Attachment 4-4

Guidance for Developing Ecological Soil Screening Levels (Eco-SSLs)

Eco-SSL Standard Operating Procedure (SOP) # 5: Wildlife TRV Data Evaluation

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Standard Operating Procedure (SOP) #5: Wildlife Toxicity Reference Value Data Evaluation for

Ecological Soil Screening Levels (Eco-SSLs)

OSWER Directive 92857-55

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1.0 INTRODUCTION

The United States Environmental Protection Agency (USEPA) Office of Emergency and Remedial Response (OERR) with a multi-stakeholder workgroup developed risk-based based soil screening levels (Eco-SSLs). Eco-SSLs are concentrations of contaminants in soils that are protective of ecological receptors that commonly come into contact with soil or ingest biota that live in or on soil. Eco-SSLs are derived separately for four groups of ecological receptors: mammals, birds, plants, and soil invertebrates. As such, these values are presumed to provide adequate protection of terrestrial ecosystems.

The Eco-SSLs are used in the baseline ERA process to identify the contaminants that need to be evaluated further in the characterization of exposure, effects and risk characterization. The Eco-SSLs are used during Step 2 of the Superfund ERA process, the screening-level risk calculation. This step normally is completed at a time when limited soil concentration data are available, and other site-specific data (e.g., contaminant bioavailability information, area use factors) are not available. It is expected that the Eco-SSLs will be used to screen the site soil data to identify those contaminants that are not of potential ecological concern and do not need to be considered in the subsequent baseline ERA.

Plant and soil biota Eco-SSLs were developed from available plant, soil invertebrate and microbial toxicity data. The mammal and bird Eco-SSLs were the result of back-calculations from a Hazard Quotient (HQ) of 1.0. The HQ is equal to the dose (associated with the contaminant concentration in soil) divided by a toxicity reference value (TRV). Generic food chain models were used to estimate the relationship between the concentration of the contaminant in soil and the dose for the receptor (mg per kg body weight per day). The TRV represents a numerical estimate of a no adverse level (dose) for the respective contaminant.

The procedure(s) for deriving the oral TRVs needed for calculation of Eco-SSLs for mammals and birds are contained within four standard operating procedures (SOPs) that are sequentially numbered with those used to derive plant and soil invertebrate Eco-SSLs:

- Eco-SSL SOP #3 Wildlife TRV Literature Search and Retrieval (Attachment 4-2)
- Eco-SSL SOP #4 Wildlife TRV Literature Review, Data Extraction and Coding (Attachment 4-3)
- Eco- SSL SOP #5 Wildlife TRV Data Evaluation (Attachment 4-4)
- Eco-SSL SOP #6 Derivation of the Oral TRV (Attachment 4-5)

This document serves as SOP #5 (Attachment 4-4) and describes the procedure for evaluation of data extracted from toxicological studies for applicability in the derivation of wildlife TRVs.

The scored data is then used to derive TRVs for mammals and birds, according to the procedures outlined in SOP #6 (Attachment 4-5).

2.0 PURPOSE

TRVs are derived from the available literature reporting the toxicity of a contaminant to different mammalian and avian species. The toxicological study results (there may be more than one result reported within a study) are identified for each contaminant based on the results of literature reviews implemented as described in Attachment 4-2. Not all studies resulting from the literature search process are equally relevant to the derivation of oral TRVs.

The purpose of this SOP is to describe the procedure used for the review of attributes of a toxicological study that tend to increase or decrease their respective usefulness for the derivation of wildlife TRVs. The SOP establishes a standard system for scoring the relevance and reliability of the findings of each toxicological study result.

3.0 THE SCORING SYSTEM

Each study result with attributes extracted as described in Attachment 4-3 is evaluated and scored according to the following described system. In instances within one paper where more than one "experiment" (i.e., different combinations of receptor, dose, exposure route, exposure duration, and endpoint) is reported, the individual "experiments"are scored separately so that each may be evaluated.

The scoring system assigns an "attribute" score ranging from zero (no merit in setting a TRV) to 10 (extremely valuable and relevant to setting a TRV) to each of 10 toxicological study attributes. The ten attributes of the toxicological study include data source, dose route, test substrate, the contaminant form, dose quantification, endpoint, dose range, statistical power, exposure duration and test conditions. The evaluation of each attribute is described in Section 4.0. Note that a low score does not necessarily imply the study itself was poor, only that the study design was not optimal for the narrow goal of developing an oral TRV.

