



國科會計畫涉及動物實驗之3R文件調整說明 如何做好動物實驗規劃

國家實驗動物中心 秦咸靜主任

NAR Labs
國家實驗研究院

課程大綱

1. 國科會計畫涉及動物實驗之3R文件調整說明
2. 動物實驗規劃 (I) 實驗動物與統計方法
3. 動物實驗規劃 (II) 實驗流程及結果分析
4. 動物實驗規劃 (III) 傷害利益評估



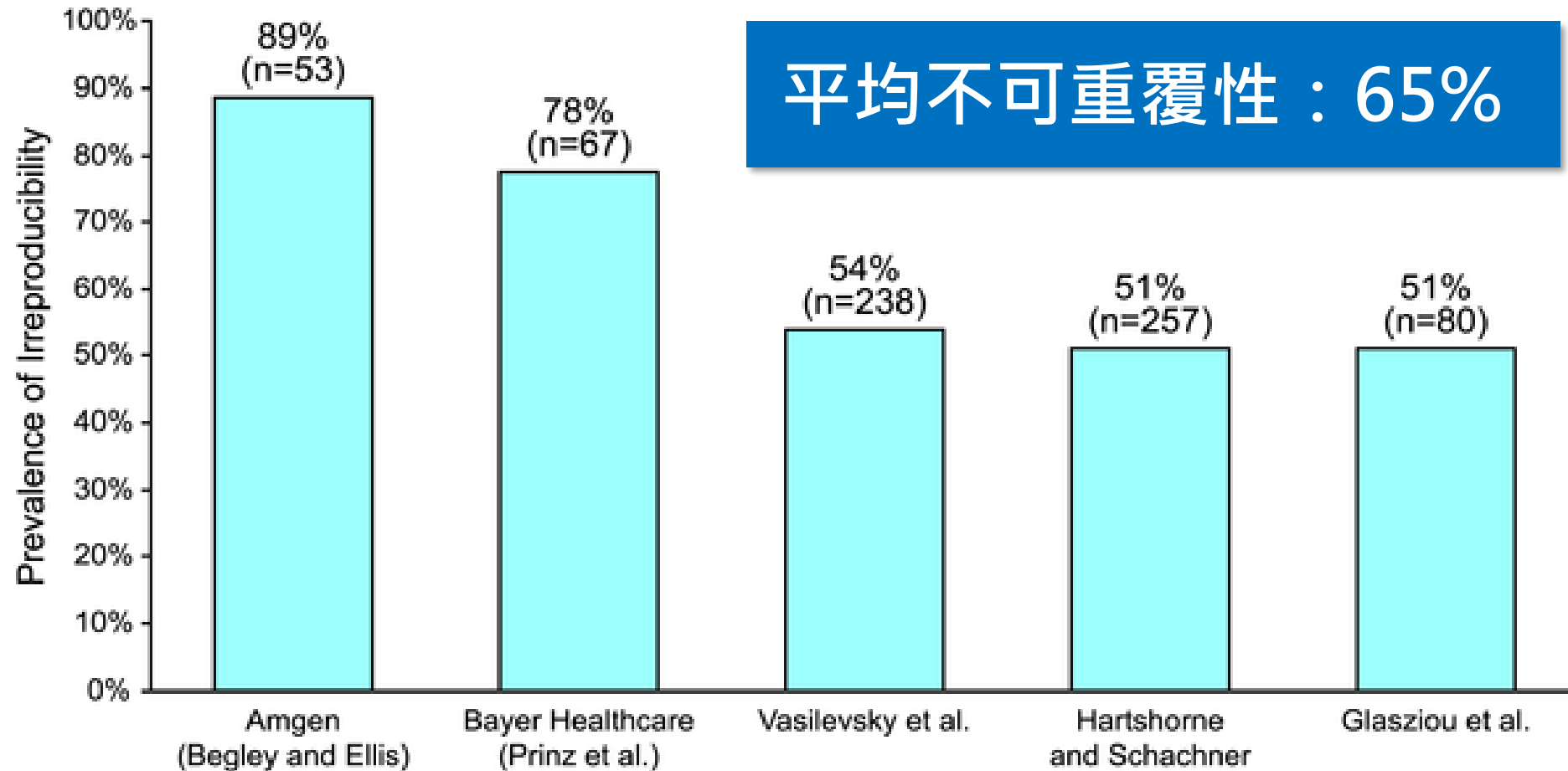
第一部份

國科會計畫涉及動物實驗之3R文件調整說明

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動物實驗的挑戰- 再現性不足



Freedman LP, Cockburn IM, Simcoe TS (2015)
The Economics of Reproducibility in Preclinical Research.
PLoS Biol 13(6): e1002165. doi:10.1371/journal.pbio.1002165

動物實驗成果發表- 欠缺實驗細節

OPEN ACCESS Freely available online

PLoS one

Survey of the Quality of Experimental Design, Statistical Analysis and Reporting of Research Using Animals

Carol Kilkenny^{1*}, Nick Parsons², Ed Kadyszewski³, Michael F. W. Festing⁴, Innes C. Cuthill⁵, Derek Fry⁶, Jane Hutton⁷, Douglas G. Altman⁸

- The survey identified key areas for improvement:

Experimental design

Most papers did not report randomisation (88%) or blinding (86%) to reduce bias in animal selection and outcome measurements.

Statistical analysis

Only 70% of publications fully described statistical methods and presented the result with a measure of variability.

Reporting of studies

Only 59% included three important pieces of information: hypothesis, number of animals and characteristics of animals.

ARRIVE guidelines

The ARRIVE guidelines (Animal Research: Reporting of *In Vivo* Experiments) are a checklist of recommendations for the full and transparent reporting of research involving animals – maximising the quality and reliability of published research, and enabling others to better scrutinise, evaluate and reproduce it.

[ARRIVE guidelines >](#)



ARRIVE指南目標在**改善動物實驗成果報導品質**

不是注重吸引人的實驗成果，而是注重**嚴謹的實驗規劃與執行細節**，增加可信度

Title

1. Accurate & concise description

Abstract

2. Background, objectives, methods, key findings and conclusions

Introduction

3. Background
4. Objectives

Methods

5. Ethical statement
6. Study design (blinding/randomisation)
7. Experimental procedures (How? When? Where? Why?)
8. Experimental animals (species, sex, weight)
9. Housing and husbandry
10. Sample size
11. Allocation experimental groups
12. Experimental outcomes
13. Statistical methods

Results

14. Baseline Data
15. Numbers Analysed
16. Outcomes & estimation
17. Adverse events

Discussion

18. Interpretation & implications
19. Generalisability and translation
20. Funding

The ARRIVE guidelines are endorsed by journals, funders and learned societies.

Journals



Over 400 journals have incorporated the ARRIVE guidelines in their Instructions to Authors

Funders



The major funding bodies of biomedical research in the UK support the ARRIVE guidelines.

Universities



Universities endorse the ARRIVE guidelines by encouraging staff and students to use the guidelines.

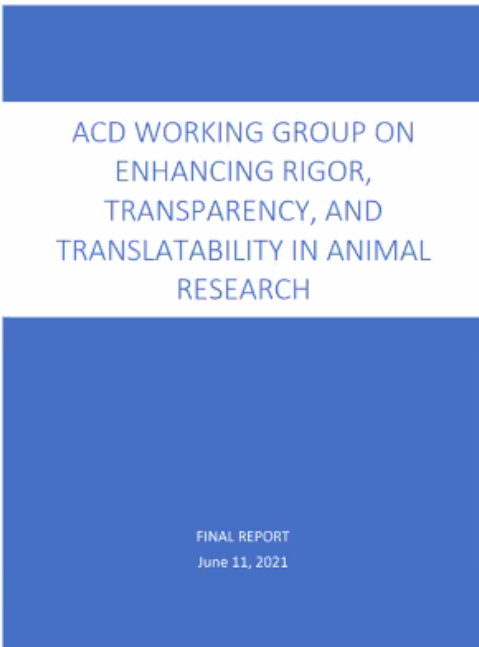
Learned Societies



A growing number of learned societies endorse the ARRIVE guidelines and share the guidelines with their members.

NIH建議採用ARRIVE Essential 10

NIH Encourages the Use of the ARRIVE Essential 10 Checklist in all Publications Reporting on the Results of Vertebrate Animal and Cephalopod Research



When ARRIVE 2.0 should be followed:

Writing stage

AND

Entire research process

“Strengthening these elements **across the life of a study, from planning to execution and publication**, will result in a higher-quality knowledge base and will better inform future research.”

實驗規劃

執行計畫

成果發表

ARRIVE Essential 10

- **ARRIVE 1.0 - 如何發表動物實驗相關之論文**
- **ARRIVE 2.0 (Essential 10)- 精簡為10項在計畫申請時應完備的規劃項目**
- **好的科學不光是要做到，還要讓別人看到**

1. 實驗設計	4. 隨機 Randomisation	7. 統計方法
2. 樣本數	5. 盲法 Blinding	8. 實驗動物
3. 樣本納入及排除	6. 結果評量指標	9. 實驗程序
		10. 結果

PREPARE GUIDELINE

PREPARE: guidelines for planning animal research and testing

Adrian J Smith¹, R Eddie Clutton², Elliot Lilley³,
Kristine E Aa Hansen⁴ and Trond Brattelid⁵

Abstract

There is widespread concern about the quality, reproducibility and translatability of studies involving animals. Although there are a number of reporting guidelines available, there is very little overarching guidance on how to *plan* animal experiments, despite the fact that this is the logical place to start ensuring quality. In this paper we present the PREPARE guidelines: Planning Research and Experimental Procedures on Animals: Recommendations for Excellence. PREPARE covers the three broad areas which determine the quality of the preparation for animal studies: formulation, dialogue between scientists and the animal facility, and quality control of the various components in the study. Some topics overlap and the PREPARE checklist should be adapted to suit specific needs, for example in field research. Advice on use of the checklist is available on the Norecopa website, with links to guidelines for animal research and testing, at norecopa.no/PREPARE.

