Threshold Values for Selenium in Great Salt Lake: Selections by the Science Panel

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The purpose of this technical memorandum is to provide a summary and documentation of the Science Panel's discussions relative to toxicity thresholds for exposure of birds to selenium at the Great Salt Lake. It is generally recognized that the most significant exposure of birds occurs through their diet, and that the best-documented and most readily-monitored effects are those on reproductive success (particularly egg hatchability). Thus, much of the focus of this technical memorandum is on those exposures and endpoints, because they can be most readily applied toward establishment of a site-specific water quality standard for selenium in the open waters of the Great Salt Lake.

Before the Science Panel meeting on November 29-30, 2006, I prepared a technical memorandum (Subject: Threshold Values for Selenium in Great Salt Lake; dated November 28) to provide the following:

- a summary of potential threshold values identified by Science Panel members for consideration in establishing a water quality standard for selenium in the open waters of the Great Salt Lake, and
- supporting documentation and literature provided by Panel members to be used as the basis of discussion by the Panel.

Bill Adams, Anne Fairbrother, Theresa Presser, and Joe Skorupa provided input concerning threshold values to be considered and sent supporting literature (either as citations or copies of publications), in addition to providing their views on the threshold values themselves. The entire Panel discussed that material and related information from other sources on November 30. From the available information, the Panel narrowed the ranges of values for bird diets and eggs to those listed in Tables 1 and 2 (Attachment A [tables modified from the compilation of field and laboratory data presented in Table 15 of Presser and Luoma, 2006]) and then identified "working values" for the ranges of acceptable selenium concentrations in bird diets and in bird eggs (those shaded in the tables). It is understood that the values will likely be refined during future phases of work (including consideration of site-specific data currently being generated by the Great Salt Lake research effort) and discussion related to establishing a site-specific standard for Great Salt Lake.

A previous draft of this technical memorandum (dated December 8) provided a brief summary of the threshold values that were selected by the Panel during those discussions. For both diet and eggs, the ranges of selenium concentrations selected by the Panel are the lower and upper 95 percent confidence intervals (95% CIs; also referred to as the 5 percent lower confidence limit [LCL] and the 95 percent upper confidence limit [UCL]) for the mean selenium concentration that is associated with a 10 percent reduction (i.e., the 10 percent effect concentration or EC_{10}) in the hatchability of mallard eggs. Those values were reported by Ohlendorf (2003), based on the analysis of data from six laboratory studies (Heinz et al. 1987, 1989; Heinz and Hoffman 1996, 1998; Stanley et al. 1994, 1996). Essentially, there is 95 percent confidence that the mean dietary or egg selenium concentration that causes a 10 percent reduction of egg hatchability is within the identified ranges, which are illustrated in the figures below.

The Panel agreed by consensus that the 95% CIs on mean selenium concentrations in mallard diet and eggs associated with the EC_{10} for egg hatchability would be reasonably protective for birds nesting at the Great Salt Lake, and that the ranges of values represented by the 95% CIs included the concentrations proposed by various Panel members for consideration. Rationale supporting selection of the 95% CIs is provided by the previous technical memorandum (dated November 28) and through discussion at the Panel meeting.

Panel members provided comments on the December 8 draft version of this technical memorandum summarizing threshold values (Attachment B), and Bill Adams provided further data analyses of effect levels in diets and eggs of mallards that are included in this revised draft. Additional considerations and qualifications about the selected dietary and egg concentrations are presented below in the Discussion section.

All concentrations in bird diets or eggs mentioned below are expressed on dry-weight basis.

Selenium in Bird Diets

The dietary selenium EC_{10} for mallards was reported as 4.87 mg/kg, with 95% CIs of 3.56 to 5.74 mg/kg based on reproductive toxicity (egg hatchability) (Ohlendorf 2003). The EC_{10} of 4.87 mg/kg was estimated by fitting a logistic regression model (Figure 1). It should be noted, however, that the mallard studies used a “dry diet” that had about 10 percent moisture. Ohlendorf (2003) used the reported dietary selenium concentrations without adjustment for that moisture content, but an upward adjustment of the values (by 11 percent) would be appropriate to account for the moisture content of the duck diet.

In Adams et al. (2003), hockey-stick regression was used to model relationships between egg selenium concentrations and adverse effects in order to derive toxicity thresholds, such as EC_{10} values. Hockey-stick regression is a model that has been used elsewhere to define a threshold when an underlying background level of response is unrelated to the dose (see Adams comments in Attachment B). Thus, such a model may be relevant to naturally occurring elements that are essential to birds and a wide variety of other organisms and particularly useful for elements such as selenium, which has a narrow range between levels that are essential and those that are toxic to birds so that variance around the inflection point (threshold) in the model is small. As shown in Figure 2 below, a threshold clearly

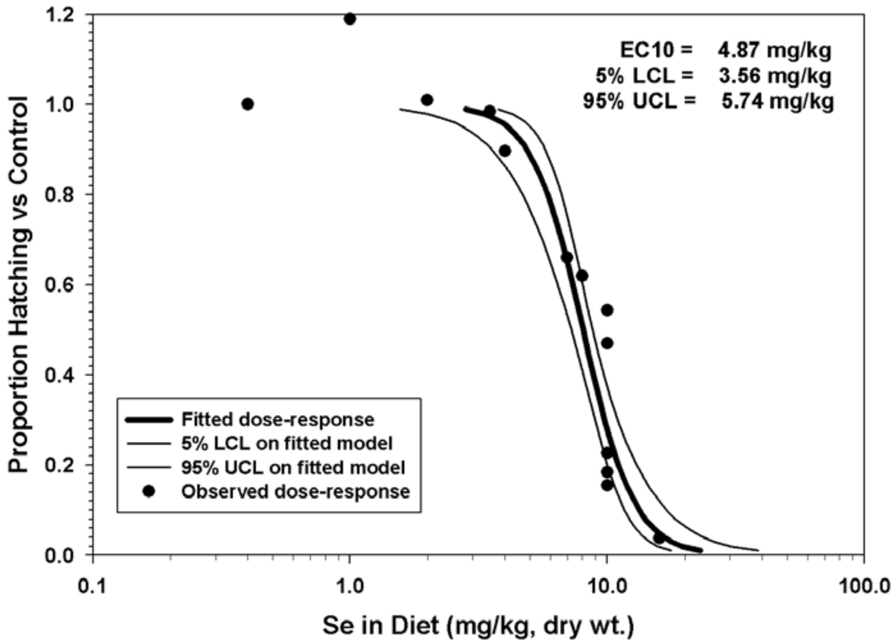

Figure 1. Mallard egg hatchability vs control as a function of selenium concentration in diet.

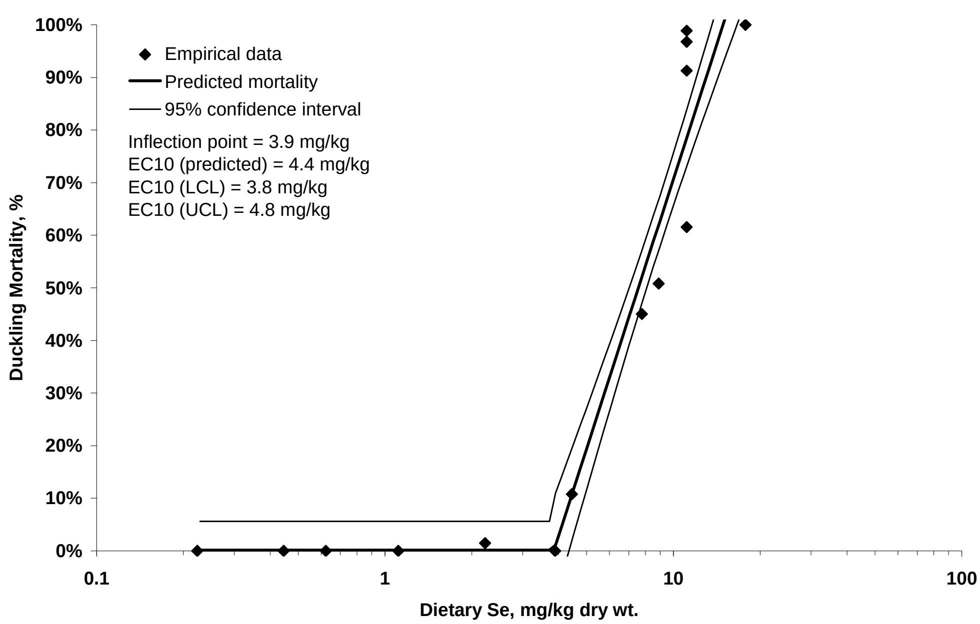

Figure 2. Hockey stick regression of laboratory mallard duckling mortality versus dietary selenium.

appears to exist when dietary selenium is plotted versus duckling mortality (which incorporated the cumulative effects of fertilization success and hatchability). The inflection point occurs at a dietary selenium concentration of 3.9 mg/kg. (The Discussion section below describes uncertainty around the inflection point.) The predicted EC_{10} is 4.4 mg/kg (just slightly above the inflection point) and the 95% CI around the predicted EC_{10} ranges from 3.8 to 4.8 mg/kg. The predicted EC_{10} of 4.4 mg/kg is slightly lower than Ohlendorf's (2003) EC_{10} of 4.9 mg/kg, and the 95% CI is narrower using hockey stick regression than when using logistic regression.