The total score is calculated by adding the results of the evaluation of each attribute. The total score may range from a minimum of 36 to a maximum of 100. The total scores are interpreted as follows:

80 to 100	High confidence
71 to 79	Medium confidence
66 to 70	Low confidence
0 to 65	Not Used in Eco-SSL Derivation

4.0 EVALUATION AND SCORING OF STUDY ATTRIBUTES

4.1 Data Source

The source of the toxicological study (e.g., peer reviewed vs. non-peer reviewed) is not expected to be an indication of the quality of the study nor its applicability in use as part of the data set to derive a TRV. Many peer reviewed studies in the toxicological literature may have little or no merit in setting oral TRVs, and some non-peer reviewed studies may be excellent sources of data for the derivation of oral TRVs. It is a requirement, however, that all studies being considered for the derivation of a TRV must be acquired and reviewed in primary form. That is, secondary descriptions of a study should not be used. Secondary reports often contain errors of fact, include only a subset of all of the data and findings, and may contain interpretations or judgements not supported by the primary data.

Scoring factors:

10 = Primary source is acquired and reviewed

0 = Primary source is not acquired and reviewed

4.2 Consideration of Absorption Fraction and Contaminant Form

Oral TRVs are expressed in units of ingested dose (mg/kg-day). It is important to recognize that the use of a TRV expressed as units of ingested dose implicitly assumes that absorption of the contaminant from the test medium is the same as for the site medium. This assumption may be reasonable when the two media are the same (e.g., both water, both similar food items), but may not be true if the two media are different (e.g., test medium = water, site medium = soil). To account for the potential difference in absorption between different media, it is necessary to convert both the ingested dose and the TRV to units of absorbed dose:

Site Dose (absorbed) = Site Dose (ingested) · Absorption fraction from site medium

TRV(absorbed dose) = TRV(ingested dose) · Absorption fraction in test medium

For this reason toxicological studies reporting the known oral absorption fraction from the test medium are preferred to those where the absorption fraction is not known. If the absorption fraction is known (either from the TRV study itself or from other studies in the same test medium), then the TRV can be used to evaluate hazard from any other medium with a known or estimated absorption fraction. For the Eco-SSLs it is conservatively assumed that absorption (bioavailabilty of the contaminant from the soil) is 100%.

The assumption of equal absorption of the contaminant from the test and site medium is reasonable when the form of the contaminant is the same in the test medium versus the site

medium. Some contaminants are more absorbed and more biologically active than others. The preferred toxicological studies use the same form of contaminant in the exposure medium compared to that found in the site medium. Table 3 in Attachment 4-3 provides a list of the contaminant forms considered for the wildlife TRVs and identifies if the are expected to occur in soils (site medium). For example, the acetate forms of metals are not expected to occur as such in the soil matrix and are scored lower than those that are expected (chlorides, oxides, etc...,). Most organic forms of metals are excluded from consideration including organic forms of arsenic used as herbicides, triethyl and tetraethyl lead, and chromium picolinate. Mixtures of contaminants are also excluded (e.g., lead chromate and mixtures of lead and arsenic). Lead shot studies are also excluded (although these were identified and labeled for further special consideration) as this metal form represents metal alloys with different combinations of metals. Acetate forms of metals are retained for use as these forms are used most often in water and quickly dissociate.

The contaminant form is considered in evaluation of the toxicological study according to the following scoring factors:

10	=	Contaminant form is known and is the same or similar to that found in the medium of concern
5	=	Contaminant form is irrelevant to absorption or biological activity
4	=	Contaminant form is not reported

4.3 Test Substrate Concentrations

An important issue in evaluation of the quality of a toxicological study for use in wildlife TRV derivation is if nominal or measured concentrations of the contaminant in the exposure medium (diet in particular) are reported and used in the determination of the dose-response relationship in the study. Using only nominal concentrations can introduce a large error into the determination of a toxicity "threshold". Studies that do not report measured concentrations are given less weight than those that provide measured concentrations. Gavage studies are considered measured, and are scored as a 10.