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[sagepub.co.uk/
journalsPermissions.nav](http://sagepub.co.uk/journalsPermissions.nav)
DOI: 10.1177/0023677217721
journals.sagepub.com/t



The PREPARE guidelines cover 15 topics, grouped in three main sections:

A. Formulation of the study

1. Literature searches
2. Legal issues
3. Ethical issues, harm-benefit assessment and humane endpoints
4. Experimental design and statistical analysis

B. Dialogue between scientists and the animal facility

5. Objectives and timescale, funding and division of labour
6. Facility evaluation
7. Education and training
8. Health risks, waste disposal and decontamination

C. Quality control of the components in the study

9. Test substances and procedures
10. Experimental animals
11. Quarantine and health monitoring
12. Housing and husbandry
13. Experimental procedures
14. Humane killing, release, reuse or rehoming
15. Necropsy

PREPARE GUIDELINE

- PREPARE (**P**lanning **R**esearch and **E**xperimental **P**rocedures on **A**nimals: **R**ecommendations for **E**xcellence)
- **動物實驗開始前應檢視的15個重點項目**

1. 系統性文獻檢索	6. 動物設施評估	11. 檢疫及健康監測
2. 法規	7. 教育訓練	12. 飼養管理
3. 倫理- 3R之落實模式	8. 環安, 生安及職安	13. 實驗流程
4. 實驗設計及統計	9. 測試物質	14. 人道終點與再應用
5. 實驗專案管理	10. 實驗動物	15. 解剖及採樣

The PREPARE Guidelines Checklist

Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

Adrian J. Smith¹, R. Eddie Clutton², Elliot Lilley³, Kristine E. Aa. Hanssen⁴ and Trend Brattøld⁵

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⁴Section of Experimental Biomedicine, Department of Production Animal Clinical Sciences, Faculty of Veterinary Medicine, Norwegian University of Life Sciences, P.O. Box 8148 Dep., 0033 Oslo, Norway; ⁵Division for Research Management and External Funding, Western Norway University of Applied Sciences, 5020 Bergen, Norway.

PREPARE¹ consists of planning guidelines which are complementary to reporting guidelines such as ARRIVE². PREPARE covers the three broad areas which determine the quality of the preparation for animal studies:

1. Formulation of the study
2. Dialogue between scientists and the animal facility
3. Quality control of the components in the study

The topics will not always be addressed in the order in which they are presented here, and some topics overlap. The PREPARE checklist can be adapted to meet special needs, such as field studies. PREPARE includes guidance on the management of animal facilities, since in-house experiments are dependent upon their quality. The full version of the guidelines is available on the Norecopa website, with links to global resources, at <https://narecopa.no/PREPARE>.

The PREPARE guidelines are a dynamic set which will evolve as more species- and situation-specific guidelines are produced, and as best practice within Laboratory Animal Science progresses.

Topic	Recommendation
(A) Formulation of the study	
1. Literature searches	<input type="checkbox"/> Form a clear hypothesis, with primary and secondary outcomes. <input type="checkbox"/> Consider the use of systematic reviews. <input type="checkbox"/> Decide upon databases and information specialists to be consulted, and construct search terms. <input type="checkbox"/> Assess the relevance of the species to be used, its biology and suitability to answer the experimental questions with the least suffering, and its welfare needs. <input type="checkbox"/> Assess the reproducibility and translatability of the project.
2. Legal issues	<input type="checkbox"/> Consider how the research is affected by relevant legislation for animal research and other areas, e.g. animal transport, occupational health and safety. <input type="checkbox"/> Locate relevant guidance documents (e.g. EU guidance on project evaluation).
3. Ethical issues, Harm-Benefit Assessment and humane endpoints	<input type="checkbox"/> Construct a lay summary. <input type="checkbox"/> In dialogue with ethics committees, consider whether statements about this type of research have already been produced. <input type="checkbox"/> Address the 3Rs (Replacement, Reduction, Refinement) and the 3Ss (Good Science, Good Sense, Good Sensibilities). <input type="checkbox"/> Consider pre-registration and the publication of negative results. <input type="checkbox"/> Perform a Harm-Benefit Assessment and justify any likely animal harm. <input type="checkbox"/> Discuss the learning objectives, if the animal use is for educational or training purposes. <input type="checkbox"/> Allocate a severity classification to the project. <input type="checkbox"/> Define objective, easily measurable and unequivocal humane endpoints. <input type="checkbox"/> Discuss the justification, if any, for death as an end-point.
4. Experimental design and statistical analysis	<input type="checkbox"/> Consider pilot studies, statistical power and significance levels. <input type="checkbox"/> Define the experimental unit and decide upon animal numbers. <input type="checkbox"/> Choose methods of randomisation, prevent observer bias, and decide upon inclusion and exclusion criteria.



The ARRIVE Guidelines Checklist

Animal Research: Reporting In Vivo Experiments

Carol Kilkenny¹, William J. Browne², Innes C. Cuthill³, Michael Emerson⁴ and Douglas G. Altman⁵

¹The National Centre for the Replacement, Refinement and Reduction of Animals in Research, London, UK; ²School of Veterinary Science, University of Bristol, Bristol, UK; ³School of Biological Sciences, University of Bristol, Bristol, UK; ⁴National Heart and Lung Institute, Imperial College London, UK; ⁵Centre for Statistics in Medicine, University of Oxford, Oxford, UK.

	ITEM	RECOMMENDATION	Section/ Paragraph
Title	1	Provide an accurate and concise description of the content of the article as possible.	
Abstract	2	Provide an accurate summary of the background, research objectives, including details of the species or strain of animal used, key methods, principal findings and conclusions of the study.	
INTRODUCTION			
Background	3	a. Include sufficient scientific background (including relevant references to previous work) to understand the motivation and context for the study, and explain the experimental approach and rationale. b. Explain how and why the animal species and model being used can address the scientific objectives and, where appropriate, the study's relevance to human biology.	
Objectives	4	Clearly describe the primary and any secondary objectives of the study, or specific hypotheses being tested.	
METHODS			
Ethical statement	5	Indicate the nature of the ethical review permissions, relevant licences (e.g. Animal [Scientific Procedures] Act 1986), and national or institutional guidelines for the care and use of animals, that cover the research.	
Study design	6	For each experiment, give brief details of the study design including: <ol style="list-style-type: none"> a. The number of experimental and control groups. b. Any steps taken to minimise the effects of subjective bias when allocating animals to treatment (e.g. randomisation procedure) and when assessing results (e.g. if done, describe who was blinded and when). c. The experimental unit (e.g. a single animal, group or cage of animals). A time-line diagram or flow chart can be useful to illustrate how complex study designs were carried out. 	
Experimental procedures	7	For each experiment and each experimental group, including controls, provide precise details of all procedures carried out. For example: <ol style="list-style-type: none"> a. How (e.g. drug formulation and dose, site and route of administration, anaesthesia and analgesia used [including monitoring], surgical procedure, method of euthanasia). Provide details of any specialist equipment used, including supplier(s). b. When (e.g. time of day). c. Where (e.g. home cage, laboratory, water maze). d. Why (e.g. rationale for choice of specific anaesthetic, route of administration, drug dose used). 	
Experimental animals	8	a. Provide details of the animals used, including species, strain, sex, developmental stage (e.g. mean or median age plus age range) and weight (e.g. mean or median weight plus weight range). b. Provide further relevant information such as the source of animals, international strain nomenclature, genetic modification status (e.g. knock-out or transgenic), genotype, health/immune status, drug or test naïve, previous procedures, etc.	

The ARRIVE guidelines. Originally published in *PLoS Biology*, June 2010⁷

國科會3R說明文件優化方案

- 以**提高動物實驗再現性為目標**，比照美國NIH作法，以「**動物實驗規劃與評估查檢表**」協助研究人員確認ARRIVE及PREPARE指南之內容已於計畫書詳細說明，以提高計畫書撰寫品質。
- **修訂NSCB04 3R說明文件**，導入ARRIVE及PREPARE指南之要件，同時鼓勵運用損害利益評估 (Harm-Benefit Analysis) 進行動物實驗優化評估，綜合納入查檢表確認。
- **涉及動物實驗需檢附文件及審查流程：**
 - 計畫申請時檢附「**IACUC 審查同意書**」。IACUC 審查同意書若因計畫申請時尚未審查完畢，最遲應於計畫核定前補件完成。(同現行作法)
 - 計畫申請時檢附「**動物實驗規劃與3R評估查檢表**」。(取代現行3R說明表格)
 - 提醒審查委員確認查檢表內容是否有在計畫書內容清楚說明，並於**計畫評核時納入考量**。

動物實驗規劃流程



- 文獻回顧
- 替代方法
- 系統性文獻回顧

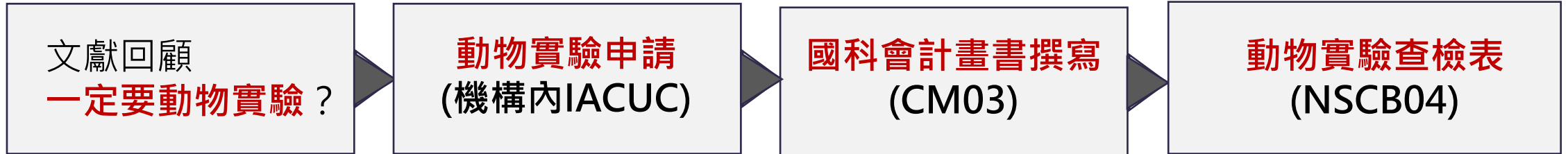
- 人員教育訓練
- 實驗動物選擇及來源
- 動物設施的運作
- 職安、環安及生安
- 3R之落實策略