Selenium in Bird Eggs

Similar to the dietary values calculated by Ohlendorf (2003) for reproductive toxicity for mallards, the EC_{10} in eggs was reported as 12.5 mg/kg, with 95% CIs of 6.4 to 16.5 mg/kg (Figure 3). The EC_{10} of 12.5 mg/kg was estimated by fitting a logistic regression model to the results of the six laboratory studies with mallards.

As noted in Table 2, the EC_{10} for duckling mortality, as reported in Adams et al. (2003), ranged from 12 to 16 mg/kg (see Adams comments in Attachment B). These EC_{10} values are based on a synthesis of laboratory studies in which the final endpoint was duckling mortality (the same effects data used in the dietary EC_{10} evaluation with hockey-stick regression above) and the range of EC_{10} values reflects different statistical approaches for analyzing the data. An adaptation from Figure 3 in Adams et al. (2003) is provided below (Figure 4), with the 95% CI included. As shown, the inflection point occurs at an egg selenium concentration of 9.8 mg/kg, with a predicted EC_{10} comparable to that derived by Ohlendorf (2003). (See Discussion for comments concerning uncertainty around the inflection point.) However, the 95% CI using hockey-stick regression is much narrower (9.7 to 13.6 mg/kg) than that derived by Ohlendorf using logistic regression (6.4 to 16.5 mg/kg). Given that there is a clear egg-selenium threshold at which effects begin to be observed, a unimodal model, such as logistic regression, may result in exaggerated confidence intervals, particularly in the tails.

Discussion

Additional discussion is presented below concerning the basis for selection of threshold values, uncertainty surrounding the hockey-stick regression inflection points, hormetic effects of selenium, and other qualifications and points discussed during the Panel meeting in November, as reflected in comments from Panel members (Attachment B).

Basis for Selection of Threshold Values

The Science Panel can choose a scientifically-based threshold value or acceptable "benchmark" concentration based on the consensus confidence limits described by analysis of available data (presented above), but ultimately, a choice of numbers from within the consensus confidence limits for regulatory purposes is not a scientific decision. Choices of a specific number or numbers from within those confidence ranges are philosophical/legal decisions that depend on how precautionary the State of Utah wants to be (a matter of philosophy) and on how much potential for legal liability the State is comfortable with exposing itself to. The key decision the State must make is whether they want to regulate to a "NEC" (no effects concentration, which is not the same as a NOEC [no observed effects

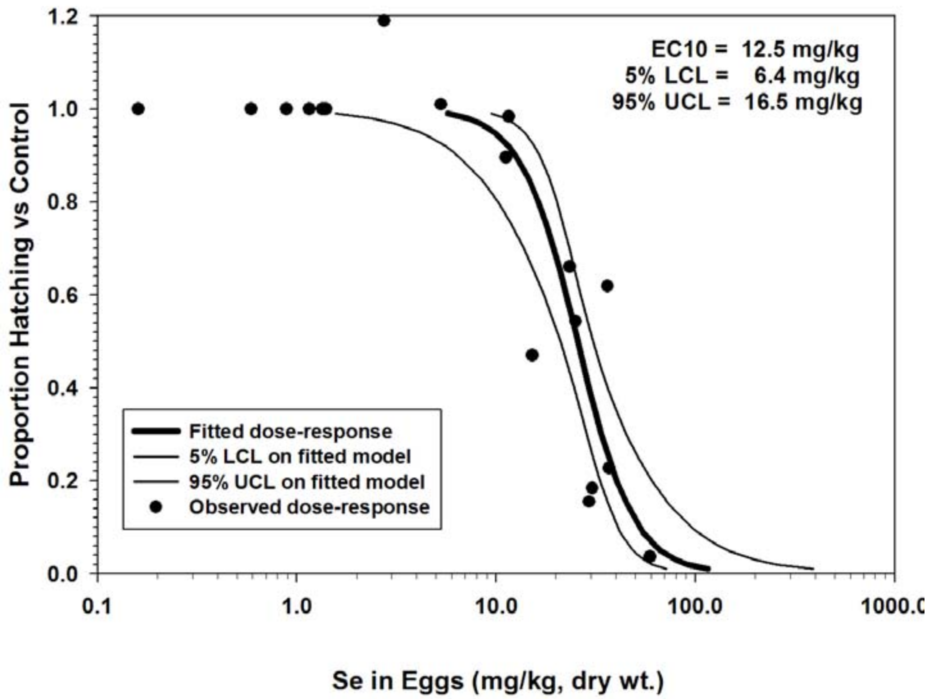

Figure 3. Mallard egg hatchability vs control as a function of selenium concentration in eggs.

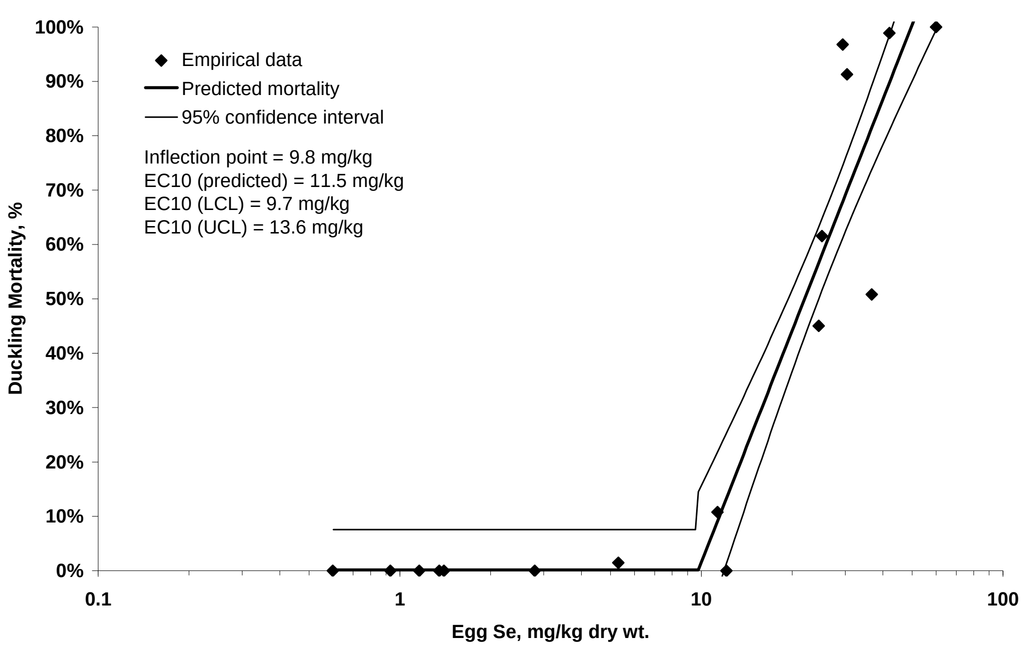

Figure 4. Hockey stick regression of laboratory mallard duckling mortality versus egg selenium.

concentration]) standard or to some version of a "tolerably toxic" standard such as an EC_{10}, an EC_{20}, or an EC_{05}, etc.

Conceptually, a benchmark concentration is defined as the location on the exposure-response curve that is the threshold between absence and presence of a given effect or endpoint (i.e., the threshold between an EC_{00} and an EC_{01} concentration [see: www.epa.gov/ecotox/ecossl/pdf/ecossl_attachment_3-2.pdf; p. A-6]). Benchmark concentrations are estimated as the lower 95 percent confidence boundary on the EC_{10} (see: Meister and Van Den Brink [2000], pp. 114-116 in particular; and USEPA [2000]).

Uncertainty Surrounding the Hockey-Stick Regression Inflection Points

To determine the inflection point between the hockey-stick "blade" and "handle", or any parameter in the model, initial parameter values are input to the software program SPlus® and an iterative technique is used to search for more exact parameter values that will minimize the sum of squared deviations between the observed effects data and effects values predicted by the model. Variance in the estimate of the inflection point value is affected by the spacing of the measured X values as well as the scatter or trend in Y values in the vicinity of the estimated inflection point. If, for example, there are few measured dietary selenium concentrations near the predicted inflection point, the uncertainty in the location of the inflection point will be greater because it will be difficult to determine the exact concentration at which the inflection point occurs (i.e., it could be between two of the measured values). Uncertainty around the predicted Y (EC) values at the predicted inflection point is affected by the number of Y values and the scatter of the Y values at that particular X value (which, when calculating the confidence interval around Y, is assumed to be estimated without error). Thus, both the spacing of the measured X values and the variance in the response variable affects the uncertainty around the inflection point. The tighter spacing and less ambiguous effects response after the inflection point causes the 95% CI around the dietary selenium-based inflection point (3.0 to 4.9 mg/kg) to be narrower than that for the egg selenium-based inflection point (6.4 to 14.9 mg/kg).