The following scoring factors are applied:

10	=	Test substance concentrations reported as actual measured values or unmeasured but analytically verified
5	=	Test substance concentrations reported as nominal values
1	=	Test substance concentrations calculated

0 = Test substance concentrations not reported

4.4 Dose Quantification

Knowledge of the actual doses ingested by animals in a laboratory study (or field study) can often be imprecise, especially when the exposure route is via food or water. Many studies measure the amount of water or food consumed (water and food intake rates), and hence the average ingested dose (assuming there has been no loss of contaminant) can be calculated. However, some studies do not measure and do not report water or food intake rates. This can cause errors in dose estimation, especially in cases where the presence of the test contaminant in the water or food causes a direct reduction in intake due to taste aversion, odor aversion or illness. For wildlife TRV derivation studies which report actual doses are preferred over those where the doses need to be estimated based on reported intake rates and body weights. The following scoring factors are applied:

10 = Administered doses reported as mg per kg-BW

7 = Administered doses need to be calculated and intake rates and body weights provided.

6 = Administered doses need to be calculated and only one value (intake or body weight provided)

5 = Administered doses need to be calculated based on estimated intake rates and body weights.

0 = Administered doses cannot be calculated from the information provided and the study is rejected. This includes studies where the exact dose or concentrations units or amount administered is not reported clearly or is obviously incorrect.

If the study uses an exposure method of gavage, capsule or other oral exposure where the administered amount is known then some more specific rules for scoring apply as follows:

- If the amount administered by gavage or capsule is reported in units of mg/kg body weight, a score of 10 is assigned.
- If the amount administered is in units of mg/organism, it must be divided by body weight to convert to dose units of mg/kg/day. If the body weight is reported in the study, a score of 7 is assigned.
- If the body weight is not reported and the value needs to be estimated based on a default, a score of 6 is assigned.

4.5 Dose Range

By definition, a TRV is intended to represent the location on the dose-response curve that is the threshold between absence and presence of the effect of concern (i.e., the toxicological endpoint selected as most relevant). There were two methodologies considered for establishing this threshold.

The first methodology involves identification of two values from the toxicological study including a no observed adverse effect level (NOAEL) and a lowest observed adverse effect level (LOAEL). The LOAEL is defined as the lowest administered dose that did cause a statistically significant adverse effect and the NOAEL as the lowest administered dose that did not cause a statistically significant adverse effect. Experimentally, the value of the threshold is estimated by assuming that it lies between the NOAEL and the LOAEL. Therefore, studies that use a series of doses that span the threshold region and which identify both a NOAEL and a LOAEL are much more valuable in estimating the threshold than a study which uses only one dose, or which uses multiple doses that do not bracket the threshold.

The second methodology involves the use of a modeling approach derived from the benchmark dose methodology being evaluated by EPA for use in human health risk assessment. This model estimates an exposure-response distribution. The dose level (and 95% confidence limits) are then identified from the distribution (e.g., ED_5 to ED_{50}). This method was considered in the development of the wildlife TRVs for Eco-SSLs but was not used due to limitations in the dose-response data available for wildlife. This methodology may be considered further in future revisions of the wildlife TRV procedures.

In the case of both methodologies, the same type of scoring system for evaluation of dose-range applies as it is desirable to have the "threshold" bracketed. Any study that does not contain a suitable control group cannot be used to establish a dose-response value as the TRV for calculation of an Eco-SSL.

Scoring factors:

10 = Both a NOAEL and a LOAEL are identified; values are within a factor of 3

8 = Both a NOAEL and a LOAEL are identified; values are within a factor of 10

6 = Both a NOAEL and a LOAEL are identified; values are not within a factor of 10

4 = Only a NOAEL or a LOAEL is identified

0 = Study lacks a suitable control group

4.6 Dose Route

The Eco-SSLs reflect the concentrations of contaminants in soil protective of oral exposure via ingestion of soil or food items. Dietary studies are preferred to oral exposure via gavage or capsule because they represent the closest approximation of the intake route under natural conditions. Gavage and capsule studies are less desirable because they do not generally reflect natural feeding behaviors and the vehicle used to deliver the gavage dose can alter the kinetics of absorption. Drinking water is the least desirable among the acceptable routes of administration because the Wildlife TRVs are derived for use to evaluate ingestion of soil or food items rather than drinking water.

Studies that report results for non-oral exposures (inhalation, interperitoneal injections, dermal, intravenous, subcutaneous) are not used to establish TRVs and are rejected as "not oral" using the literature rejection criteria discussed in Attachment 4-3.