- 實驗設計與分組
- 測試物質
- 樣本的選擇與排除
- 避免實驗偏誤 (盲法及逢機)
- 統計方法的選擇

- 動物實驗專案管理
- 量測指標的選擇
- 解剖與採樣
- 人道試驗終點
- 實驗數據的呈現

國科會計畫送件準備



- 依明確的實驗目的檢索
- 檢索範圍應包括替代方案的考量、正反面實驗結果
- 解釋所選用的動物模式如何能夠滿足研究目的

- 清楚說明動物實驗設計、樣本及分組、統計方法
- 清楚說明實驗動物來源、品質及照護環境
- 清楚說明實驗流程及量測分析方法

※ 本 (NSCB04) 表格：請將下列 2 項文件依序合併後之 PDF 檔案上傳至系統。

一、「動物實驗規劃與 3R 評估」查檢表

- (一) 凡執行研究計畫涉及動物實驗者，請考量「取代 (Replace)」、「減量 (Reduce)」及「優化 (Refine)」之實驗動物福祉 3R 精神，依所執行動物實驗之「傷害-利益評估 (Harm & Benefit Analysis, HBA)」，減少對動物的傷害，並增加實驗的效益與可行性 (查檢表第一項)。
- (二) 上述傷害-利益評估主要查檢項目如下：
1. 減少實驗對於動物的傷害：評估所提研究計畫是否有其他非動物替代方案、針對可能對動物造成傷害的實驗步驟進行優化、建立疼痛評估與人道終點，精進實驗團隊的操作技術。
 2. 增加實驗的效益與可行性：避免進行已發表的重覆 (me-too) 實驗、善用種原庫資源，避免重覆開發基因改造鼠、完善動物飼育品質及實驗環境、優化實驗品質，提高實驗再現性等。
- (三) 鼓勵遵循 PREPARE guidelines (動物實驗開始前應檢視之重點項目)、ARRIVE guidelines (動物實驗發表時應檢視之重點項目)，優化動物實驗品質。上述指南可協助團隊在動物實驗執行前完備相關實驗設計規劃，並以正確的報導方式，公平的呈現動物實驗結果，以提高實驗再現性，增加動物實驗可信度 (查檢表第二項)。

研究團隊應在動物實驗3R精神下，完成機構內動物實驗申請程序，並利用傷害-利益評估進行優化自評。

傷害-利益評估主要目的是要達成「減少傷害」及「增加可信度」。

ARRIVE指南及PREPARE指南的目的都在輔助「增加動物實驗可信度」，以期達到預期效益。

二、實驗動物照護及使用委員會 (或小組) 審查同意書

NSCB04 表格

「動物實驗規劃與 3R 評估」查檢表

一、動物實驗 3R 聲明 (3R+HBA):

勾選	說明
<input type="checkbox"/>	本計畫已依農業部動物實驗管理相關規定，提送機構內動物實驗申請，並已考量「取代 (Replace)」、「減量 (Reduce)」、及「優化 (Refine)」之實驗動物福祉3R精神，於該申請表中評估確認無其它適合之替代方法、已採用最少動物隻數與完成傷害-利益評估，以求動物福利最佳化。

確認已提送機構 IACUC 申請，國科會計畫核定前需先取得 IACUC 同意文件

二、請確認 CM03 計畫書內容及研究方法已評估以下項目 (PREPARE、ARRIVE)，並依實際 CM03 撰寫內容勾選符合之項目，若有不適用或未勾選之項目，請補充說明：

1. 本計畫在動物實驗設計時，已納入以下評估項目，以提升實驗可信度，減少重覆實驗：

<input type="checkbox"/>	已說明動物實驗的實驗組/對照組與實驗單元 (Experimental unit)
<input type="checkbox"/>	已考慮性別對實驗的影響並估算動物之性別比例，採用單一性別應充份說明。
<input type="checkbox"/>	已考量樣本數 (Sample size) 之可驗證性及動物減量原則，說明樣本數的決定方法，並評估實驗動物總使用量。
<input type="checkbox"/>	已考量樣本 (或動物) 被納入及排除的原則。
<input type="checkbox"/>	已考量採用逢機分組策略 (Randomization) 或採用盲法 (Blinding)，以減少系統偏誤。
<input type="checkbox"/>	已考量實驗結果的量測指標 (例如生物標記、行為分析項目、細胞死亡數等)，確認可藉由量測指標項目回答實驗假說。
<input type="checkbox"/>	已評估及說明使用之統計方法 (Statistical methods)、統計軟體或工具。

確認7項動物實驗設計要件已於國科會CM03計畫書中說明

確認5項動物實驗管理要件已於國科會CM03計畫書中說明

2. 本計畫在動物實驗優化上，已納入以下評估項目：

<input type="checkbox"/>	已評估使用動物的細節，包括物種、品系、次品系、性別、年齡或體重、特殊基因型或表現型及採用正確實驗動物命名原則。
<input type="checkbox"/>	動物來源，已優先考量自 AAALAC 認可之供應單位取得實驗動物。
<input type="checkbox"/>	已評估動物實驗流程之內容及項目完整，可回答實驗假說，同時維持動物福祉 (含動物實驗項目、測試物質、疼痛評估及人道試驗終點之設定、解剖及檢體收集規劃等)。
<input type="checkbox"/>	已評估動物設施之管理品質符合動物實驗執行之品質要求 (設施維運、健康監測及農業部查核評比結果等)。
<input type="checkbox"/>	已評估執行團隊之技術與執行能力可避免動物因操作不當而影響動物福祉。

3. 若有不適用或未勾選之項目，請補充說明：

計畫主持人簽名/簽署日期：

檢視CM03計畫書內容，涉及動物實驗說明部份：

本計畫擬利用32隻小鼠 (C57BL/6JNarl) 進行中風藥物功效之初步確認，將利用MCA occlusion (MCAo) 建立中風模式後投藥，並以行為分析 (步態分析、跑輪、認知能力) 做為藥效判斷依據 (Ref)。若動物之腦血流於MCAo術後低於60% (以laser Doppler flowmetry判讀) 則納入本計畫，並以電腦逢機編號分為4組 (高、中、低濃度測試組及陰性對照組)，起始樣本數每組6-8隻 (公母各半)。若動物於行為測試前死亡，則予以排除。行為測試時因實驗室人力有限無法進行blinding，但行為分析採用錄影及電腦系統分析運算，可以減少偏誤。

1. 本計畫在動物實驗設計時，已納入以下評估項目，以提升實驗可信度，減少重覆實驗：

<input checked="" type="checkbox"/>	已說明動物實驗的實驗組 / 對照組與實驗單元 (Experimental unit)
<input checked="" type="checkbox"/>	已考慮性別對實驗的影響並估算動物之性別比例，採用單一性別應充份說明。
<input type="checkbox"/>	已考量樣本數 (Sample size) 之可驗證性及動物減量原則， <u>說明樣本數的決定方法</u> ，並評估實驗動物總使用量。
<input checked="" type="checkbox"/>	已考量樣本 (或動物) 被納入及排除的原則。
<input checked="" type="checkbox"/>	已考量採用逢機分組策略 (Randomization) 或採用盲法 (Blinding) ，以減少系統偏誤。
<input checked="" type="checkbox"/>	已考量實驗結果的量測指標 (例如生物標記、行為分析項目、細胞死亡數等) ，確認可藉由量測指標項目回答實驗假說。
<input type="checkbox"/>	已評估及說明使用之統計方法 (Statistical methods) 、統計軟體或工具。

檢視CM03計畫書內容，涉及動物實驗說明部份：

本計畫使用之實驗小鼠 (C57BL/6JNarl, 8wk, 16M16F) 擬由國家實驗動物中心取得，後續動物代養及照顧則在本校實驗動物房進行，本校實驗動物設施每季進行健康檢測，有專業獸醫師及維運團隊負責動物照護，前次農業部查核評比結果為良，符合動物實驗執行品質。本計畫所列之主題及實驗流程，在本實驗室已執行多年 (Ref)，所需之MCAo技術、腹腔注射技術等，操作人員均通過機構內部技術訓練，實驗流程可能衍生之疼痛觀察及人道試驗終點之設定，已詳實說明於IACUC申請書中，由機構核定執行。

2. 本計畫在動物實驗優化上，已納入以下評估項目：

<input checked="" type="checkbox"/>	已評估使用動物的細節，包括物種、品系、次品系、性別、年齡或體重、特殊基因型或表現型及採用正確實驗動物命名原則。
<input checked="" type="checkbox"/>	動物來源，已優先考量自AAALAC認可之供應單位取得實驗動物。
<input checked="" type="checkbox"/>	已評估動物實驗流程之內容及項目完整，可回答實驗假說，同時維持動物福祉 (含動物實驗項目、測試物質、疼痛評估及人道試驗終點之設定、解剖及檢體收集規劃等)。
<input checked="" type="checkbox"/>	已評估動物設施之管理品質符合動物實驗執行之品質要求 (設施維運、健康監測及農業部查核評比結果等)。
<input checked="" type="checkbox"/>	已評估執行團隊之技術與執行能力可避免動物因操作不當而影響動物福祉。