However, although there is uncertainty surrounding the inflection point, use of the best estimate of the inflection point results in the best fit of the regression model to the data. In Figure 4, for example, if the inflection point occurred at either end of the 95% CI of egg selenium concentration (6.4 to 14.9 mg/kg dry wt.) one can easily visualize that the fit of the regression to the data points above the inflection point would not pass through the measured values in the same way.

Hormetic Effects of Selenium

Consideration of the hormetic effects of selenium may result in lowering of thresholds (for hormetic substances and endpoints one has to distinguish between valid control responses and hormetic deficiency responses before a valid baseline to compare toxic responses against can be identified). The hormetic bias in the data used for the Ohlendorf (2003) regressions has not yet been fully considered by the Science Panel. If such consideration were to result in changes, those changes could only be in the direction of a downward shifting of the threshold confidence limits. (For example, preliminary unpublished analyses that adjusted for hormetic effects in the mallard data yielded a revised EC_{10} for diet of

4.1 mg/kg, with a 95% CI of 1.3 to 5.8 mg/kg, and a revised EC_{10} for eggs of 9.22 mg/kg, with a 95% CI of 4.11 to 13.07 mg/kg.).

Other Qualifications and Points Discussed

The Panel also discussed the following additional qualifications and points relative to toxicity threshold values:

- Applicability of laboratory data to field situations is not certain (note that field data were retained in compilation of egg-selenium concentrations in Table 2), and it is important to collect site-specific field data on selenium concentrations in bird eggs (e.g., current data gathering effort at the Great Salt Lake).
- Applicability of mallard data to species at Great Salt Lake is uncertain, because relative sensitivity of all species nesting there is not known.
- Threshold values discussed are for the hatchability endpoint (based on diet and avian egg) but non-reproductive adverse effects endpoints (e.g., avian blood endpoint) also may be important. However, interpretive values for selenium in avian blood are not available; although selenium concentrations in blood indicate exposure of the birds, that endpoint is not considered useful for setting a water quality standard.
- Phalaropes are seasonally numerous at the Great Salt Lake and should be added to the list of species to be monitored because they represent species with a feeding rate that is a large percentage of body weight (affecting energy consideration in determining wildlife criterion).

Recommended Next Steps

The issues summarized in this technical memorandum should be discussed/considered further by the Panel, particularly to refine the selection of threshold values for bird diets and eggs with respect to effects documented elsewhere (in field and laboratory studies) and considering the results being developed through research at the Great Salt Lake. In parallel, it will be important to know what level of protectiveness the State and EPA will apply in the development of the site-specific standard for selenium on the Great Salt Lake (i.e., EC_{20}, EC_{10}, EC_{05}, etc.) so that the Science Panel can most effectively make recommendations that can be applied toward that purpose.

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ATTACHMENT A

Tables

TABLE 1
Diet Concentrations

mg/kg	Approach or Site	Effects	Species	Reference(s)
4.87 **(CI 3.56 - 5.74)**	Synthesis of lab Data	Hatchability in mallards (10% effect level/95% confidence boundaries)	Mallard	Ohlendorf 2003
4.4 (CI 3.8 - 4.8)	Synthesis of lab data	EC_{10} for duckling mortality	Mallard	Bill Adams analyses presented in Attachment B
3.85 - 7.7 (diet based on 10% moisture)	Lab	Reduced hatching success in mallards (33% at 7.7 µg/g); reduced growth and weight in hatchlings	Mallard	Stanley et al. 1996
7.7 (diet based on 10% moisture)	Lab	Reduction in number of surviving mallard ducklings produced per female	Mallard	Stanley et al. 1996
8.8 4.4/6.2 (diet based on 10% moisture)	Lab	8.8 - LOAEL, 4.4 - NOAEL, 6.2 - Geometric Mean Reduction (17%) in survival of mallard ducklings; mean decrease (43%) in number of 6-day-old ducklings	Mallard	Heinz et al. 1989
6	Lab	Adverse effect on body condition of male American kestrels	American Kestrels	Yamamoto and Santolo, 2000
7.7 - 8.8 (diet based on 10% moisture)	Lab	Dietary threshold of teratogenic effects in mallards; above upper threshold, rate of deformity rises sharply	Mallard	Stanley et al. 1996
7.7 - 8.8 (diet based on 10% moisture)	Lab	Dietary threshold of mallard duckling mortality (parental exposure)	Mallard	Stanley et al. 1996

Note: Highlighted cells are the threshold values for bird diets identified by consensus of the Science Panel on November 30, 2006.

TABLE 2
Egg Concentrations

mg/kg (dry wt.)	Approach or Site	Effects	Species	Reference(s)
12.5 **(CI 6.4 - 16.5)**	Synthesis of lab data	Hatchability in mallards (10% effect level/95% confidence boundaries)	Mallard	Ohlendorf 2003
10	Synthesis of lab data	NOAEL	Mallard	Adams et al. 2003
12 - 16	Synthesis of lab data	EC_{10} for duckling mortality	Mallard	Adams et al. 2003
9	Synthesis of lab data	Impaired clutch viability (8.2% effects level)	Mallard	Lam et al. 2005
8.2 (or 7.3) (egg based on 73% moisture)	Field	16% depression in egg viability **(*7.3 in paper*)**	Spotted Sandpiper	Harding et al. 2005
6	Synthesis of field data	Threshold (3% effect level) of hatchability	Stilts	Skorupa, 1998; Skorupa, 1999
5.1 (egg based on 78.4% moisture)	Field	15% depression in egg viability	American dipper	Harding et al. 2005

Note: Highlighted cells are the threshold values for bird eggs identified by consensus of the Science Panel on November 30, 2006.

ATTACHMENT B

Comments on December 8, 2006, Draft Technical Memorandum

ATTACHMENT B

Comments on December 8, 2006, Draft Technical Memorandum

Comments of Bill Adams

Following are comments on Harry Ohlendorf's draft technical memorandum to the Great Salt Lake Science Panel entitled *Threshold Values for Selenium in Great Salt Lake: Selections by the Science Panel* (December 8, 2006).

Selenium in Bird Diets

As noted in the draft memorandum, the mallard studies used in Ohlendorf (2003) as the basis for a dietary selenium EC10 in birds was based on a "dry diet" containing about 10% moisture. Although the moisture content of the mallard diet was low, we recommend that standard convention should be used to properly adjust the dietary selenium concentrations to a dry weight basis. The equation for the wet weight-to-dry weight conversion is included in Attachment 1 to this memorandum.

In Adams et al. (2003), hockey-stick regression was used to model relationships between egg selenium concentrations and adverse effects in order to derive toxicity thresholds, such as EC10 values. Hockey-stick regression is a model that has been used to define a threshold when an underlying background level of response is unrelated to the dose. Thus, such a model may be relevant to naturally occurring elements that are essential to birds and a wide variety of other organisms and particularly useful for elements such as selenium, which has a narrow range between levels that are essential and levels that are toxic to birds so that variance around the inflection point (threshold) in the model is small. As shown in Figure 1 below, a threshold clearly appears to exist when dietary selenium is plotted versus duckling mortality (which incorporated the cumulative effects of fertilization success and hatchability). The inflection point occurs at a dietary selenium concentration of 3.9 mg/kg dry wt. (please see discussion at end of comments concerning uncertainty around the inflection point). The predicted EC10 is 4.4 mg/kg dry wt. (just slightly above the inflection point) and the 95% confidence interval around the predicted EC10 ranges from 3.8 to 4.8 mg/kg dry wt. The predicted EC10 of 4.4 mg/kg dry wt. is slightly lower than Harry Ohlendorf's EC10 of 4.9 mg/kg dry wt., but the 95% confidence interval is narrower using hockey stick regression.

Selenium in Bird Eggs

As noted in Table 2 of the draft memorandum, the EC10 for duckling mortality, as reported in Adams et al. (2003), ranged from 12-16 mg/kg dry wt. These EC10 values are based on a synthesis of laboratory studies in which the final endpoint was duckling mortality (the same effects data used in the dietary EC10 evaluation above) and the range of EC10 values reflects different statistical approaches for analyzing the data. An adaptation from Figure 3 in Adams et al. (2003) is provided below, with the 95% confidence interval included. As shown, the inflection point occurs at an egg selenium concentration of 9.8 mg/kg with a predicted EC10 comparable to that derived by Harry Ohlendorf (please see discussion at end of comments concerning uncertainty around the inflection point). However, the 95% confidence interval using hockey stick regression is much narrower (9.7 to 13.6 mg/kg dry wt.) than that derived by Harry using logistic regression (6.4-16.5 mg/kg dry wt.). Given that there is a clear egg selenium threshold at which effects begin to be observed, a unimodal model, such as logistic regression, may result in exaggerated confidence intervals, particularly in the tails.

