insert information on minimal level of quantitation by Test America, Inc. Added lines 211 – 213.
5. Inserted spreadsheet origin of Tables 4a & 4b of Analysts' Report and its subsequent rearrangement and file name change; lines 286-288 & line 292.
6. Inserted quantitative limit values from Test America for feed and water analyses; lines 343-345.
7. Inserted text in lines 379 – 381 and deleted a block of text from lines 384-387. Extra lines inserted to push Table 1 to top of next page.
8. Added “on the other hand” and removed “likewise” to beginning of sentence on line 402.
9. Added “tables 2 and 3” to line 420.
10. Editorial changes to Table 2.
 - a. Delete “*” footnote and reference to results from Test America Inc.
 - b. Move footnote references from line 424 to end of second footnote paragraph, line 426 of revised footnotes.
 - c. Change units from “ppb” to “µg/kg” and added extra line.
11. Round off decimals to a constant three decimal places and to correct a typographical error.
12. Change units from “ppb” to “µg/kg” and “ppm” to “mg/kg” in lines 441 – 449.
13. Removed reference to ONADE division/team and NADA#.
14. Consolidated text and changed units as #12 in lines 451 - 462.
15. Revised lines 464 – 475 to address equivalent concentrations of inorganic arsenic species in control and medicated feed and lack of involvement of rice hulls that might contribute to contamination in medicated feed.
16. Inserted new sentence in lines 479 – 480 that identifies source table for analyses of arsenic species in liver tissues.
17. Editorial corrections to lines 487 – 492.
18. Editorial corrections to lines 507 – 513.
19. Corrected units and use of LLOQ instead of LOQ in lines 521 – 547.
20. Line 552 – corrected concentration units.
21. Added “amended” to document title to indicate that it has been amended; line 592.

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- 47 22. Inserted “sequence” in line 604.
- 48 23. Corrected units and edited next sentence at line 611.
- 49 24. Corrected units on line 670.
- 50 25. Corrected units on line 725.
- 51 26. Insert new files under “Analytical Method and Results” section of the attachment list,
- 52 lines 764 – 766: Signed Analysts Report with Attachments.pdf, Chicken liver speciation
- 53 summary-rev20110114.xls; Amendment to Final Report for Study 27530.doc (pdf
- 54 version).
- 55 27. Replace signature page.

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57 Reason for Change(s): (*1, 2, 3, etc.*)

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- 59 1. Incorrect formatting.
- 60 2. Same as #1.
- 61 3. Same as #1.
- 62 4. This level of sensitivity was not described in the initial report.
- 63 5. Needed to document origin of Table 4 in this report.
- 64 6. Needed to define lower limits of quantitation for these two matrixes.
- 65 7. Inserted information of lower level of quantitation; deleted comments about lack of
- 66 agreement of results between contract lab and FDA analysts’ results; added lines
- 67 provided increased readability.
- 68 8. “Likewise” was used inappropriately.
- 69 9. Needed to refer to both tables and not just Table 2.
- 70 10. Editorial changes:
 - 71 a. Extraneous and basically incorrect.
 - 72 b. Consolidation of footnotes for clarity.
 - 73 c. Eliminate use of unclear concentration units.
- 74 11. Inappropriate use of significant digits implies a degree of accuracy not available; a
- 75 comma is used instead of a period for decimal value.
- 76 12. Eliminate use of unclear concentration units.
- 77 13. Not necessary.
- 78 14. Consistency in use of concentration units.
- 79 15. Clarified/corrected results.
- 80 16. Need to identify source table used in the discussion of this section.
- 81 17. Correction/clarification of sentences.
- 82 18. Correction/clarification of statements.
- 83 19. Same as #18.
- 84 20. Units’ consistency.
- 85 21. Clarification.
- 86 22. Clarification.
- 87 23. Units’ consistency and clarification.
- 88 24. Units consistency.
- 89 25. Units consistency.
- 90 26. New and/or amended files.
- 91 27. Significant revisions required new approvals by management.
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J. C. Kawabak 14 February 2011
Study Director Date

J. J. Land 2/14/11
Division Director Date

Amendment to Final Report for Study 275.30

Study No.: 275.30

Amendment No.: 2

Effective Date: 16 May 2011

Study Title: Provide data on various arsenic species present in broilers treated with roxarsone: Comparison with untreated birds.

Change(s): (1, 2, 3, etc.)

1. Corrected erroneous language in second sentence of paragraph running from pages 2-3 to eliminate terminology concerning "safe level"; and corrected the So and Sm values cited. The entire paragraph is revised (old corrected language shown with strikethrough and new language shown in italics) to read:

The characterization and comparison of the arsenic profiles in tissues of control and treated chickens will allow CVM/FDA to make some conclusions about future regulatory activities for the organic arsenicals. CVM has determined ~~that a safe level~~ the So and Sm of inorganic arsenic ~~is << 1ppb (So = 0.039 ppt; Sm (muscle, liver) = 0.2 ppt and 0.6 ppt, respectively)~~ to be: *So = 1.56 ppt and Sm (muscle, liver) = 8 ppt and 23 ppt, respectively.* (Summary of iAs Carcinogenic RA_Tong20100427_10-22-10.doc). Therefore any new animal drug that contributes to the overall inorganic arsenic burden is of potential concern.

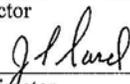
2. Corrected inorganic As species averages for days 0, 3, and 5 withdrawal on pages 26 & 29. Use values from latest statistician report: 7.8, 1.7, and 1.4 ppb for withdrawal days 0, 3, and 5, respectively.

Reason for Change(s): (1, 2, 3, etc.)

1. During preparation and review of final report, values were recalculated by ONADE to correct a computational error. (Email from Z Tong to W Flynn with attachment, dated 10-22-2010).
2. Used data from a preliminary statistical report dated 2 September 2010.



Study Director 16 May 2011
Date



Division Director 5/16/2011
Date

Amendment to Final Report for Study 275.30

Study No.: 275.30

Amendment No.: 3

Effective Date: 26 May 2011

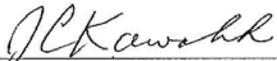
Study Title: Provide data on various arsenic species present in broilers treated with roxarsone: Comparison with untreated birds.

Change(s): (1, 2, 3, etc.)

1. Make the following corrections to Table 3b of the Analysts' Report:
The n in column 1 row 3 should be **15** not **46**
The n in column 1 row 7 should be **11** not **42**

Reason for Change(s): (1, 2, 3, etc.)

1. In preparing the table, the primary author, MC, manually counted the number of data points and erred in the final count.



Study Director 25 May 2011
Date



Division Director 5/25/11
Date