**Industry Benchmarking Survey**

**Blind vs. Non-Blind Histopathology Evaluation Practices**

**SURVEY OVERVIEW**

Purpose

The purpose of this survey is to obtain information regarding current institution decision-making practices for determining the use of “blind” and “non-blind” (or informed) histopathologic evaluations for GLP-compliant animal toxicity studies conducted at the institution or contracted externally by the institution.

How the Information Will Be Used

The results of this survey will be summarized for publication in *Toxicologic Pathology* as a Toxicologic Pathology Forum Opinion.

Survey Organization

There are two sections:

1. *Demographic Information* – 2 to 3 minutes
2. *Benchmarking Survey* – 12-20 minutes; a series of multiple-choice, check-box questions to determine how institutions make decisions regarding the use of “blind” vs. “non-blind” histopathologic evaluation.

Survey Completion

The SRPC requests completion of this survey by coordinating group toxicologic pathologists through a designated toxicologic pathologist point of contact responder for each individual institution site location within any given multi-site corporate, non-profit or government institution.

The reasons for this direction are (1) to reduce the possibility of duplicate responses from a single site while (2) meeting the purpose of this survey to gain feedback and perspective specifically from working toxicologic pathologists, and (3) including as many toxicologic pathologists as possible.

**PART 1 – DEMOGRAPHIC INFORMATION**

**Demographic Information –Section A: Pathology Experience** (*will not be included in any publication or presentation*, the intent is to understand the extent of responder toxicologic pathology experience and to reduce the potential for double counting institution sites.

1. Name of responder \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ [free text area]
2. Position / Title of responder: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_[free text area]
3. Years of experience as a toxicologic pathologist: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_[free text area]

**Pathology credentials:**

1. **Advanced training:** **(select all that apply)**
	* MS
	* PhD
	* Formal residency
	* None
	* Other (Please specify): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ [free text area]
2. **Certification in pathology / toxicologic pathology: Specialty** **(select all that apply)**
	* Anatomic pathology
	* Clinical pathology
	* Toxicologic pathology
	* None
	* Other (Please specify): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ [free text area]
3. **Certification type: Credential review** **(select all that apply)**
	* FIATP
	* None
	* Other (Please specify): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ [free text area]
4. **Certification type: Examination**: **(select all that apply)**
	* DABT
	* DABVT
	* DACVP
	* DECVP
	* DJSTP
	* ERT
	* MRCPath
	* None
	* Other (Please specify): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ [free text area]
5. **Institution of responder:**\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_[free text area]
6. **Site location** **of responder:** (for institutions with multiple sites)**:** \_\_\_\_\_\_\_\_\_\_\_ [free text area]

**Demographic Information – Section B: Institution:** (*compiled results to be published*)

1. **Type of organization (select one)**
	* Academic: research laboratory
	* Government: regulatory agency
	* Government: research laboratory
	* Industry: agrochemical
	* Industry: biopharmaceutical
	* Industry: contract research organization
	* Industry: medical device
	* Private consulting practice
	* Other: (Please indicate)
2. **Organization size:** Number of all employees in organization at the responder’s site  **(select one)**
	* < 50
	* 50 to 500
	* 501 to 5,000
	* 5,001 to 20,000
	* >20,000
3. **Number of toxicologic pathologists at the responder’s site covered by the survey responses** \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ [free text area]
4. **Institutional Location (select one)**
* Africa only
* Asia / India only
* Australia / New Zealand only
* Europe / Russia only
* North America only
* South / Central America only
* Multi-national
1. Additional comments regarding Part 1: (optional) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ [free text area]

**PART 2 – BENCHMARKING CURRENT STRATEGIES FOR APPLYING “BLIND” AND “NON-BLIND” HISTOPATHOLOGIC EVALUATION IN YOUR INSTITUTION**

**Section A: Primary Pathology Read:**

1. Does your institution perform histopathologic evaluation for evaluation for GLP-compliant animal studies using a “blind” histopathology evaluation strategy? **(select one)**
	* A) **Yes, all entire studies are always read “blind.”**
	* B) **Yes, some entire studies are read “blind”**, with the decision to do so dependent on the purpose and/or type of study.
	* C) **Yes, within-study ‘targeted’ “blind” evaluation**, where blind evaluation of selected subsets of organs, tissues, and / or animal groups is conducted after an initial informed read.
	* D) B and C
	* E) No, never

*If you answered "A" please GO TO Question 18 (skip questions 16 & 17).*

*If you answered "E" please GO TO Question 27, Peer Review (skip questions 16-26)*