Uncertainty Surrounding the Hockey-Stick Regression Inflection Points

To determine the inflection point between the hockey-stick "blade" and "handle", or any parameter in the model, initial parameter values are input to the software program SPlus® and an iterative technique is used to search for more exact parameter values that will minimize the sum of squared deviations between the observed effects data and effects values predicted by the model. Variance in the estimate of the inflection point value is affected by the spacing of the measured X values as well as the scatter or trend in Y values in the vicinity of the estimated inflection point. If, for example, there are few measured dietary selenium concentrations near the predicted inflection point, the uncertainty in the location of the inflection point will be greater because it will be difficult to determine the exact concentration at which the inflection point occurs (i.e., it could be between two of the measured values). Uncertainty around the predicted Y (EC) values at the predicted inflection point is affected by the number of Y values and the scatter of the Y values at that particular X value (which, when calculating the confidence interval around Y, is assumed to be estimated without error). Thus, both the spacing of the measured X values and the variance in the response variable affects the uncertainty around the inflection point. The tighter spacing and less ambiguous effects response after the inflection point causes the 95% confidence interval around the dietary selenium-based inflection point (3.0 to 4.9 mg/kg dry wt.) to be narrower than that for the egg selenium-based inflection point (6.4 to 14.9 mg/kg dry wt.).

However, although there is uncertainty surrounding the inflection point, use of the best estimate of the inflection point results in the best fit of the regression model to the data. In Figure 2, for example, if the inflection point occurred at the either end of the 95% confidence interval of egg selenium concentration (6.4 to 14.9 mg/kg dry wt.) once can easily visualize that the fit of the regression to the data points above the inflection point would not pass through the measured values in the same way.

Figure 1. Hockey stick regression of laboratory mallard duckling mortality versus dietary selenium.

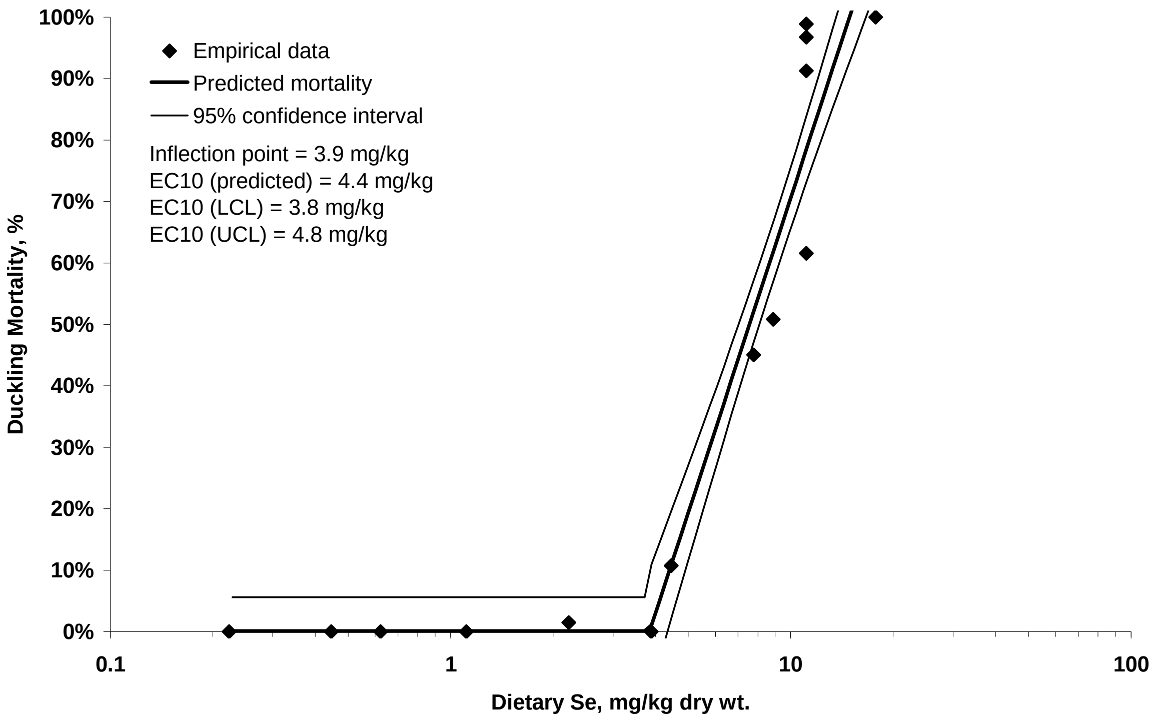
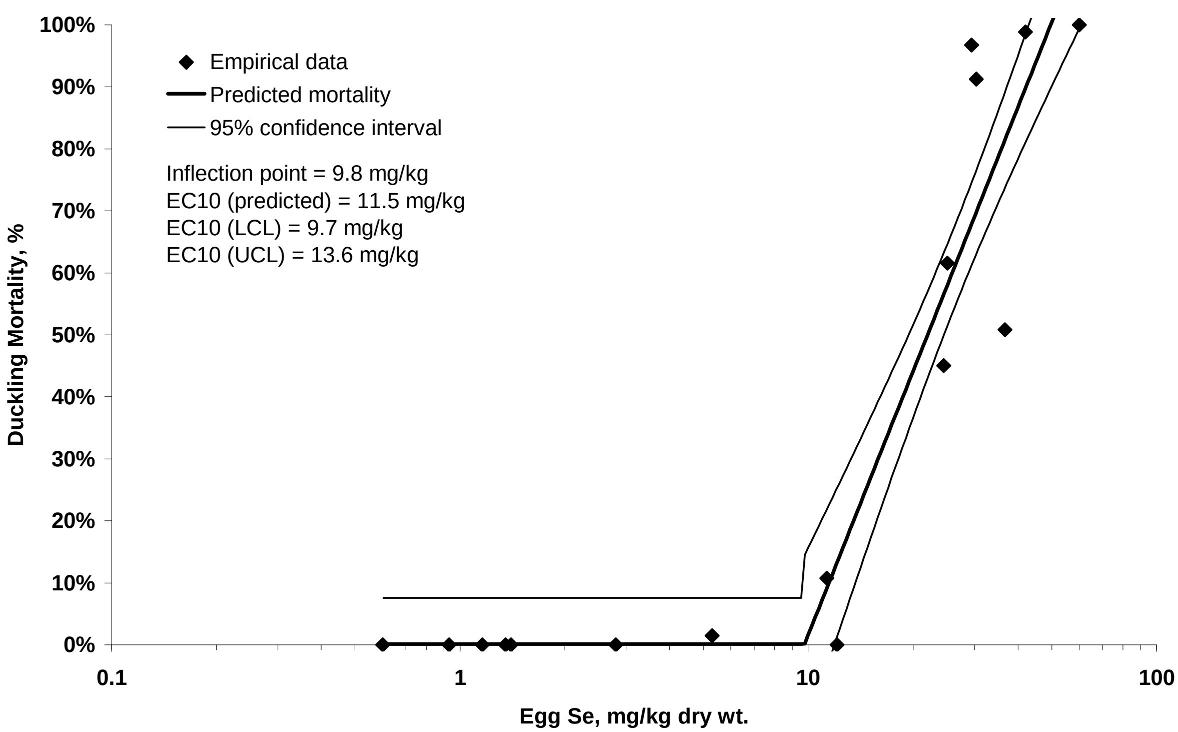


Figure 2. Hockey stick regression of laboratory mallard duckling mortality versus egg selenium.



ATTACHMENT 1

WET WEIGHT-TO DRY WEIGHT CONVERSION FOR DIETARY SELENIUM CONCENTRATIONS IN MALLARD STUDIES

$$\text{Dry Weight Concentration} = \frac{\text{Wet Weight Concentration}}{f_{\text{solids}}}$$

Where: f_{solids} = fraction solids in diet (i.e., 0.9 in a diet containing 10% moisture)

Comments of Anne Fairbrother

I realize that I am late (the last?) on providing comments and feedback on the report you pulled together from our last Salt Lake City meeting on threshold values. I was sort of hoping to see the data from Bill Adams' re-analysis of the dose-response before replying... Absent that, here are my thoughts and comments.

I think you did an appropriate job pulling together what was discussed at the meeting in regard to diet and egg threshold levels. However, the more I look at the data in regard to selenium uptake and effects, the more convinced do I become that we are dealing with a threshold phenomenon, likely because of the essential nature of the element. I do believe that the mean value for the EC10 that was selected for both endpoints is likely to remain pretty much the same regardless of what dose-response model is used, but the standard error about the mean may be different. Likely it will be smaller when using a threshold model since a logistic model tends to spread out the CI's at its tails. So, for now, I am willing to approve the document as a report of what was discussed at the meeting, but not as a final say on what we have agreed to for the EC10 and its confidence intervals.