3. 若有不適用或未勾選之項目，請補充說明

範例:

1. 採用單一性別說明: 本計畫進行乳癌藥物測試，故僅使用母鼠進行研究。
2. 統計分析說明: 本計畫所列動物為實驗所需細胞來源，在採樣前未分組，採樣後即犧牲。

現行版本自113年起，不再適用國科會專題計畫申請

現行國科會NSCB04

NSCB04 表格

※ 本(NSCB04)表格上傳時，請將下列第一項及第二項兩份文件先合併為一個 PDF 檔案，再將該合併檔上傳。

一、 動物實驗同意文件。

二、 動物實驗倫理 3R 說明：

(一) 凡執行研究計畫涉及動物實驗者，請考量「取代(Replace)」、「減量(Reduce)」、及實驗「精緻化(Refine)」之實驗動物福祉 3R 精神，並說明如何在動物實驗倫理 3R 下做最佳化實驗設計。

(二) 上述實驗動物福祉查檢主要評估項目如下：

1. 動物實驗替代方案評估：所提研究計畫是否考量有其他替代方案、考量減量、技術訓練、實驗環境改善及實驗流程改善等符合動物福祉。
2. 避免重覆開發生產：所提研究計畫若涉及基因改造實驗動物，是否已在國內及國際種原庫搜尋。如已在但因不易取得需重新開發者，開發完成之基因改造實驗動物應如何妥善保存或分享其它研究使用的規劃。
3. 研究成果進一步形...

不適用

現行農業部動物實驗申請書 附錄二

附錄二(若有申請補助計畫需檢附 3R 說明時，請填寫本說明。)

動物實驗人道管理替代、減量及精緻化(3R)說明 (範例)

本研究計畫涉及動物實驗，已考量「替代 (Replace)」、「減量 (Reduce)」及「精緻化 (Refine)」之 3R 精神，將實驗設計最佳化，並說明如下：

一、3R 原則：

- 本實驗計畫已經本人及機構內「實驗動物照護及使用委員會 (或小組)」詳實審查，無其他替代方案。
- 本實驗計畫已經本人及機構內「實驗動物照護及使用委員會 (或小組)」詳實審查，已使用最少數量動物。
- 本實驗計畫已經本人及機構內「實驗動物照護及使用委員會 (或小組)」詳實審查，已做到精緻化，或動物福利最佳化。包含：
 - 已考慮並要求執行動物疼痛評估
 - 已考慮並要求執行適當減輕動物痛苦方式 (如： 麻醉劑、 止痛劑、 設定人道安樂死時機)
 - 其他(請說明)：_____

二、教育訓練：

為促進 3R 精神之落實，本研究實際負責進行動物實驗之教育與訓練經歷：

- 實驗動物人道管理(例如：動物福利、動物照護)
- 實驗專業技術訓練
- 其他(請說明)：_____

三、使用動物來源：

為確保本研究計畫實驗動物來源為：

- AAALAC 認證繁殖機構
- 其他繁殖機構 (請說明名稱及地址等)
- 其他 (請說明) _____

不適用

小結

- 國科會優化動物實驗3R評估NSCB04表格，自113年起，若專題研究計畫涉及動物實驗，將採用新的NSCB04 動物實驗規劃與3R評估查檢表
- 配合新的查檢表，請研究人員於計畫書CM03之內容，詳細說明：
 - 動物實驗設計、樣本及分組、統計方法
 - 實驗動物來源、動物房品質及照護環境
 - 實驗流程及量測分析方法、技術能力



國科會計畫涉及動物實驗之3R文件調整說明

如何做好動物實驗規劃

國家實驗動物中心 秦咸靜主任

NAR Labs
國家實驗研究院



第二部份

動物實驗規劃 (I) – 樣本與統計

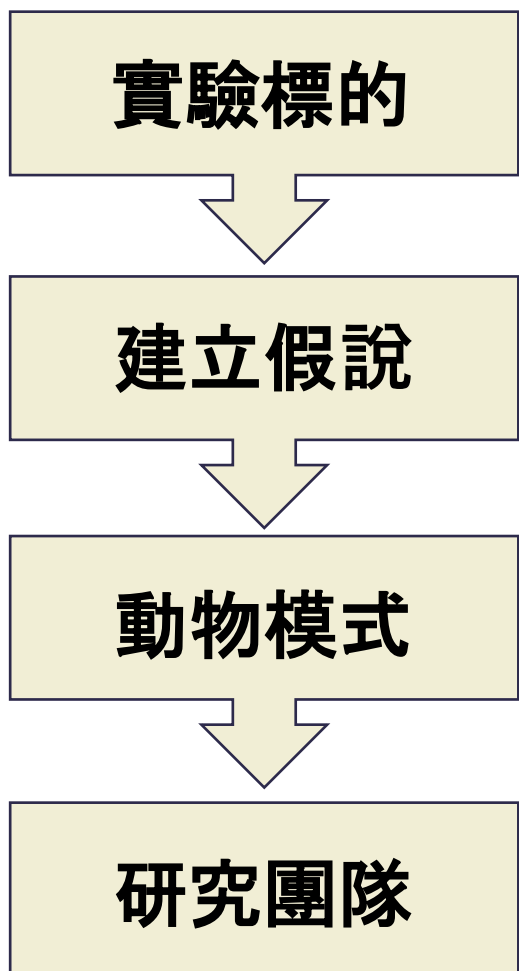
國家實驗動物中心 秦咸靜主任

NAR Labs
國家實驗研究院

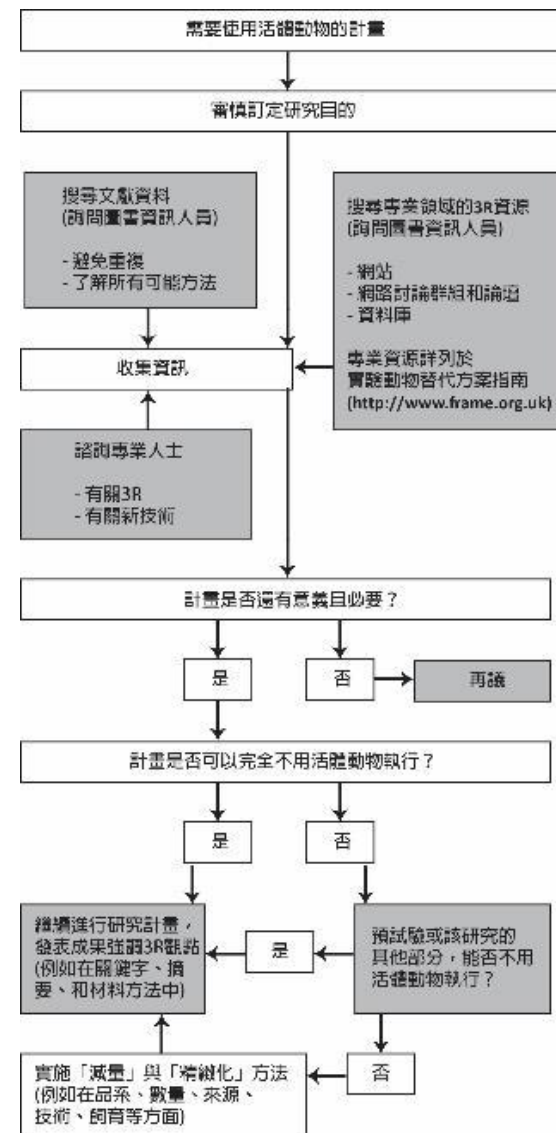
課程大綱

1. 國科會計畫涉及動物實驗之3R文件調整說明
2. 動物實驗規劃 (I) 實驗樣本與統計方法
3. 動物實驗規劃 (II) 實驗流程及結果分析
4. 動物實驗規劃 (III) 傷害利益評估

實驗規劃- STEP1 確認實驗主軸

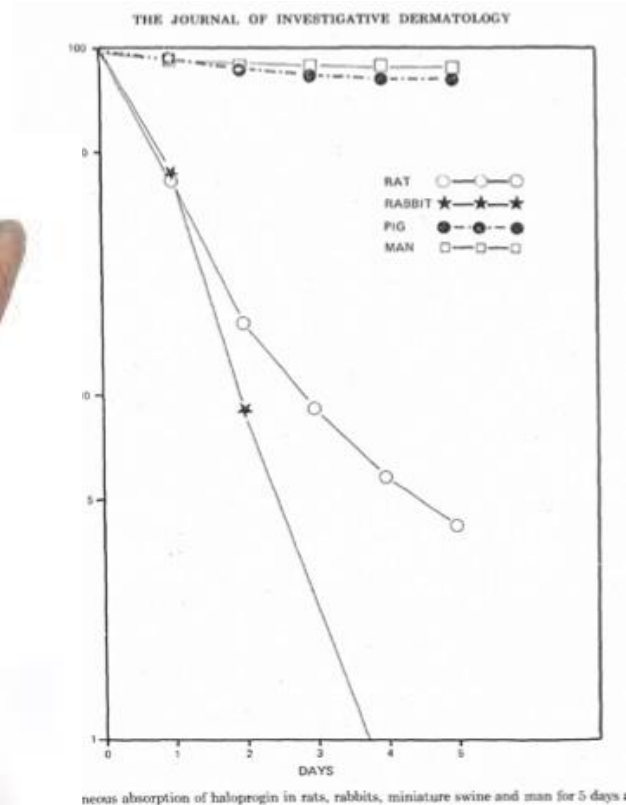


- 動物實驗規劃
 - 一定要使用動物嗎?
 - 動物模式能回答問題嗎?
 - 選擇正確的物種/ 品系
 - 動物如何取得/ 運輸
 - 動物如何適應及飼養
 - 良好的實驗設計
 - 適當的統計方法
 - 結果的呈現方式



WHO IS IN THE STUDY?