The following scoring factors are applied to evaluate dose route:

10	=	Dietary
8	=	Other oral, solid exposures (gavage, capsule)
5	=	Other oral, liquid exposures
0	=	Not oral (inhalation, intravenous, subcutaneous, dermal); or choice between contaminated and non-contaminated media; or dose route not reported.

4.7 Endpoint

In most ecological risk assessments (ERAs), assessment endpoints focus on the effects of long term exposures of contaminants on population sustainability. The specific toxicological endpoints used as measurements of population sustainability in ERAs are site-specific. For the purposes of the identification and derivation of a TRV for calculation of an Eco-SSL, the endpoints are predefined. The following endpoints are selected in order of preference for derivation of TRVs.

- Studies measuring reproductive endpoints are considered the most appropriate and are preferred. Reproductive endpoints are assigned a score of 10. Within the coding system, this includes any endpoint within the reproduction (REP) effect group (Attachment 4-3; Table 16).

- Studies measuring mortality or survival (chronic) as an endpoint are also considered appropriate but are less preferable to reproductive endpoints. These study endpoints are assigned a score of 9. Within the coding system, this includes any endpoint within the mortality (MOR) effect group (Attachment 4-3; Table 16).

- Studies measuring growth are also considered appropriate for establishing TRVs. These study endpoints are assigned a score of 8. Within the coding system, this includes any endpoint within the (GRO) effect group (Attachment 4-3; Table 16).

- Studies measuring organ function, behavior or neurological function are considered less useful in establishing TRVs. This applies to endpoints within the pathology (PTH), behavior (BEH) or physiology (PHY) effect groups in the TRV coding system (Attachment 4-3; Table 16). These study endpoints are assigned a score of 4. The User may elect to score such studies lower if it is decided that the effect does not have an adverse effect on organism "fitness" or health.

- Studies measuring biochemical effects or changes that are either hormonal, chemical or enzymatic in nature are considered the least useful in establishing TRVs. These study endpoints are assigned a score of 1. This evaluation includes any endpoint in the biochemical (BIO) effect group of the Wildlife TRV coding system (Attachment 4-3; Table 16). The User may elect to score such study measures higher if it is decided that the measure can be related to organism "fitness" or health. Biomarkers of exposure are always scored as a 1.

4.8 Exposure Duration

The usefulness of a study result for derivation of a TRV is partially dependent on the duration of the exposure. Chronic and multiple generation exposures are preferred to subchronic exposures. Acute exposures are defined as single oral exposures and other exposures of less than 14 days. Chronic exposures are generally more representative of the type of exposure which may occur at a contaminated site.

The Exposure Duration score is based on the duration of the study exposure and the lifespan of the test organism. A summary of typical laboratory test organism's lifespan is provided in Table 22 of Attachment 4-3. If the exposure duration encompasses multiple generations of the test organism, a score of 10 is selected. If the duration of exposure is at least 0.1 times the expected lifespan of the test organism or occurs during a critical lifestage, a score of 10 is selected.

A lifestage is defined as critical if it is critical to the survival and reproduction of the species. These lifestages may or may not be more sensitive to contaminant exposure. Critical lifestages are listed in the following table. There may be some cases where professional judgement is used to classify certain exposures as critical outside of these listed.

Lifestage Code Descriptions	
Lifestage	**Critical (Yes or No)**
adult	No

Lifestage Code Descriptions	
Lifestage	**Critical (Yes or No)**
egg	Yes
embryo	Yes
immature	Yes
juvenile; includes yearling,	Yes
mature	No
multiple	Yes
not reported, unknown	No
subadult	No
sexually immature	No
sexually mature	No
young	Yes
young of year	Yes
Gestational Exposures	Yes
Lactation	Yes

To assess if the exposure duration is representative of the expected lifespan, the test organism lifespan is multiplied by 0.1. For example, if the test organism is a gerbil with an assumed lifespan of 2.5 years (2.5 years * 0.1 = 0.25 years or 12 weeks), an exposure duration of 9 weeks is less than 0.1 times the expected lifespan. If the duration of exposure is less that 0.1 times the expected lifespan of the test organism and multiple dosing intervals occur, a score of 6 is selected. If the duration of exposure is less that 0.1 times the expected lifespan and only a single dose interval occurs, a score of 3 is assigned. If the exposure duration is acute (a single oral dose), a score of 0 is selected.