Comments of Theresa Presser

Suggested additions to threshold discussion write-up of 12/8/06:

1) Page 1: Note that compilation of data for consideration was adapted from Presser and Luoma (2006), table 15.

2) Page 1: Note that in addition to laboratory data, a compilation of field data for egg concentrations was retained.

3) Page 1: Note that any final determination must take into account site-specific data currently being generated by the Great Salt Lake research effort.

4) Page 2 wording: "The panel agreed by consensus that the 95% CIs on mean selenium concentrations in mallard diet and eggs would be reasonably protective for birds nesting at the Great Salt Lake, and the range of values included the concentrations proposed by various panel members for consideration. Rational supporting selection of the 95% CIs is provided by the previous technical memorandum and through discussion at the panel meeting."

    a) Did you mean here the 95% CIs on the mean EC10 for hatchability?

    b) The phrase "would be reasonably protective for birds nesting at the Great Salt Lake" does not adequately convey all parts of the extensive discussion that took place. I did not perceive that a consensus had been reached as to protectiveness, only that a consensus had been reached as to the interpretation of data from mallard lab experiments. Therefore, I suggest incorporating into the wording of a summary statement the following qualifications and points that were discussed at the meeting:

        1) Applicability of lab data to field situations (note retention of compilation of field data in table 2 and current data gathering effort at the Great Salt Lake; points 2 and 3 listed above)

        2) Applicability of mallard data to species at Great Salt Lake (sensitivity issue)

        3) Applicability of hatchability endpoint (diet and avian egg) and non-reproductive adverse effects endpoints (e.g., avian blood endpoint)

        4) Level of protection and precautionary regulation as exemplified by benchmark concentration regulation. Specifically add excerpt from page 8 of 11/28/06 memo as clarification of 95% CI: "Conceptually, a benchmark concentration is defined as the location on the exposure-response curve that is the threshold between absence and presence of a given effect or endpoint, i.e., the threshold between an EC00 and an EC01 concentration (see: www.epa.gov/ecotox/ecossl/pdf/ecossl_attachment_3-2.pdf; p. A-6)….. Benchmark concentrations are estimated as the lower 95% confidence boundary on the EC10 (see: Meister, R., and P.J. Van Den Brink. 2000. The analysis of laboratory toxicity experiments. Pages 99-118 in T. Sparks (ed.), Statistics in Ecotoxicology. John Wiley & Sons, LTD, New York, NY: [pp 114-116 in particular]; and see: USEPA. 2000. Benchmark Dose Technical Guidance

Document. [External Review Draft]. EPA/630/R-00/001. U.S. Environmental Protection Agency, Washington, DC)."

5) Addition of phalarope to list of species to be monitored to represent species with a feeding rate that is a large percentage of body weight (energy consideration in determining wildlife criterion).

6) Potential lowering of thresholds through consideration of hormesis data (for hormetic substances and endpoints one has to distinguish between valid control responses and hormetic deficiency responses before a valid baseline to compare toxic responses against can be identified).

5) References: Add Presser and Luoma, 2006.

6) Table 1:"Bill Adams suggestion" needs to be documented as how his entry differs from entry #1 in table 1.

Comments of Joe Skorupa

In Table 1 I don't believe the science panel wanted the value of 4.87 to be presented in bold type, only the confidence limits (for comparison see Table 2 where I think you have it the way the science panel intended).

Adjusting for 10% moisture would result in an 11% increase in the dietary values, not an upward adjustment of 10% as stated.

I didn't feel like your draft write-up adequately conveyed our (sci. panel's) discussion concerning the fact that, ultimately, a choice of numbers from within the consensus confidence limits is not a scientific decision. That confidence range is as far as science can bring us... choosing a specific number or numbers from within those confidence ranges are philosophical/legal decisions that depend on how precautionary the State of Utah wants to be (a matter of philosophy) and on how much potential for legal liability the State is comfortable with exposing itself to. The key decision the State must make is whether they want to regulate to a "NEC" (no effects concentration... which is not the same as a NOEC) standard or to some version of a "tolerably toxic" standard such as an EC-10, or EC-20, or EC-05 etc.

Finally, I think on the scientific side of things we would be remiss in our duty as experts not to include some discussion indicating that the issue of hormetic bias in the data used for the Ohlendorf (2003) regressions has not yet been fully considered by the science panel (at Bill Adams request to defer it so that he could preview Beckon's SETAC presentation before I presented any of it to the panel... although it seemed to be acceptable to everyone to see Kennecott's U. of Wyoming presentation without any opportunity for anyone other than Bill A. to preview it... seems like a double standard to me), and that if such consideration were to result in changes, those changes could only be in the direction of a downward shifting of the threshold confidence limits.

For example, remember that the analysis that Brad Sample re-ran to adjust for hormetic effects in the mallard data yielded a revised EC-10 for diet of 3.7 ppm ww [4.1 ppm dw] with a 95% confidence interval of 1.15 - 5.18 ppm ww [1.3 - 5.8 ppm dw] and a revised EC-10 for eggs of 9.22 ppm dw with a 95% confidence interval of 4.11 - 13.07 ppm dw.

Threshold Values for Selenium in Great Salt Lake: Refined Selections by the Science Panel

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The purpose of this technical memorandum is to provide a summary and documentation of the Science Panel's further discussions during the recent Panel meetings (March 21 to 22, 2007, and July 31 to August 1, 2007) relative to refining toxicity thresholds for exposure of birds to selenium at the Great Salt Lake (GSL), and to define some of the terms used. During the most recent meetings, the Panel continued its review of available information to determine threshold values that should be considered for development of the site-specific standard for selenium in the open waters of GSL. Previous considerations are summarized in the following two technical memorandums: Subject: Threshold Values for Selenium in Great Salt Lake, dated November 28, 2006; and Subject: Threshold Values for Selenium in Great Salt Lake: Selections by the Science Panel, dated February 28, 2007.

Briefly, key considerations for the threshold values are as follows:

- It is generally recognized that the most significant exposure of birds occurs through their diet.
- The best-documented and most readily-monitored effects are those on reproductive success (particularly egg hatchability, assessed indirectly for GSL on the basis of selenium concentrations in food-chain organisms and bird eggs).
- Laboratory studies with mallards provide the best available data to evaluate avian exposure and effects; because the mallard is relatively sensitive to the effects of selenium, using those threshold values builds in conservatism so that the result can be considered protective of other species.
- The 95% lower confidence interval (CI) on the mean selenium concentrations in mallard diet and eggs associated with the EC_{10} for egg hatchability (explained below) would be reasonably protective for birds nesting at the GSL.

- The previous technical memoranda provide a summary and discussion of potential threshold values identified by Science Panel members for consideration in establishing a water quality standard for selenium in the open waters of the GSL.
- The degree of protectiveness to be applied by the State in setting the water quality standard is not known, and there is not complete understanding of the sensitivity of the GSL system to selenium; thus, the Panel is considering a range of values to be used in modeling and derivation of a potential standard.

From the available information, the Panel initially (in November 2006) narrowed the values to be considered by identifying "working values" for the ranges of acceptable selenium concentrations in bird diets and eggs. For both diet and eggs, the Panel selected the ranges of selenium concentrations provided by Ohlendorf (2003); they include the 95% CI (also referred to as the 5% lower confidence limit [LCL] and the 95% upper confidence limit [UCL]) for the mean selenium concentration that is associated with a 10% reduction (i.e., the 10% effect concentration or EC_{10}) in the hatchability of mallard eggs. The Panel selected the EC_{10} as the appropriate endpoint because it is conventionally used as an endpoint in toxicological studies and the related literature, and it represents a lower limit of sensitivity for assessment of effects at a population level.

For bird diets, the 95% CI = 3.56 to 5.74 mg Se/kg (mean = 4.87 mg Se/kg); in bird eggs, the 95% CI = 6.4 to 16.5 mg Se/kg (mean = 12.5 mg Se/kg). (All concentrations in bird diets or eggs mentioned in this technical memorandum are expressed on dry-weight basis.) Those values were based on the analysis of data from six laboratory studies (Heinz et al. 1987, 1989; Heinz and Hoffman 1996, 1998; Stanley et al. 1994, 1996). Essentially, there is 95% confidence that the mean dietary or egg selenium concentration that causes a 10% reduction of egg hatchability is within the identified ranges, which are illustrated in Figures 1 and 2.

At the July 31 to August 1 meeting, Joe Skorupa suggested an alternative way of communicating the selected threshold values that de-emphasizes the EC_x terminology. Those values, shown in Table 1, relate the mean, LCL, and UCL as a selenium concentration in the diet or in bird eggs to the degree of reduction in egg hatchability (as percent reduction) associated with those selenium concentrations. For each concentration, the table lists the range of reduction in hatchability that can be expected to occur. The range represents the least to the most reduction that is associated with the selenium concentration, with 95% confidence that the level of effect falls within that range. The table also lists the "maximum likelihood" value for each concentration; that value is the best estimate of the expected decrease in hatchability.