- **實驗動物：**
 - 物種、品系、次品系、年齡、性別、體重、繁殖狀態、健康狀態
 - 來源 (供應商/ 品系碼/ 供應地)
 - 所用實驗動物是否
 - 是否適合進行實驗所需之操作
 - 是否具代表性



(Bartek, LaBudde, Maibach, 1972)



Outbred 逢機品系 vs Inbred 近親品系

紐西蘭白兔



倉鼠



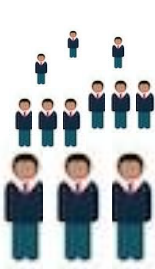
SD大鼠



ICR小鼠



outbred



Inbred 1



Inbred 2

B6小鼠



db/db小鼠

DBA小鼠

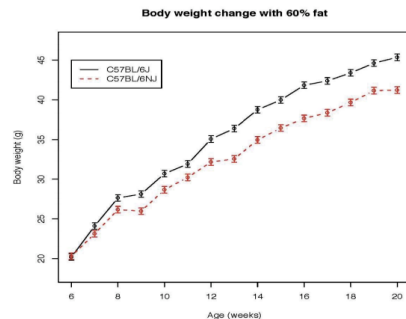
BALB/c小鼠

次品系: C57BL/6J vs C57BL/6N

<h2>C57BL/6J NarI</h2>	<h2>C57BL/6N Blw</h2>
 <p>NAR Labs 國家實驗研究院 國家實驗動物中心 National Laboratory Animal Center</p>	 <p>樂斯科生物科技</p>

Metabolic Differences (DIO)

B6J gains more weight than B6N on high fat diet (HFD)



- C57BL/6J ([000664](#)) vs C57BL/6N ([005304](#))
- Mice fed a 60 kcal% high fat diet
 - Beginning at 6 weeks of age

Nicholson, A et al. 2010. *Obesity* 18(10): 1902-1905. PMID: [20057372](#)

Neurological Differences

Vision - Avoid Common Research Mistakes

C57BL/6N (*Crb1^{rd8}*); consequences of retinal degeneration

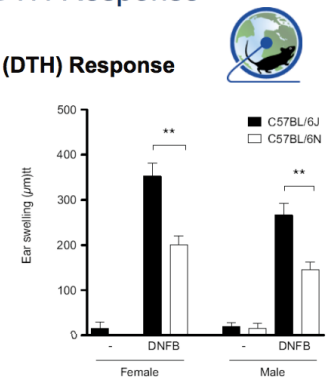
- Complication in interpretation of genes influencing diseases, phenotypes & developmental biology of sight & neurobiology
- Phenotypic analysis of genes implicated in cognitive function (behavioral tests that require visual cues)
- Research areas impacted:
 - Alzheimer's
 - Autism
 - Down Syndrome
 - Rhatt Syndrome
 - Neurodegenerative disorders

Immunological Differences

B6J mice show greater DTH Response

Delayed Type Hypersensitivity (DTH) Response

- Sensitization and challenge with dinitrofluorobenzene (DNFB)
- B6J males & females show greater inflammatory response



Genetic Analysis

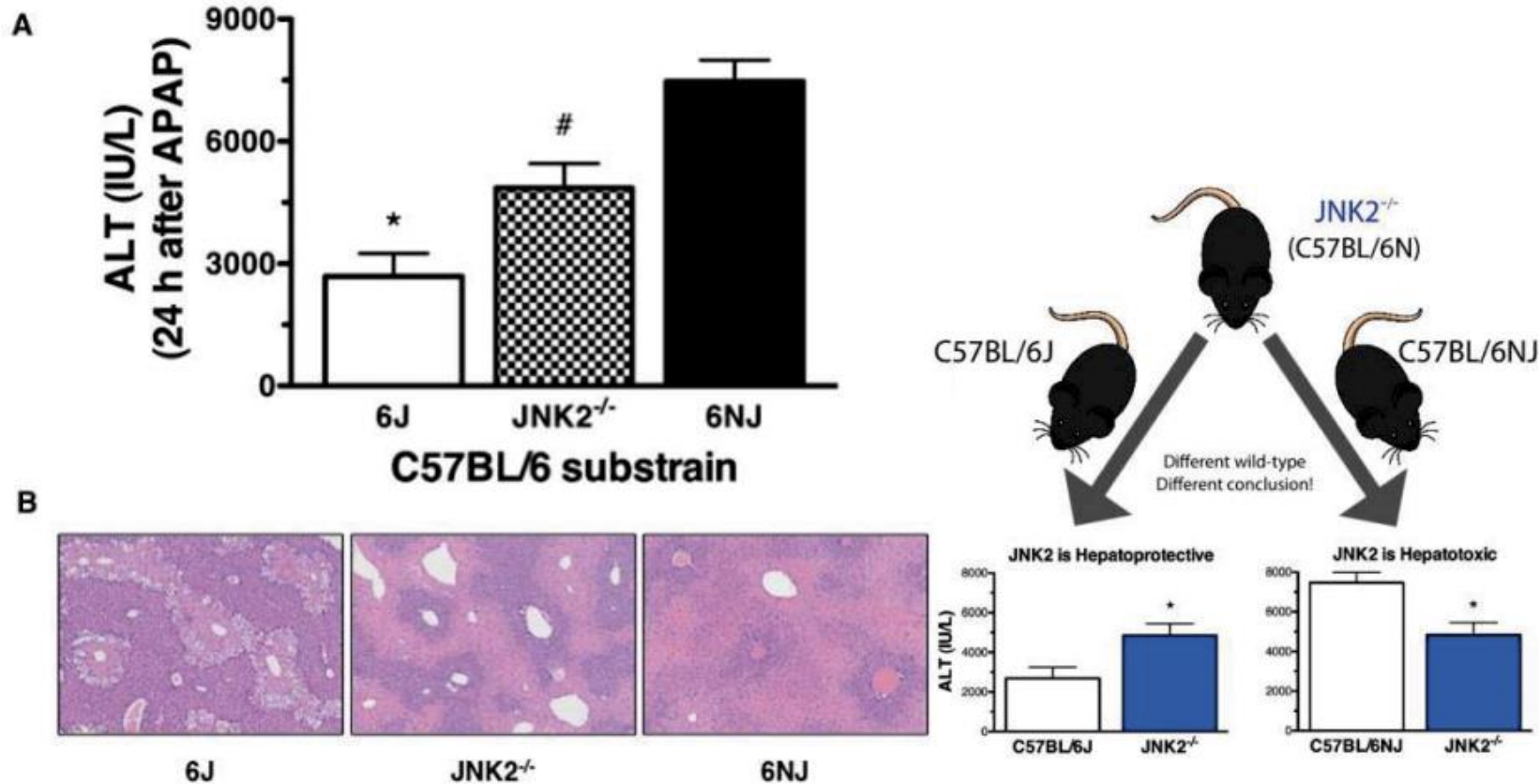
- Identified multiple SNPs & Indels
- Genomic structural variants

Simon, M. M., et al. (2013). *Genome Biology* 14(7): R82. PMID: [23902802](#)

Select The Proper C57BL/6 Control

Avoid Common Research Mistakes

Effects of *Mapk9* (*Jnk2*) on acetaminophen-induced liver injury (ALI)



疾病模式與合作夥伴



自發性突變

肥胖及糖尿病 (db/db)

高血壓鼠 (SHR rat)