Scoring:

10 = Exposure duration encompasses multiple generations of test species

10 = Exposure duration is at least 0.1 times the expected life span of the test species or occurs during a critical life phase.

6 = Exposure duration is shorter than 0.1 times the expected life span of the test species but multiple dosing intervals occur

3 = Exposure duration is shorter than 0.1 times the expected life span of the test species and only one dose interval occurs.

0 = Acute exposure or single oral dose.

4.9 Statistical Power

A NOAEL is defined as the highest dose that does not cause a significant effect in the selected endpoint when compared to the control. However, the ability to detect an effect (i.e., the reliability of the NOAEL) depends on a number of factors. The most important are:

1) the variability of the measurement endpoint in both the control and the dosed groups
2) the number of animals in each group

That is, as variability in the measurement endpoint goes up and the number of experimental animals goes down, the ability to detect an effect becomes very poor, and a dose which actually causes an effect may be incorrectly identified as a NOAEL. There are a number of standard statistical procedures available for calculating the power of a study to detect an effect which can be used to evaluate the reliability of NOAEL values. The statistical power test used for the toxicological Data Evaluation process for establishing Wildlife TRVs is based on Rosner (1995) and is described in detail in Appendix B of Attachment 4-3.

The NOAEL is normally defined at the highest exposure level in a study that did not cause a statistically significant difference in mean response from the control group. The test for statistical significance that is most often used to compare the control group and an exposed group is the one-sided t-test assuming equal variance:

$$t = \frac{m_2 - m_1}{s_p \sqrt{1/n_1 + 1/n_2}}$$

$$s_p = \sqrt{\frac{(n_1 - 1) \cdot {s_1}^2 + (n_2 - 1) \cdot {s_2}^2}{n_1 + n_2 - 2}}$$

where:

m = mean response of control group (m_1) or test group (m_2)
s = standard deviation of control group (s_1) or test group (s_2)
s_p = pooled standard deviation
n = number of animals in control group (n_1) or test group (n_2)

Power is the ability of a particular experimental study to detect a statistically significant difference between the control group and the exposed group, if the true difference in the means is some specified value (Δ). The method used to calculate power for the difference in the means of two normal distributions with equal variance in a one-tailed test is as follows:

$$Power = \Phi\left(Z_\beta\right) = \Phi\left(\frac{\Delta}{s_p \sqrt{1/n_1 + 1/n_2}} - Z_{1-\alpha}\right)$$

where:

ϕ = Standard normal distribution function

Δ = Assumed difference between the means of the exposed and control groups (i.e., the difference that is of concern to you as a biologically significant effect). Choosing the value of Δ to use is this calculation is subjective. For the purposes of evaluating toxicological studies as candidates for derivation of TRVs, **a default value of 20% of control is used as Δ.** This is based on the assumption that most experimental studies cannot detect smaller changes with acceptable power, and that changes of 20% or less will often not result in population level impacts, at least for many endpoints.

α = Statistical significance level used to declare an effect different from control. **The default value of α is 0.05.**

If it is not convenient to calculate the standard normal distribution function of Z_β exactly, the approximate power of a study can be determined using the following table of critical values:

Z_b (Critical)	Power
-0.674	25%
0.000	50%
0.674	75%
0.842	80%
1.282	90%
1.645	95%

For example, if the calculated value of Z_β is 0.93, then the power of the study to detect a difference of size Δ at the 0.05% confidence level is greater than 80% but less than 90%. A similar approach has been used in the Wildlife TRV database to evaluate the results of the power calculation and assign a power score.

Choosing the value of Δ to use is this calculation is difficult. For example, for some receptors and some endpoints, rather large effects (e.g., 30 to 40% of control) might not be of biological significance, while for other endpoints and other receptors, even small differences (e.g., 5-10%, or even less) might be of concern. For the purposes of evaluating toxicological studies as candidates for derivation of TRVs, a default value of 20% of control is used for Δ. This is based on the assumption that most experimental studies cannot detect smaller changes with acceptable power, and that changes of 20% or less will often not result in population level impacts, at least for many endpoints.

Scoring factors:

10 = At least 90% chance of seeing a difference that is biologically significant

8 = At least 75% chance of seeing a difference that is biologically significant

6 = At least 50% chance of seeing a difference that is biologically significant

3 = Less than a 50% chance of detecting a difference that is biologically significant

1 = STDEV and/or N not reported; the power of the NOAEL cannot be determined.