Basis for Selection of Threshold Values

As mentioned above, the dietary selenium EC_{10} for mallards was reported as 4.87 mg/kg, with 95% CI of 3.56 to 5.74 mg/kg based on reproductive toxicity (egg hatchability) (Ohlendorf 2003). The EC_{10} was estimated by fitting a logistic regression model (Figure 1). Similar to the dietary values calculated by Ohlendorf (2003) for reproductive toxicity for mallards, the EC_{10} in eggs was reported as 12.5 mg/kg, with 95% CI of 6.4 to 16.5 mg/kg (Figure 2). This EC_{10} also was estimated by fitting a logistic regression model to the results of the six laboratory studies with mallards.

Supportive/Corroborative/Other Considerations

The Panel considered two approaches to hockey-stick regression and also the possible effects of hormesis as ways of modifying the results of the logistic regression model described above, but decided they should be considered informational and corroborative, rather than as providing a basis for adjustment of the values given above. Hockey-stick regression and hormesis results are briefly described below. In addition, the Panel also discussed other considerations, such as the degree of protectiveness the State may want to take into account in setting the standard as well as several additional qualifications, during its meetings.

Hockey-stick Regression

Adams et al. (2003) used hockey-stick regression to model relationships between egg selenium concentrations and adverse effects in order to derive toxicity thresholds, such as EC_{10} values. (Hockey-stick regression is discussed in more detail in the technical memorandum of February 2007.) As shown in Figure 3, a threshold clearly exists when dietary selenium is plotted versus duckling mortality (which incorporates the cumulative effects of fertilization success and hatchability). The inflection point occurs at a dietary selenium concentration of 3.9 mg/kg (Table 2). The predicted EC_{10} is 4.4 mg/kg (just slightly above the inflection point) and the 95% CI around the predicted EC_{10} ranges from 3.8 to 4.8 mg/kg.

The hockey-stick analysis described above was based on data that were adjusted for the response of "control" ducks in the studies. When the data were not adjusted (normalized) on the basis of the control birds, the inflection point was 3.2 mg/kg (Figure 4 and Table 2), slightly lower than the LCL for logistic regression (3.6 mg/kg; Figure 1) or the inflection point when data were normalized for response of controls (3.9 mg/kg; Figure 3 and Table 2).

For eggs, an adaptation from Figure 3 in Adams et al. (2003) is provided below as Figure 5, with the 95% CI included. As shown in the figure and in Table 3, the inflection point occurs at an egg selenium concentration of 9.8 mg/kg, with a predicted EC_{10} comparable to that derived by Ohlendorf (2003). However, the 95% CI using hockey-stick regression is much narrower (9.7 to 13.6 mg/kg) than that derived by Ohlendorf using logistic regression (6.4 to 16.5 mg/kg). When data are not adjusted (normalized) for the response of the "control" mallards, the inflection point is 6.7 mg/kg (Figure 6 and Table 3). This is near the LCL for logistic regression (6.4 mg/kg; Figure 2) and lower than the inflection point when data were normalized for response of controls (9.8 mg/kg; Figure 5 and Table 3).

Overall, the Panel considered the results of the hockey-stick regression analyses to corroborate the use of the EC_{10} (and associated CI) from logistic regression, rather than indicating a need to adjust those threshold values.

Hormetic Effects of Selenium

Consideration of the hormetic effects of selenium may result in lowering of thresholds (for hormetic substances and endpoints, one has to distinguish between valid control responses and hormetic deficiency responses before a valid baseline to compare toxic responses against can be identified). The hormetic bias in the data used for the Ohlendorf (2003) regressions was discussed by the Science Panel. If modifications were to be made on the basis of hormetic effects, those changes could only be in the direction of a downward shifting of the threshold confidence limits. (Preliminary unpublished analyses that adjusted for hormetic effects in the mallard data yielded a revised EC_{10} for diet of 4.1 mg/kg, with a 95% CI of 1.3 to 5.8 mg/kg, and a revised EC_{10} for eggs of 9.22 mg/kg, with a 95% CI of 4.11 to 13.1 mg/kg.)

The Panel agreed that the available information does not indicate a need to modify the range of values presented in Table 1 for use in modeling and evaluation of avian exposure and effects. Instead, hormesis, like hockey-stick regression, is a factor the Panel will consider but the ranges of values in Table 1 are considered adequate for that purpose.

Desired Degree of Protectiveness

The Science Panel can choose a scientifically-based threshold value or acceptable "benchmark" concentration based on the consensus confidence limits described by analysis of available data (presented above), but ultimately, a choice of numbers from within the consensus confidence limits for regulatory purposes is not a scientific decision. Choices of a specific number or numbers from within those confidence ranges are philosophical/legal decisions that depend on how precautionary the State of Utah wants to be (a matter of philosophy) and on how much potential for legal liability the State is comfortable with exposing itself to. This issue is discussed in more detail in the technical memorandum of February 2007.

Other Qualifications and Points Discussed

The Panel also discussed several additional qualifications and points relative to toxicity threshold values. The principal ones included the applicability of laboratory data to field situations, applicability of mallard data to species at GSL, importance of non-reproductive adverse effects endpoints, and possible effects on phalaropes or other seasonally numerous birds with smaller body weight (and consequently a higher feeding rate) at the GSL. However, in the end, the Panel agreed to focus primarily on those species for which information was available or for which assessment could be more readily completed.

Recommended Next Steps

The threshold values summarized in this technical memorandum (Table 1) should be used for purposes of modeling and evaluation toward development of the recommended standard. In parallel, it will be important to know what level of protectiveness the State and USEPA will apply in the development of the site-specific standard for selenium on the GSL (i.e., EC_{10}, LEL, UCL, or some other value) so that the Science Panel can most effectively make recommendations that can be applied toward that purpose.

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Tables

TABLE 1
Range of Values for Use in Modeling and Evaluation
Threshold Values for Selenium in Great Salt Lake: Refined Selections by the Science Panel

Concentration	95% Effects	Maximum Likelihood
Diet		
3.6 ppm	< 1% - 10%	3%
4.9 ppm	4% - 24%	10%
5.7 ppm	10% - 32%	18.5%
Egg		
6.4 ppm	< 1% - 10%	1.5%
12.5 ppm	3.5% - 26.5%	10%
16.5 ppm	10% - 37.5%	21%

TABLE 2
Hockey-stick Regression Results for the Bird Diet Endpoint
Threshold Values for Selenium in Great Salt Lake: Refined Selections by the Science Panel

	Inflection Point	LCL	EC_{10}	UCL
Data adjusted for control	3.9	3.8	4.4	4.8
Data not adjusted for control	3.2			

Note: EC_{10}, LCL, and UCL for data without adjustment for control not calculated due to varying confidence interval.

TABLE 3
Hockey-stick Regression Results for the Bird Egg Endpoint
Threshold Values for Selenium in Great Salt Lake: Refined Selections by the Science Panel

	Inflection Point	LCL	EC_{10}	UCL
Data adjusted for control	9.8	9.7	11.5	13.6
Data not adjusted for control	6.7			

Note: EC_{10}, LCL, and UCL for data without adjustment for control not calculated due to varying confidence interval.

Figures

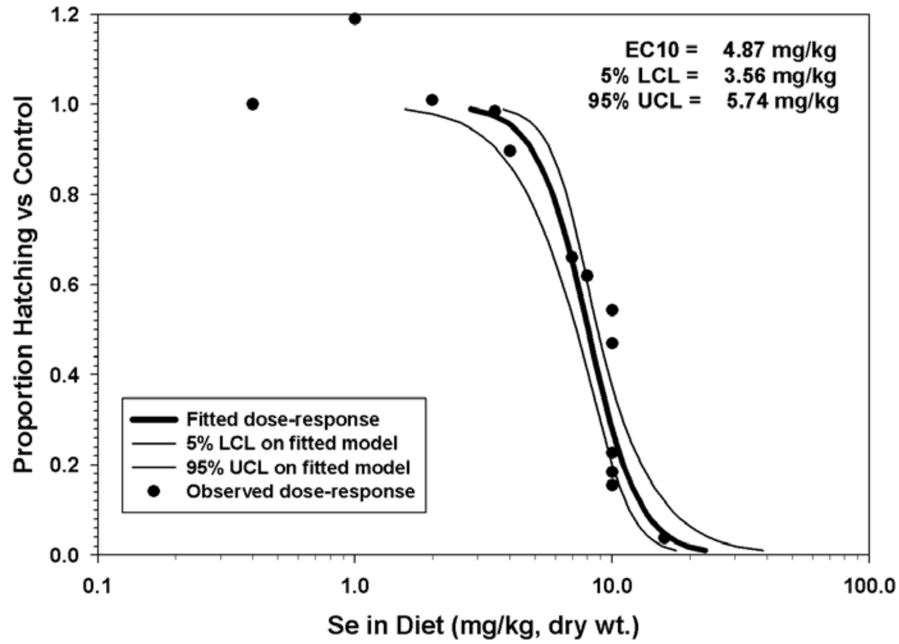

FIGURE 1
Mallard Egg Hatchability versus Control as a Function of Selenium Concentration in Diet