*If you answered "B,” “C,” or "D" please GO TO Question 16 (the next question).*

1. Reply only if your answer to Survey Question 15 was “B”, “C”, or “D”: Out of a hypothetical 100 animal studies at your institution, **approximately what percent use “blind” histopathologic evaluation as a *pre-determined* strategy** in the initial evaluation (i.e., prescriptive strategy defined in the study plan / protocol)?  **(select one)**
	* 0
	* ≤5%
	* 6 to 10%
	* 11% to 20%
	* 21 to 50%
	* 51-75%
	* >75%
	* Unknown
2. Reply only if your answer to Survey Question 15 included either “C” or “D”: Out of a hypothetical 100 animal studies at your institution, **approximately what percent use ‘targeted’ “blind” histopathologic evaluation as a *post-hoc* strategy**? **(select one)**
	* 0
	* ≤5%
	* 6 to 10%
	* 11% to 20%
	* 21 to 50%
	* 50-75%
	* >75%
	* Unknown
3. **Are there certain therapeutic modalities where your institution is more likely to consider including “blind” histopathologic evaluation?**  (select all that apply)
* Small molecules
* Oligonucleotides
* Therapeutic proteins
* Therapeutic antibodies
* Gene therapy
* Other(s) (describe): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ [free text area]
* Modality type does not influence the decision to include a “blind” evaluation
1. **Rank order the top 5 reasons used in your institution when making a decision to perform a “blind” histopathologic evaluation (***as either a predetermined strategy or a post hoc addition)*. Rank the order with “1” being the most important and “5” being the least important. Do not rank options that you do not consider in making the decision to “blind” studies.
* To generate anatomic pathology information as ordinal data for statistical analysis.
* To minimize potential observational bias of data during interpretation (e.g., to test a hypothesis).
* To determine a “no observed adverse effect level” (NOAEL) or “no observed effect level” (NOEL).
* In a tiered approach to reexamine selected or all treated groups following initial non-”blind” evaluation
* To meet expectations or requests from non-pathologists that the anatomic pathology data is generated in an unbiased fashion
* Studies employing quantitative analysis of microscopic features compared across treatment groups as end points on a continuous scale
* Evaluation of well-characterized diseases or animal models a using predefined set of criteria to evaluate and score each characteristic of the finding
* To confirm the incidence / severity of a finding in treatment groups relative to the background incidence / severity seen in control animals (i.e., to confirm the potential relationship of subtle changes to treatment)
* Other(s) (describe): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ [free text area]
1. **Rank the order of how are “blind” histopathologic evaluations** *(as either a predetermined strategy or a post hoc addition)* **performed in your institution**? Rank the order with “1” being the most common practice and “4” being the least common option. Do not rank options that you do not use.
* Formal – Slides receive coded labels before being sent to the study pathologist
* Formal – The study pathologist returns slides for coding (e.g., coded covering slide labels) before proceeding to the “blind” evaluation
* Informal - The study pathologist randomizes the slides to be read, then does not read/ignores uncoded slide labels until all the slides have been graded.
* Other(s) (describe): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ [free text area]
1. **Rank order the top 5 specific types of information that are withheld from the study pathologist** **when conducting “blind” histopathologic evaluations at your institution.** Rank the order with “1” being the most important and “5” being the least important.Do not rank options that you do not use.

*For terminology reference, please the following definitions*

**“Test Article”**

* + - * + Characteristics: Modality, mechanism of action, known activities of this class of compound and vehicle

**“Target Tissues”**

* Knowledge of target organs/tissues, including the type of changes encountered in previous toxicity studies, preferred terminology / lexicon, etc.

**Study Design**

* Route of Administration: Gavage, intravenous, intramuscular, etc.
* Duration: Exposure and recovery times
* Study Protocol, Amendments, Deviations:
* Dose groups
* Control groups - Negative, wild-type, positive, vehicle, etc.