誘發式疾病模式

Covid-19 倉鼠模式

腦血管栓塞中風模式

脂肪肝及肝硬化模式

腫瘤移植模式



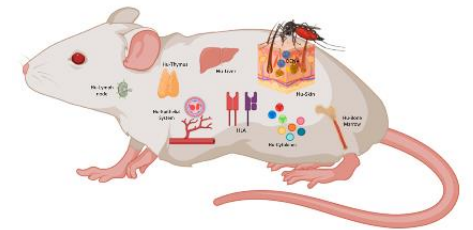
基因改造模式

自閉症/妥瑞症

多囊腎

罕見疾病

基因與疾病解碼



擬人化模式

源自病患腫瘤模式

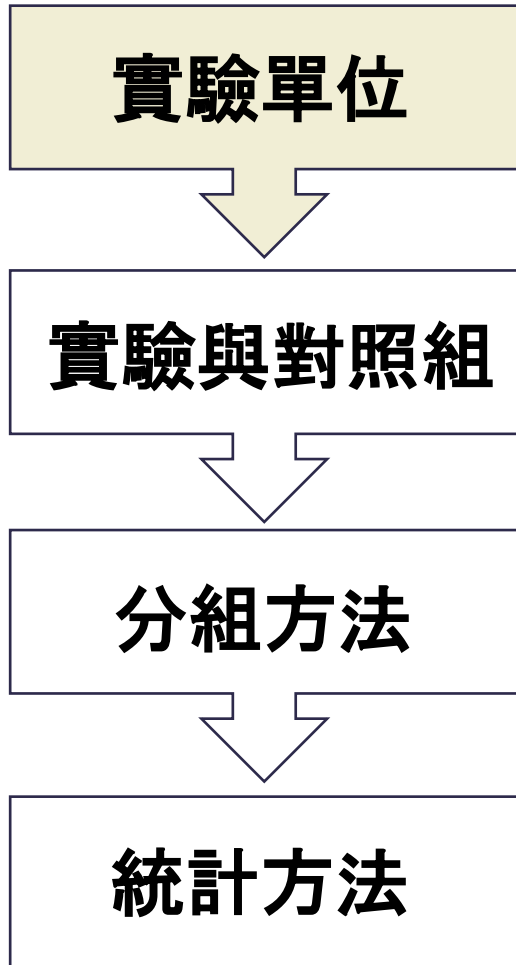
人類免疫鼠

人類腸道菌鼠

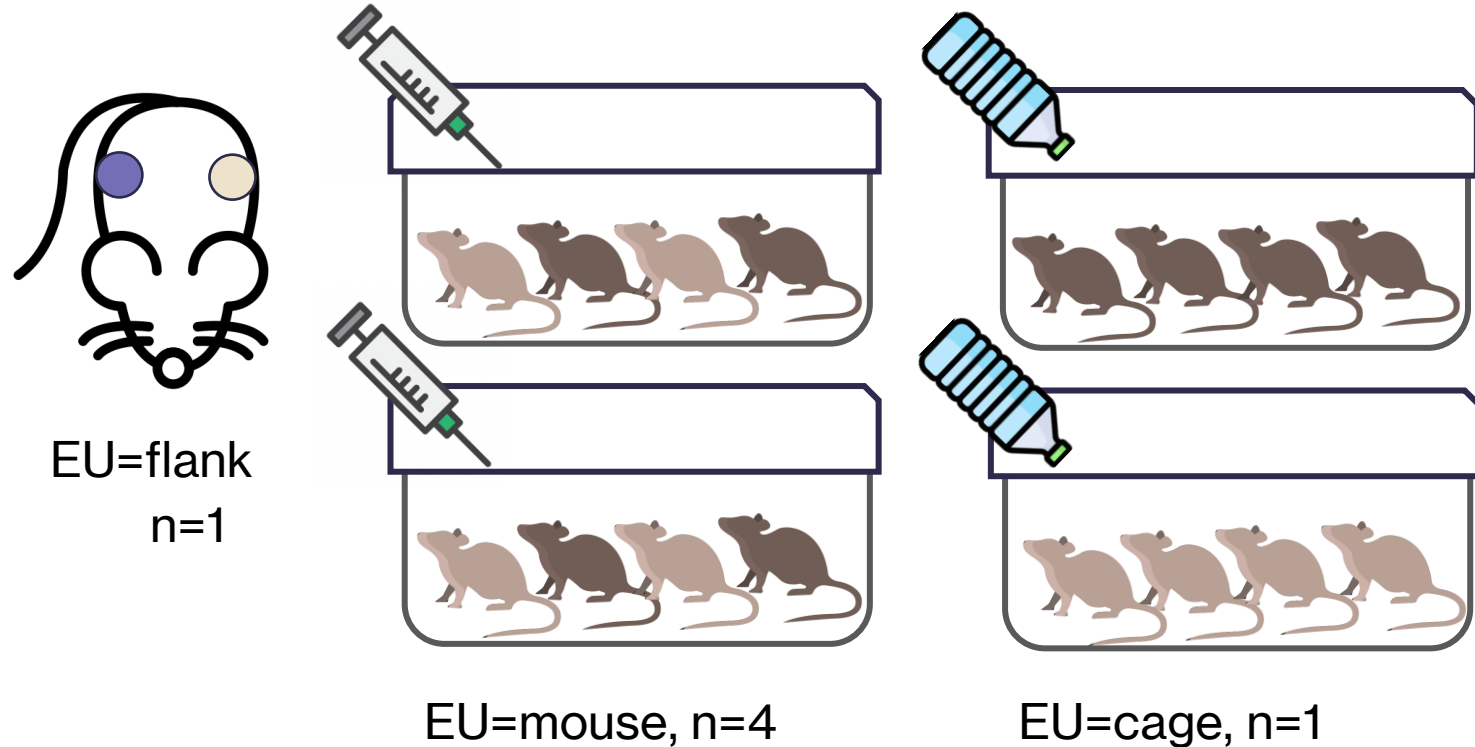


在計畫規劃階段應該確認誰是你的神隊友？訓練學生？委託專家？合作研究？

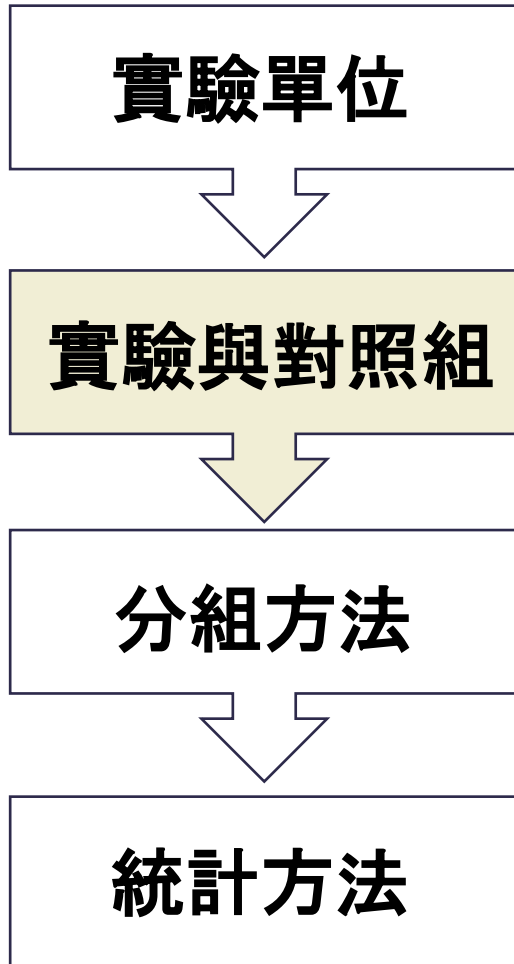
實驗規劃- STEP2 實驗樣本與統計方法



- 實驗單位 Experimental Unit (EU)
 - 統計分析的最小單位 (動物 / 籠 / 組)

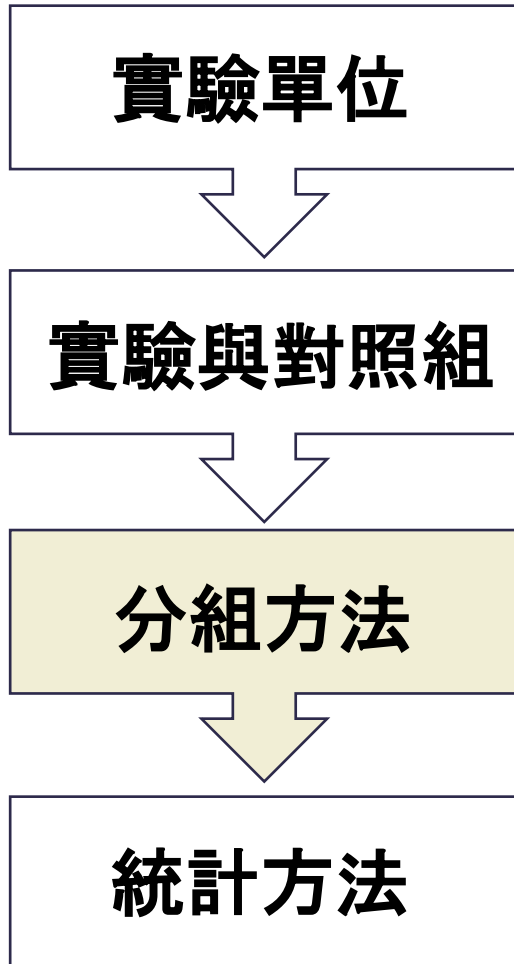


實驗規劃- STEP2 實驗樣本與統計方法



- **對照組：**
提供一個可靠的參考點，排除已知或可能存在的未知變數影響
 - 陽性對照組 (positive control):
 - 已知有變化 / 可做為比對標準，用來確保實驗正常運作
 - 陰性對照組 (negative control):
 - 已知無變化 / 可做為比對標準，用來確保未知變數不影響實驗
 - 空白對照組 (Mock) (Sham Control)
 - 模擬實驗組的過程，但實質未給予有效物質
 - 媒介物對照組 (Vehicle control)
 - 實驗使用特殊溶劑時，通常會做媒介物對照

實驗規劃- STEP2 實驗樣本與統計方法



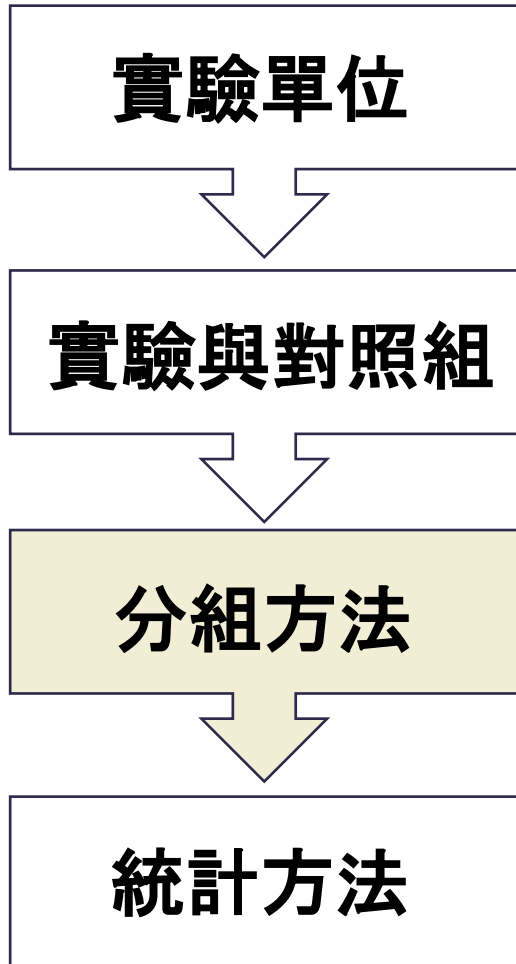
隨機分組與盲法

-減少系統性偏誤，增加實驗可信度



- **Randomization 隨機分組**
 - 說明配置實驗單元 (EU) 到實驗組與對照組的做法
 - 說明減少潛在或人為偏誤的影響
- **Blinding 盲法**
 - 分組、操作、量測、資料分析，任一階段
 - 尤其是病理分析、行為分析等需操作者判斷時
 - 說明如何避免個人判斷造成的偏誤