4.10 Test Conditions

Many aspects of the conditions under which animals are subject to toxicity tests may affect the outcome of the endpoints being measured. Testing conditions including ambient or incubator temperature, lighting regime, food presentation and composition, age of test species and source of test species have all been shown to influence toxicity results. Therefore, it is important that these parameters be reported in the study so the potential for confounding effects can be evaluated. If studies are reported as having been conducted following standard test protocols (e.g., avian reproduction test method), and if the measured conditions are reported and meet target values, they can be considered as the highest quality study. Equally of high quality are studies that did not explicitly follow a standard protocol, but reported all test conditions. Studies that followed standard protocols but did not report the measured conditions are of secondary quality. Studies that report only some of the key test conditions are of lower quality while those that do not report any of the test conditions should not be used. Standard study protocols and test condition parameters are discussed in Attachment 4-3 as part of the coding guidelines. Table 12 of Attachment 4-3 provides a summary of the standard avian and mammalian testing protocols and the parameters measured for each. The following Scoring factors are applied:

10 = Follows standard guideline and reports all measurement parameters

10 = Does not follow a standard guideline, but reports all test parameters

7 = Follows a standard guideline but does not report test parameters

4 = Does not follow a standard guideline and reports some, but not all of the test parameters

2 = Does not report any test parameters

Summary of Data Evaluation Scoring System		
Attribute	**Description**	**Score**
1. Data source	Primary	10
	Secondary	0
2. Contaminant Form	Contaminant form is known and is the same or similar to the of medium of concern	10
	Contaminant form is irrelevant to absorption or biological activity	10
	Contaminant form is known and is different from that found in the medium of concern	5
	Contaminant form is not reported (this includes situations when the contaminant is just listed as "Lead" or "Selenium")	4
3. Test Substrate	Test substance concentrations reported as actual measured values (M), verified nominal (UX) and/or doses administered by gavage	10
	Test substance concentrations reported as nominal values (U)	5
	Test substance concentrations not reported	0
4. Dose Quantification	Administered doses reported as mg/kg-BW (includes gavage doses reported in these units)	10
	Administered doses need to be calculated and intake rates and body weights provided	7
	Administered doses need to be calculated and only one value (intake or body weight) provided (if study is gavage or other capsule, intake is "provided")	6
	Administered doses need to be calculated based on estimated intake rates and body weights	5
	Administered doses cannot be calculated from the information provided	0
5. Dose Range	Both a NOAEL and a LOAEL are identified; values are within a factor of 3	10
	Both a NOAEL and a LOAEL are identified; values are within a factor of 10	8
	Both a NOAEL and a LOAEL are identified; values are not within a factor of 10	6
	Only a NOAEL or a LOAEL is identified	4
	Study lacks a suitable control group	0
6. Dose Route	Chemical incorporated into food (including mother's milk)	10
	Other oral (gavage, capsule)	8
	Chemical incorporated into drinking water	5
	Not dietary, other oral, or drinking water or not reported or choice of treated and non treated food or water	0
7. Endpoint	Reported endpoint is a reproductive or population effect (REP) (POP)	10
	Reported endpoint is lethality (chronic or subchronic exposures (MOR)	9
	Reported endpoint is reduction in growth (GRO)	8
	Reported endpoint is sublethal change in organ function, behavior or neurological function (BEH, PHY, PTH)	4
	Reported endpoint is a biomarker of exposure with unknown relationship to fitness (BIO)	1

Summary of Data Evaluation Scoring System		
Attribute	**Description**	**Score**
8. Exposure Duration	Exposure duration encompasses multiple lifestages of test species	10
	Exposure duration is at least 0.1 times the expected life span of the test species or occurs during a critical life phase	10
	Exposure duration is shorter than 0.1 times the expected life span of the test species and multiple doses or concentrations are administered	6
	Exposure duration is shorter than 0.1 times the expected life span of the test species and only a single dose or concentration is administered.	3
	Exposure duration is acute or not reported	0
9. Statistical Power	At least 90% chance of seeing a difference that is biologically significant	10
	NOAEL and LOAEL available or LOAEL only available	10
	At least 75% chance of seeing a difference that is biologically significant	8
	At least 50% chance of seeing a difference that is biologically significant	6
	Less than a 50% chance of detecting a difference that is biologically significant	3
	Only NOAEL available; insufficient data reported to determine statistical power of study	1
10. Test Conditions	Follows a standard guideline and reports all test parameters	10
	Does not follow a standard guideline, but does report all test parameters	10
	Follows a standard guideline but does not report test parameters	7
	Does not follow a standard guideline and reports some, but not all of the test parameters	4
	Does not report any test parameters	2