**Animal Information**

* Population: Age, sex, species, breed/strain
* Animal Modeling Information: Infectious disease, surgical modifications, genetic modifications, etc.
* In-Life Information: Clinical observations, body weights, food consumption, ophthalmology, etc.
* Terminal Observations: Organ weights, macroscopic (gross) observations
* Clinical Pathology & Biomarkers: Hematology, biochemistry, urinalysis, hormone concentrations, etc.
* Metabolic, pharmacokinetic, toxicokinetic: Exposure, enzyme induction, anti-drug antibodies, etc.
* “Blind” to all *(Blind to the test article (or animal model), target tissues, study design, and animal information with the intent of providing a completely random evaluation)*
* Known high-dose and control groups only *(Blind to test article characteristics, target tissues, remaining dose groups, study design, and animal information*)
* Known test article characteristics only *(Blind to all dose groups, target tissues, study design, and animal information)*
* Known test article characteristics as well as high-dose and control groups *(Blind to target tissues, remaining dose groups, study design, and animal information)*
* Known test article characteristics, target tissues, and high-dose and control groups *(Blind to remaining dose groups, study design, and animal information)*
* Other (please describe) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ [free text area]
1. **Rank the order of what type of specimens are subjected to “blind” histopathologic evaluation as either a predetermined strategy or a *post hoc* addition?** Rank the order with “1” being the most common practice and “5” being the least common option. Do not rank options that you do not use.
	* All organs and tissues
	* Potential target organs identified by an initial “non-blind” evaluation during the current study.
	* Only known target organs as identified with the specific test article in either the current or a prior study.
	* Only anticipated target organs based on prior studies with chemically-related or platform test articles.
	* Other (describe): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ [free text area]
2. **Rank the order of who most often makes the decision regarding whether the histopathologic evaluation (as either a predetermined strategy or a *post hoc* addition) will be performed using a “non-blind” vs. “blind” approach?** Rank the order regarding the decision makers, with “1” being the one who most often makes the decision and “5” the one who least often makes the decision. Do not rank options that you do not use.
	* The study pathologist
	* The study director / principal investigator
	* Institutional management (departmental managers, team leaders, etc.)
	* Standard operating procedures
	* Other (describe): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ [free text area]
3. **Rank the order of where the use of a “blind” histopathologic evaluation is documented** *(question includes both as a predetermined strategy or a post hoc addition)*. Rank the order with “1” being the document used most often and “5” the one used least often. Do not rank options that you do not use.
	* In the original study plan / protocol
	* In an amendment to the study plan / protocol
	* In the pathology sub-report
	* In an institutional standard operating procedure (SOP)
	* The decision is documented for formal (i.e., slides have coded labels) but not for informal (i.e., uncoded slide labels are ignored by pathologist) “blind” evaluations
	* The decision is not documented for either formal or informal “blind” evaluations
	* Other (describe): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ [free text area]
4. **Rank the order of where** **the use of a “blind” histopathologic evaluation is documented within the pathology report** *(question includes both as a predetermined strategy or a post hoc addition)*. Rank the order with “1” being the location used most often and “5” the one used least often. Do not rank options that you do not use.
	* No mention of the “blind” evaluation is included in the report
	* A simple mention that a “blind” evaluation was conducted
	* A more detailed description that a “blind” evaluation was performed, indicating whether it was formal or informal
	* A more detailed description that a “blind” evaluation was performed, indicating whether it was formal or informal AND why it was undertaken
	* A more detailed description that a “blind” evaluation was performed, indicating whether it was formal or informal AND who made the decision to undertake the “blind” evaluation
	* A more detailed description that a “blind” evaluation was performed, indicating whether it was formal or informal AND why it was undertaken AND who made the decision to undertake the “blind” evaluation
	* Other (describe): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ [free text area]
5. Additional comments regarding **Part 2, Section A: Primary Pathology Read:**

(Optional) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ [free text area]

**PART 2 (Continued) – BENCHMARKING CURRENT STRATEGIES FOR APPLYING “BLIND” AND “NON-BLIND” HISTOPATHOLOGIC EVALUATION IN YOUR INSTITUTION**

**Section B: Pathology Peer Review Read:**

1. Does your institution use a “blind” histopathology evaluation strategy for pathology peer review of GLP-compliant animal toxicity studies? **(select one)**
	* A. Yes, always
	* B. Yes, targeted “blind” evaluation (as needed)
	* C. No, never
	* D. It depends on the purpose and/or type of study

*If you answered “D” proceed to Question 28 (next question).*

*If you answered either “A”, “B” or C” please GO TO Question 31 (skip questions 28-30)*

*you are done with the survey. Thank you (please submit)!*

1. **If your answer to Survey Question 27 was *“D”*, for which study purposes is the pathology peer review at your institution performed using a “blind” histopathology evaluation strategy?** Rank the order, with “1” being the most common practice and “5” being the least common option. Do not rank options that you do not use.
	* Toxicity studies of 1 month duration or less
	* Toxicity studies of duration longer than one month
	* Carcinogenicity studies
	* Other (describe): \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ [free text area]
2. I**f your answer to Survey Question 27 was “D” out of a hypothetical 100 pathology peer reviews at your institution, what percent would use “blind” histopathologic evaluation as a pre-determined strategy**? (e.g. prescriptive strategy defined in the study plan / protocol) **(select one)**
	* 0
	* ≤5%
	* 6 to 10%
	* 11% to 20%
	* 21 to 50%
	* 51-75%
	* >75%
3. **If your answer to Survey Question 28 was “D,”** **out of a hypothetical 100 pathology peer reviews at your institution, what percent would use “blind” histopathologic evaluation as a *post hoc* strategy** (i.e., follow-up “blind” peer review of all organs or potential target organs)? (**select one)**
	* 0
	* ≤5%
	* 6 to 10%
	* 11% to 20%
	* 21 to 50%
	* 51-75%
	* >75%
4. **Additional comments regarding Part 2: Benchmarking Current Strategies - Section B: Pathology Peer Review Read**

(Optional) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ [free text area]

1. Are you interested in a follow-up discussion with the SRPC Working Group regarding the outcome of this survey?
	* Yes
	* No
2. The SRPC Working Group will be reviewing “blind” histopathologic evaluation practices in ***non-GLP-compliant and / or discovery-phase animal toxicity and efficacy studies*** to better understand the use of this strategy in all aspects of toxicologic pathology practice. Please indicate the most appropriate institutional site contact pathologist(s) to contact for a related short survey or phone call discussion on this topic: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_[free text area]**.**

***Congratulations - You are done with the survey!.***

***Thank you (please submit)***