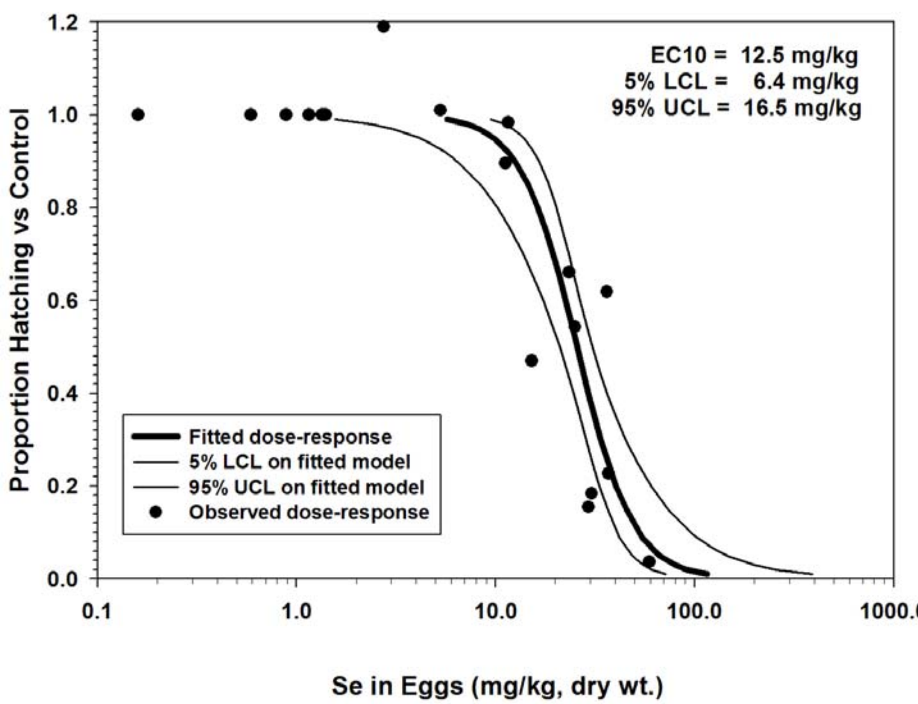

FIGURE 2
Mallard Egg Hatchability versus Control as a Function of Selenium Concentration in Eggs

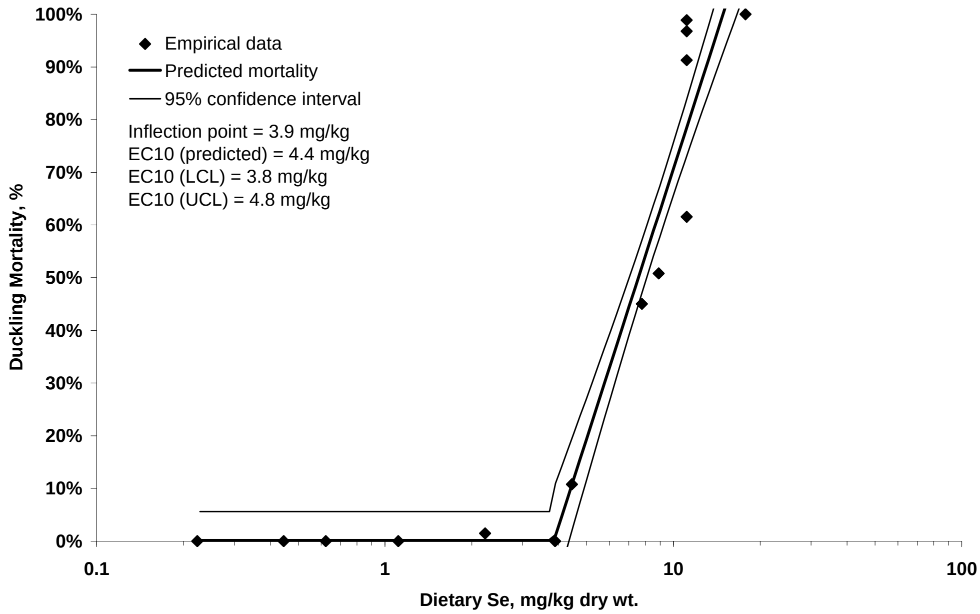

FIGURE 3
Hockey-stick Regression of Laboratory Mallard Duckling Mortality versus Dietary Selenium

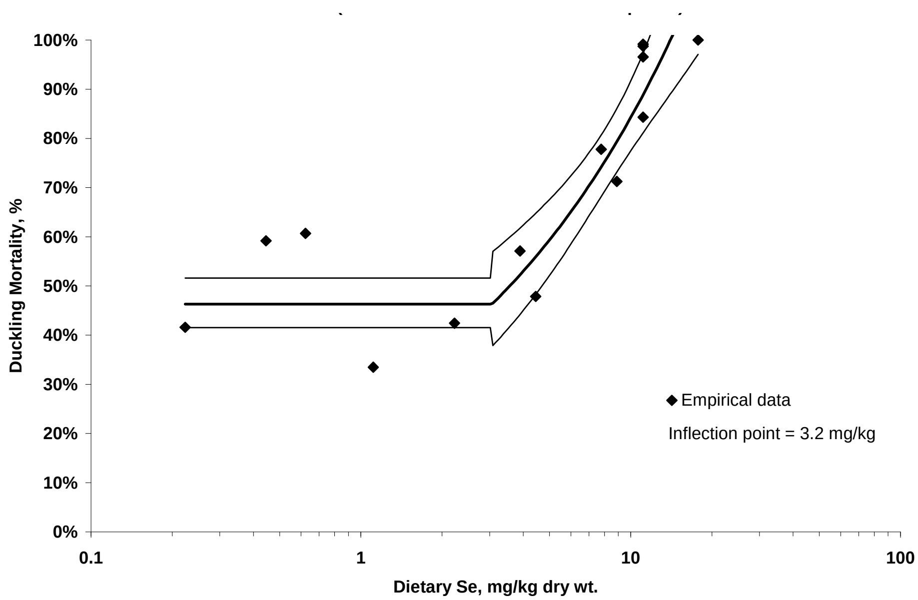

FIGURE 4
Hockey-stick Regression of Laboratory Mallard Duckling Mortality versus Dietary Selenium
(data not normalized for control response)

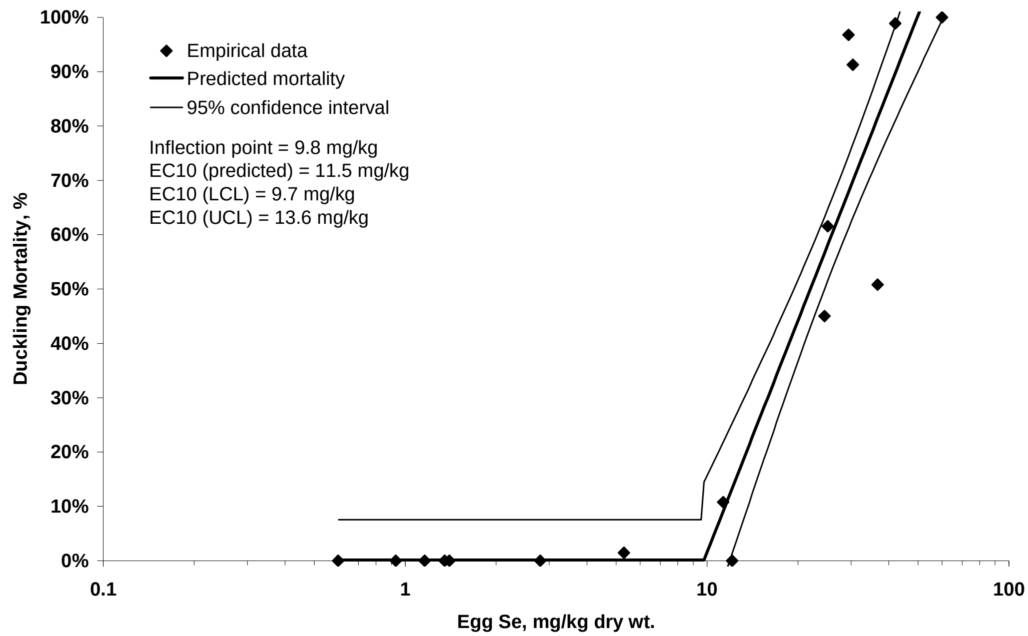

FIGURE 5
Hockey-stick Regression of Laboratory Mallard Duckling Mortality versus Egg Selenium