實驗規劃- STEP2 實驗樣本與統計方法

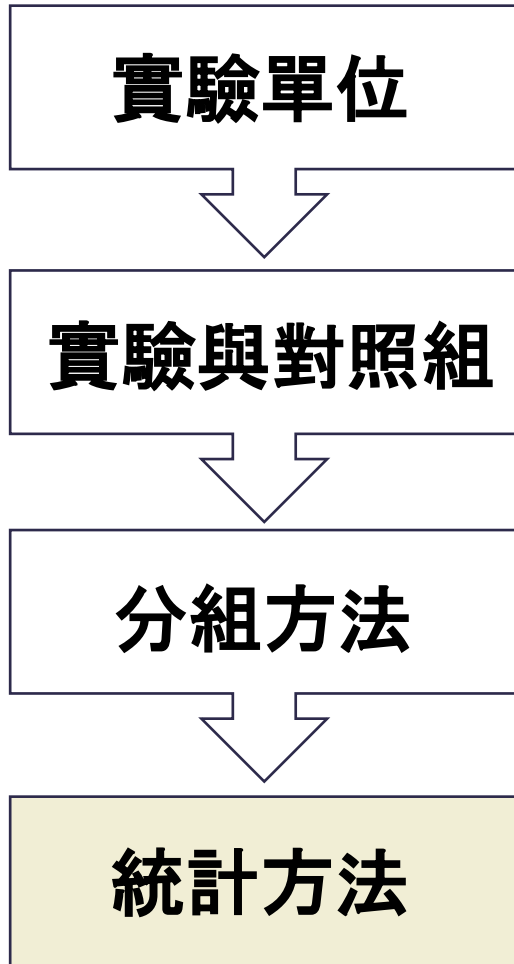


樣本的納入與排除

-預先決定最佳樣本範圍，避免依想要結果挑選樣本

- **Inclusion** 樣本納入的原則
 - 定義主要的目標族群及其具備的重要指標或特質
 - 例如：腫瘤體積超過 100mm^3
- **Exclusion** 樣本排除的原則
 - 定義會干擾實驗結果的狀況
 - 例如：動物瀕死、設備問題

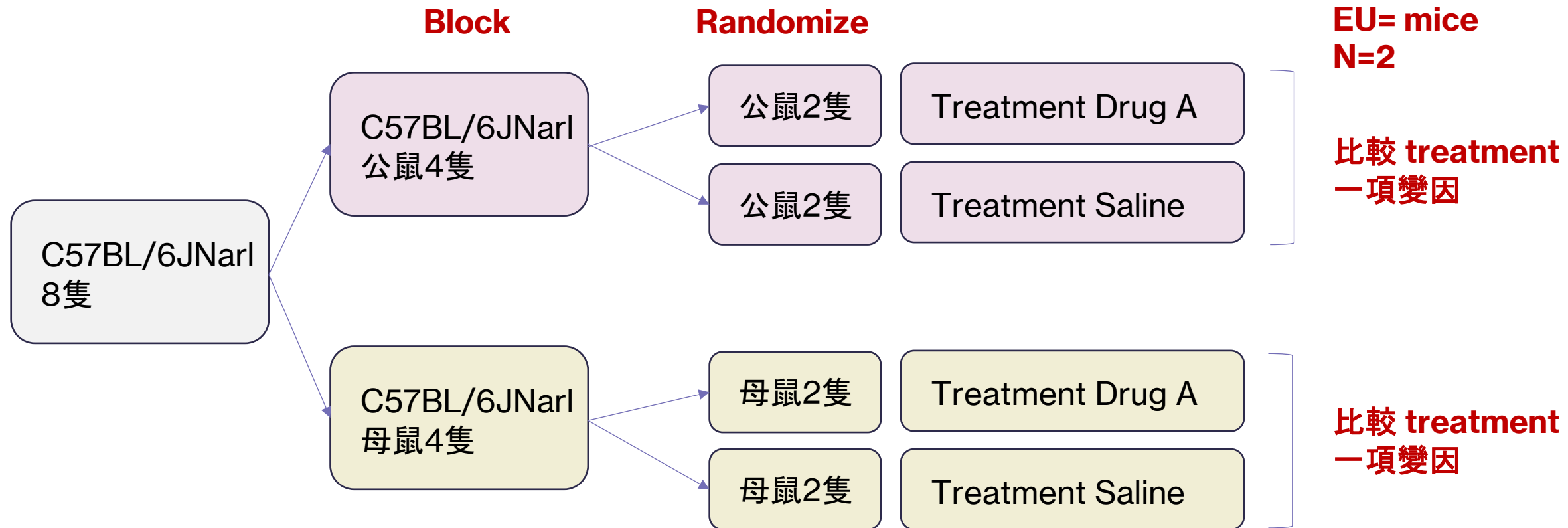
實驗規劃- STEP2 實驗樣本與統計方法



- 前導試驗- 依過往經驗，探索實驗方法及數據態樣
 - Pilot Study 預試驗
 - Exploratory Study 探索型研究
- 正式試驗- 驗證假說，需要達到顯著差異
 - Confirmatory Study
 - 運用前導試驗結果來進行樣本數預估
- 重要考量因子
 - Type of comparison
 - Primary variables: continuous/ categorical
 - Errors: type I/ type II





Randomized block design

目的：預先依照特定變因分類，減少已知變因對於實驗結果的影響



Factorial Experimental Design

- 快速篩選多個因子對實驗的影響 (2^k , k =factors)
- 可協助判斷那一個因子影響結果、判斷最適量、決定 sample size
- 一個資料多用途，資料最大化，減少動物使用 (share N)

	Control	Drug
Male	 a	 c
Female	 b	 d

EU= mice, N=2

比較- treatment及性別二項變因 (2^2)

因此

1. 共有4個組別，有4個mean (a, b, c, d)
2. Treatment差異： $(c+d)/2 - (a+b)/2$
3. 性別差異： $(a+c)/2 - (b+d)/2$
4. 性別對Treatment的影響： $((a-c) - (b-d))/2$

quantitative variable vs categorical variable

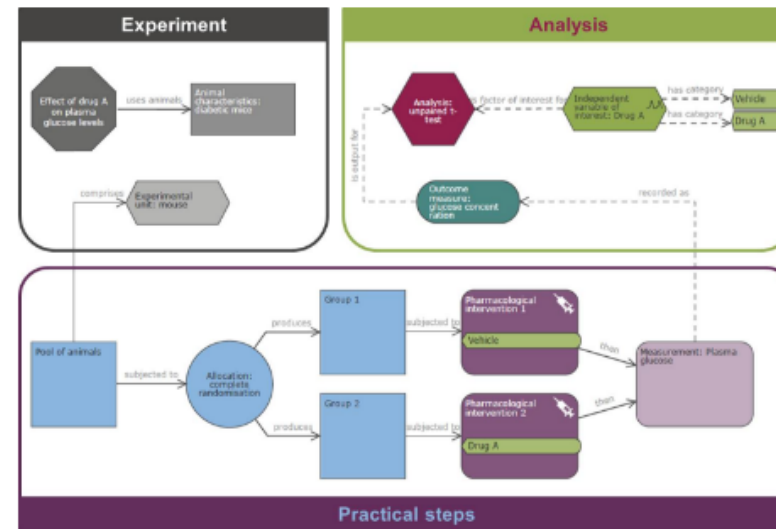
multi-way ANOVA vs ?

Welcome to the Experimental Design Assistant, a free resource from the [NC3Rs](#) to support researchers in the planning of animal experiments - ensuring robust study design and reliable and reproducible findings.

The EDA consists of a web application and a supporting website; benefits include:

- The ability to build a stepwise visual representation of your experiment
- Feedback and advice on your experimental plan
- Dedicated support for randomisation, blinding and sample size calculation
- Practical information to improve knowledge of experimental design
- Improved transparency of your experimental design, allowing you to share and discuss your plan with colleagues and collaborators

Check the [video tutorials](#) and the [user guide](#) for general information on the EDA process. Find out more about the [background](#) for this project.



