# P-247 リスクベースドアプローチを用いたGLP試験におけるプロセス調査の適用可能性

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# Availability of a risk-based approach in process-based QA inspection in GLP studies

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## Introduction and Objective

- In guidance for GLP facilities on the implementation and maintenance of a risk-based Quality Assurance (QA) program in the UK, the MHRA discusses the impact of process failures on GLP compliance and the need for assessments of process-specific cases in determining the frequency of process-based inspection.
- In this work, we evaluated the risk of issues in the experimental procedures in typical toxicity studies using a risk-based approach and examined its application in process-based inspection.

## Method

- Risk assessment was performed similarly to a Healthcare Failure Mode and Effects Analysis (HFMEA).
- As typical toxicity studies, we selected a 4-week repeated dose toxicity study (4-week TOX) and a bacterial reverse mutation assay (Ames test).
- The experimental procedure in these studies was identified and possible issues were listed.
- We evaluated the degree of severity and occurrence of possible issues, and scored according to the Evaluation Criteria.
- Criticality was calculated from severity and occurrence.
- We examined whether the testing department could detect possible issues categorized as high risk.

## What is a risk-based approach?

➢The priority of the issues to be investigated is determined based on the type and degree of risks.

➢It determines the scope, items and survey method within the survey target.

**Risk Identification** – To identify hazards considering regulatory requirements, past issues, etc.

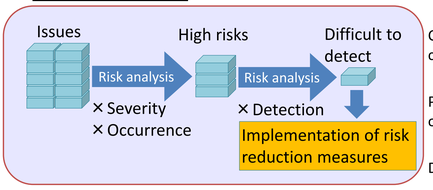
**Risk Analysis** – To estimate of the risk associated with the identified hazards: To score by occurrence (past), detection (present), severity (future).

**Risk Evaluation** – To evaluate the risks quantitatively and qualitatively.

Visualization → Extract high risk issues

**It can enable an effective and efficient survey by focusing resources on high-risk items.**

### HFMEA method




【Severity】 Criticality of the effects caused by issues

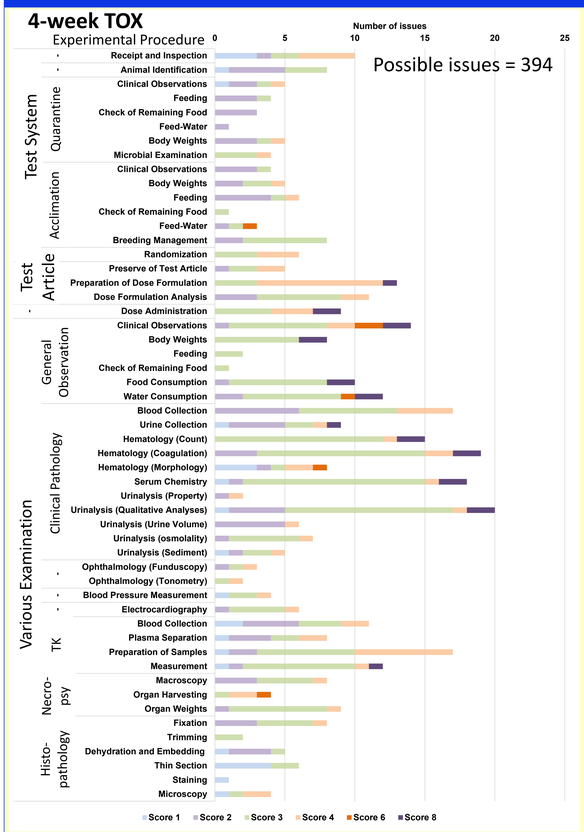
【Occurrence】 Probability or frequency of occurrence of issues

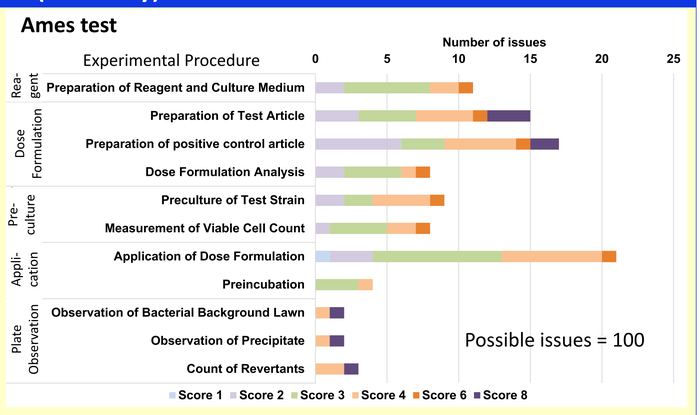
【Detection】 Detectability of issues

### Evaluation Criteria

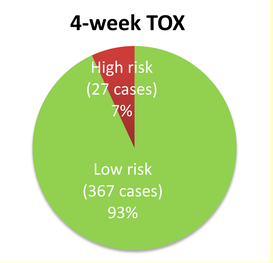
| Score | Severity | Occurrence |
|---|---|---|
| 1 | Negligible – There is no perceived risk of an unsuccessful study, and it can be corrected by oral attention. | Improbable (*e.g.*, once every few years) |
| 2 | Minor – There is no perceived risk of an unsuccessful study, but some improvement is required. | Uncommon (*e.g.*, every year) |
| 3 | Major – There is a perceived risk of an unsuccessful study, improvement is required. | Occasional (*e.g.*, once every few months) |
| 4 | Critical – Since the study is unsuccessful, drastic and urgent improvement is required. | Frequent (*e.g.*, monthly) |

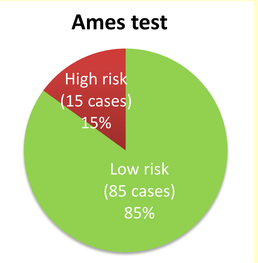
## Result (Criticality)




Criticality = Severity × Occurrence
Criteria: Low risk ≤ Criticality Score 4 < High risk




## High-risk cases

[4-week TOX]

- Approximately 60% (17 cases) of the high-risk cases were issues on computerized systems related to the ALCOA principles[1].

  Main case: Measure with the ID of another employee in the computerized systems (9 cases).

✓ Keeping the ALCOA principles is very important both in conducting tests and in determining whether process-based inspection can be applied.

[Ames test]

- Approximately 70% (10 cases) of the high-risk cases were issues related to records.

  Main case: Mistake in record of number of revertant colonies (1 case).

✓ It should be noted that record deficiencies may occasionally occur, even in experienced GLP facilities.

1) ALCOA principles by the MHRA GXP Data Integrity Guidance and Definitions:
ALCOA is an acronym for the original five principles of data integrity. Those principles are Attributable, Legible, Contemporaneous, Original and Accurate.

## Detectability of high-risk cases

[4-week TOX]

✓ It was considered that all high-risk cases would be detectable by the testing department as the procedures involved multiple staff, reporting to SD, QC checks, etc.

[Ames test]

✓ It was considered that almost all high-risk cases would be detectable by the testing department due to the checking of raw data by QC and SD.

## Conclusion

- Many issues in both studies were classified as low risk.
- The high risk rates in both studies were approximately 10%, respectively.
- It was considered that the QA inspection did not need to be performed for all experimental procedures in each study, because almost all high-risk cases would be detectable by the testing department.

◆ We conclude that process-based QA inspection is applicable to all experimental procedures in both studies.
However, it is necessary to assess the possible issues at each facility, because the possible issues of each facility differed according to the implementation system or test articles, etc.
We consider that a risk-based approach is useful for determining the applications of process-based QA inspection in GLP studies.

※The authors have no conflict of interest to disclose with respect to this presentation.