5.0 EXAMPLES

Both of the examples below are hypothetical and are intended to illustrate the basic approach that is recommended to assessing the relevance of toxicological data as the basis for deriving wildlife TRVs for use in establishing Eco-SSLs for wildlife.

5.1 Example 1

Study Summary

Smith and Jones (1984) performed a study on the effects of ingestion of dieldrin on reproduction of rats. Male and female Sprague-Dawley rats (10 per dose group) were provided with drinking water (*ad lib*.) that contained 0, 3, 10, 30, or 100 ug/L of dieldrin. Exposure began when the rats were three weeks old. At sexual maturity, males and females were randomly selected from within each dose group and were allowed to breed. After breeding, exposure of the females continued throughout gestation and lactation. The number of pups in each litter that survived to weaning was measured. Results are summarized below. Shaded cells are statistically different than control ($p < 0.05$). This result is being considered for use for derivation of the TRV for the cottontail.

Dose Group (ug/L)	Viable pups per dam (mean ± stdev)
0	7.1 ± 2.1
30	7.3 ± 2.2
100	6.8 ± 1.9
300	6.0 ± 2.4
1000	3.1 ± 1.7

Evaluation of Study Attributes

Attribute	Description	Score
Data source	Primary report was obtained and reviewed	10
Dose Route	Oral (water)	5
Test Substance	Measured concentrations are reported	10
Contaminant Form	Contaminant form in exposure medium is the same as site medium.	10
Dose Quantification	Administered doses not quantified. Ingestion rate nor body weights reported. Some effects might be due to decreased water intake by dam due to taste aversion.	5
Endpoint	Reported endpoint is a reproductive effect	10

Attribute	Description	Score
Dose Range	Both a NOAEL and a LOAEL are identified; values are within a factor of 3	10
Statistical Power	NOAEL and LOAEL reported.	10
Study Duration	Exposure duration is at least 0.1 times the expected life span of the test species and occurs during a critical life phase.	10
Test Conditions	Follows standard guideline and reports all measurement parameters	10
	Total Score	90

5.2 Example 2

Study Summary

Adams and Baker (1993) performed a study on the effects of ingestion of cadmium on renal function in dogs. Male or female animals (3 per dose group) were provided with cadmium chloride in the diet at added concentration levels of 0, 100, or 1000 mg/kg. Based on measured dietary intake, dose levels were reported to be 0, 5.2, and 41.1 mg/kg-BW per day, respectively. Urinalysis was performed for urine samples collected at days 30, 60 and 90. At day 90, animals were sacrificed and the kidneys were examined histologically. The results are summarized below.

Dose Group	Study	Urinalysis	Histopathology
5.2	30	No effect	--
	60	Mild proteinurea	–
	90	Moderate proteinurea	7% focal necrosis of renal tubule
41.1	30	Mild proteinurea	–
	60	Moderate proteinurea	–
	90	Severe proteinurea	Widespread necrosis of renal tubule

Based on these data, the authors stated that doses of 5.2 to 41.1 mg/kg-day for 90 days caused moderate to severe renal injury in dogs.

Evaluation of Study Attributes

Attribute	Description	Score
Data source	Primary report was obtained and reviewed	10
Dose Route	Oral (diet)	10
Test Substrate	Measured concentrations are reported	10
Contaminant Form	The contaminant form is the same or similar as the medium of concern.	10
Dose Quantification	Administered doses are reported as mg/kg-BW.	10
Endpoint	Reported endpoint is a sublethal change in organ function	4
Dose Range	Only a LOAEL was identified. No NOAEL can be estimated	4
Statistical Power	No NOAEL was identified; therefore this factor is not applicable	10
Exposure Duration	Exposure duration is shorter than 0.1 times the expected life span of the test species	6
Test Conditions	Does not follow a standard guideline and reports some, but not all of the test parameters	4
	Total Score	78