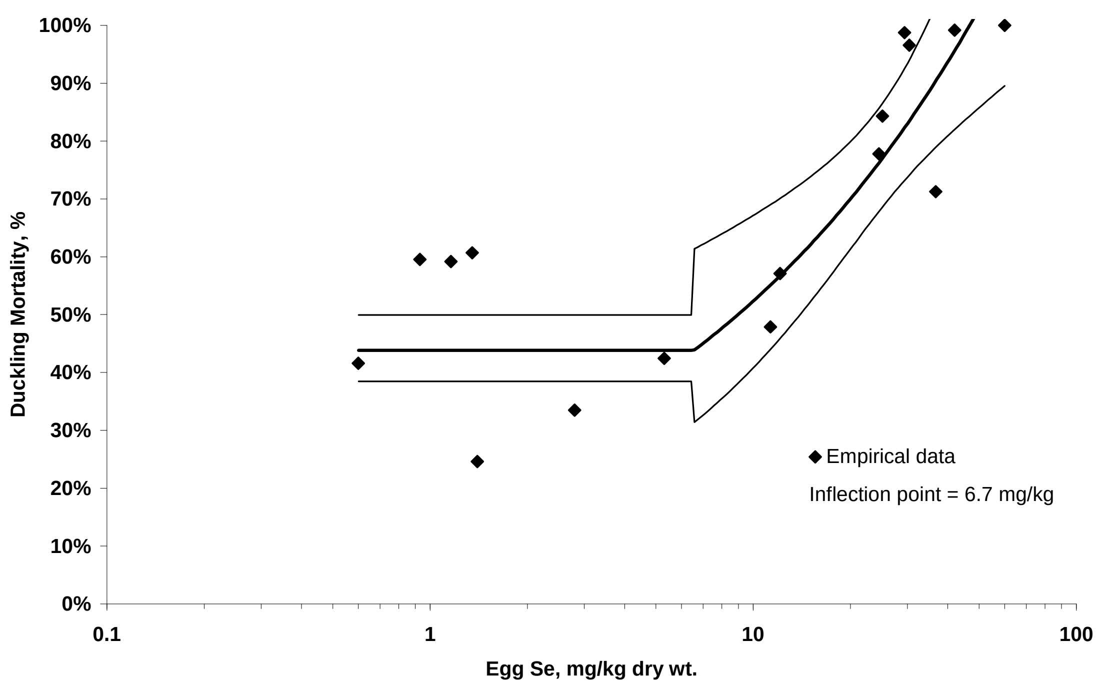

FIGURE 6
Hockey-stick Regression of Laboratory Mallard Duckling Mortality versus Egg Selenium
(data not normalized for control response)

FACT SHEET

Recommended Guidelines for a Water Quality Standard for Selenium in Great Salt Lake

The State of Utah formed a Science Panel in 2004 to study selenium (Se) in the open waters of Great Salt Lake (GSL). This fact sheet presents the Science Panel's recommended guidelines for a water quality standard for Se. A Steering Committee, comprised of various GSL stakeholders, will review the Science Panel's recommendations and define a site-specific, numeric water quality standard for Se that prevents impairment of the beneficial uses of the open waters of GSL.

Science Panel's Recommended Guidelines

It is the opinion of the Science Panel that a Se water quality standard that prevents impairment for aquatic wildlife of GSL lies within the following ranges:

- 3.6 to 5.7 mg Se/kg (mg/kg = parts per million) for bird diet items
- 6.4 to 16 mg Se/kg for bird eggs

The recommended guidelines are subject to the following qualifications and precautions:

- There is uncertainty in the guidelines, as reflected by the range of Se concentrations
- The guidelines would be applied by back-calculating from tissue concentrations to estimate a corresponding water concentration
- The Panel recognizes the need for conservatism in application of the guideline that will be recommended

What is the basis for this recommendation?

- **Why do the guidelines focus on birds?** Birds are likely the most sensitive to Se:
  - » The water quality standard will be developed to protect birds that feed primarily on open waters of GSL
  - » Exposure of birds to Se is mainly through their diet
- **How does Se affect birds?** The best-documented, most sensitive, and most readily monitored effect of Se on birds is reproductive success:
  - » Other endpoints such as body condition for migratory birds or adult mortality are important, but related Se concentrations are undetermined at this time
  - » Reproductive success is considered more sensitive than those other endpoints
- **How is the effect of Se on reproductive success studied?** Se concentration in eggs can be directly related to expected reproductive success (i.e., egg hatchability) through the use of field- or laboratory-derived relationships:
  - » Success is measured by egg hatchability (i.e., the number of eggs incubated full term that hatch vs. those that don't hatch)
  - » Field studies require extensive monitoring, eggs are sacrificed when sampled, and sampling of eggs is possible only during the nesting season (about a 2-month period)
  - » Laboratory studies describe the relationship between Se concentration in bird diet, eggs, and reproductive success
- **If collecting eggs is difficult, is there another way to link Se to reproductive success?** Field-collected food items can be used to represent the bird diet to estimate Se concentration in eggs and predict reproductive success:
  - » Samples of food items can be obtained throughout the year (though spring nesting season is most important)
  - » It is easier to obtain routine samples of food items than to sample eggs
- **What is the basis for linking Se in eggs and diet to reproductive success?** Laboratory studies provide the best available data for relating Se levels in bird diets or eggs to effects on reproductive success:
  - » Panel reviewed the literature for best data describing Se effects on egg hatchability
  - » Data set identified is from six laboratory studies of mallards fed a selenomethionine-augmented diet relating Se concentration in diet and eggs to egg hatchability
  - » Panel agreed to use values from Ohlendorf (2003)[1] to establish the range
- **Why use data for mallards, which do not nest on open waters of GSL?** Mallards as a species are more sensitive to Se than other species that commonly nest at GSL:
  - » Field studies show that birds that typically use saline, or salt water, non-marine habitats (e.g., avocets and snowy plover) seem to be less sensitive than closely related species typical of freshwater habitats (e.g., stilts and killdeer)[2]

» Mallards are a freshwater species; thus, using mallard data **builds conservatism**, or a safety factor, into any water quality standard

» The best available data set for Se effects on egg hatchability are for mallards

- **How do we link bird diet and egg concentrations to the water?** Research for the GSL Se Program included development of a model that characterizes the transfer of Se from water to the birds' diet and then to the birds' eggs:

» Allows the development of a water concentration from specific diet and egg Se concentrations (by back-calculation)

How does the range of diet and egg selenium concentrations represent levels of protection?

The Science Panel has determined that selenium-related impairment for the open waters of GSL should be defined by hatching success of birds commonly nesting on the lake. Toxicological studies have shown that a 10% reduction (called an "EC_{10}") in egg hatchability of mallards occurs when the diet contains selenium concentrations between 3.6 and 5.7 mg/kg and selenium concentrations in eggs are between 6.4 and 16 mg/kg. This range of selenium concentrations in the diet and eggs and associated reductions in egg hatchability are shown in the table below. The statistical analysis indicates the greatest probability that a 10% hatchability reduction is associated with a 4.9 mg/kg diet and 12 mg/kg in the egg. There is only a very small chance that the low or high values in the ranges provided are the true concentration where a 10% effect occurs.

Diet Selenium (mg /kg)	Reduction in Hatchability	Egg Selenium (mg/kg)	Reduction in Hatchability
3.6	3%	6.4	2%
4.9	10%	12	10%
5.7	18%	16	21%

The Steering Committee will recommend to the Utah Water Quality Board the level of hatchability reduction that should be allowed before impairment is declared. The standard will be directly linked to that reduction.

What does the ECx mean?

- ECx is the effect concentration (in the diet or egg) at which X% of the eggs that are incubated to full term do not hatch because of Se exposure (i.e., 100 - X% of the eggs hatch successfully despite Se exposure of the hen)
- Each range of values (diet or egg) is determined from a toxicity (or exposure effects) curve established in the laboratory[1]
- The curve helps define the effect, in this case a certain percentage (X%) of eggs not hatching, for a given Se concentration
- When birds are exposed to the ECx in the diet, or concentrations reach the ECx in the eggs, up to an additional X% hatching failure may occur (there are other causes that also naturally contribute to hatching failure)
- The population significance of this failure depends on other losses (e.g., predation, flooding of nests, etc.)

What does the ECx NOT mean?

- It does NOT mean that X% of the overall bird population using GSL will die
- The ECx being used considers hatching success and does not apply to other endpoints, such as effects on the adult population:

» Hatching success is a more sensitive endpoint than adult survival

What will the Science Panel provide to the Steering Committee?

- Recommended guidelines that relate tissue and water concentrations to a level of protection (ECx)
- Technical documentation of studies used to develop a model that relates Se in water to bird diet and then to bird eggs
- A palette of values relating tissue Se concentrations to water Se concentrations
- Recommendations for the water quality standard from each Science Panel member

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