Step 1

Login or Register

Start using the EDA application

Step 2

Plan your experiment as a diagram

Check the [examples](#) and the [user guide](#) for more information

Step 3

Critique your design

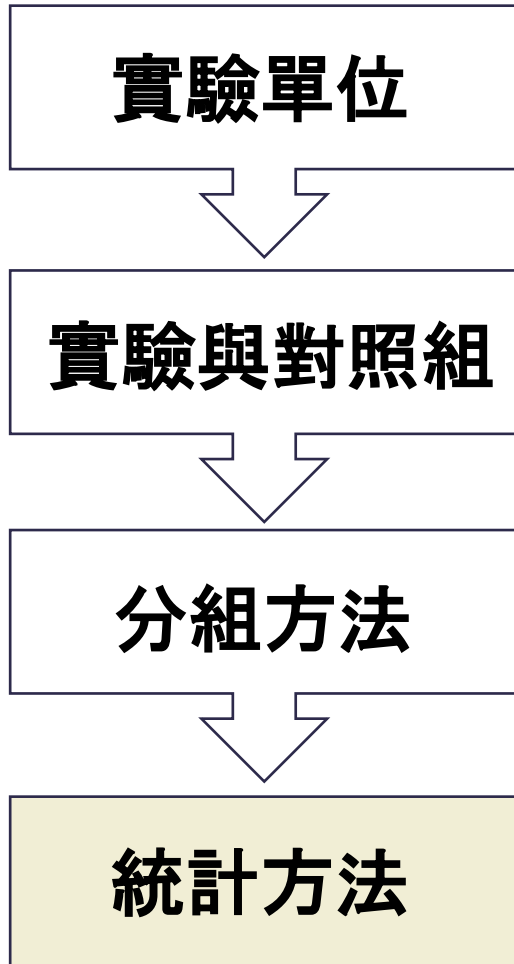
The critique function enables you to get feedback and advice on your diagram, find more information [here](#)

Step 4

Improve your design

Modify your experimental plan based on feedback from the system

實驗設計- STEP2 實驗樣本與統計方法



樣本數計算

- 樣本數 (N) 在整個實驗期間及報告撰寫時，都應該一致 (若要排除應符合排除原則，並說明)
- 運用前導試驗結果來進行樣本數預估 (用那一項指標為基準做樣本數預估?)
- 減量原則：在可得最大科學價值下，採用最少傷害的方法與最少的動物隻數
(數量太多浪費多餘的動物生命，數量太少浪費全部的動物生命)
- 不適合的做法
 - 採用文獻上未經驗證的樣本數
 - 不解釋或硬套公式

小結

- 完善的動物實驗設計是增加動物實驗可信度的重要基礎， 確認在規劃已考量下列因素：
 - 動物模式的選擇應有合理的理由及代表性
 - 如何減少人為的偏誤- 逢機分組、盲法、樣本的納入及排除
 - 選擇正確的實驗分組與統計方法
 - 運用預試驗或文獻資料， 計算合理的樣本數， 減少動物使用



國科會計畫涉及動物實驗之3R文件調整說明

如何做好動物實驗規劃

國家實驗動物中心 秦咸靜主任

NAR Labs
國家實驗研究院



第三部份

動物實驗規劃 (II) – 實驗流程與結果分析

國家實驗動物中心 秦咸靜主任

NAR Labs
國家實驗研究院

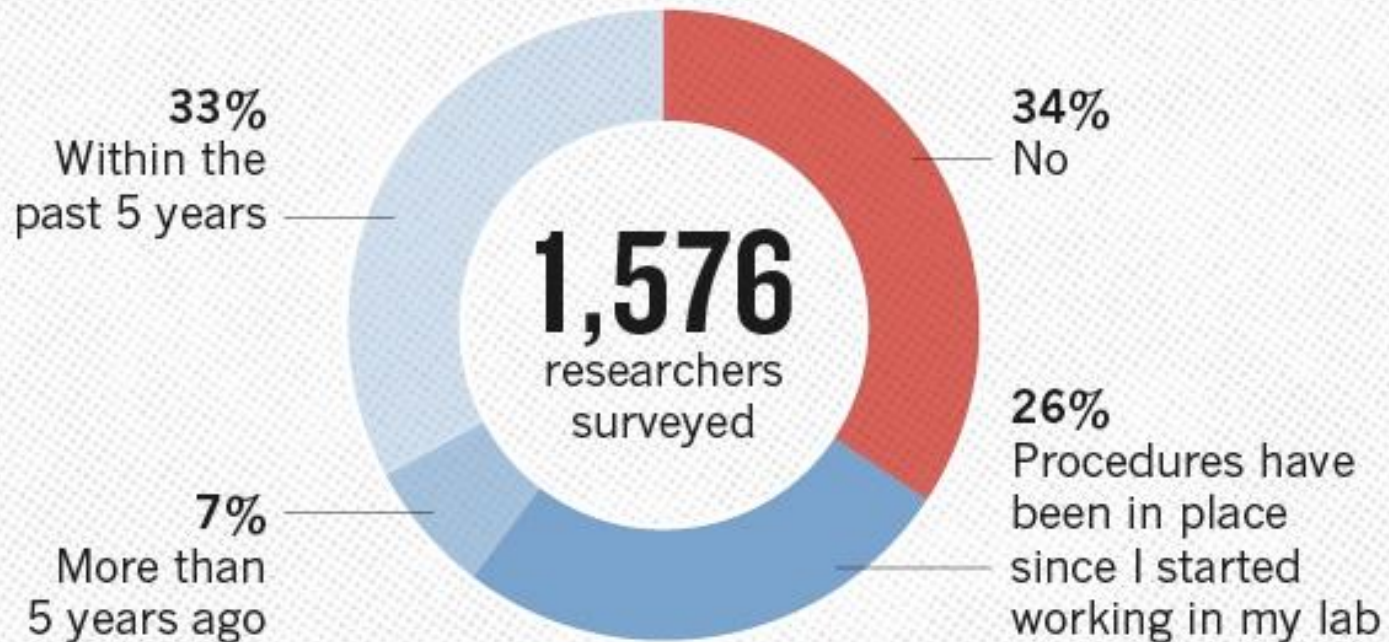
課程大綱

1. 國科會計畫涉及動物實驗之3R文件調整說明
2. 動物實驗規劃 (I) 實驗動物與統計方法
3. 動物實驗規劃 (II) 實驗流程及結果分析
4. 動物實驗規劃 (III) 傷害利益評估

實驗規劃- STEP3 實驗PROTOCOL

HAVE YOU ESTABLISHED PROCEDURES FOR REPRODUCIBILITY?

Among the most popular strategies was having different lab members redo experiments.



©nature

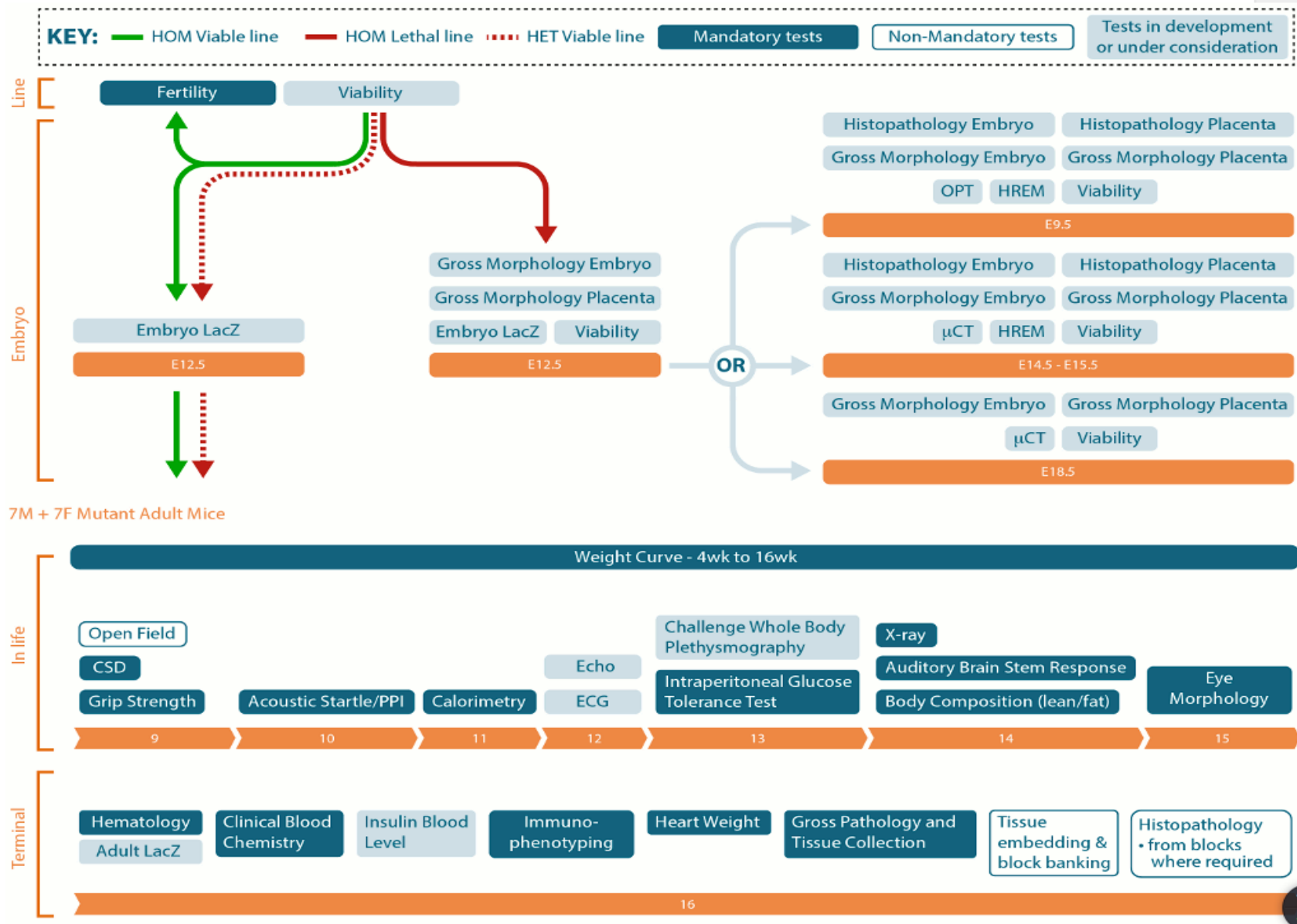


IMPC

International Mouse Phenotyping Consortium

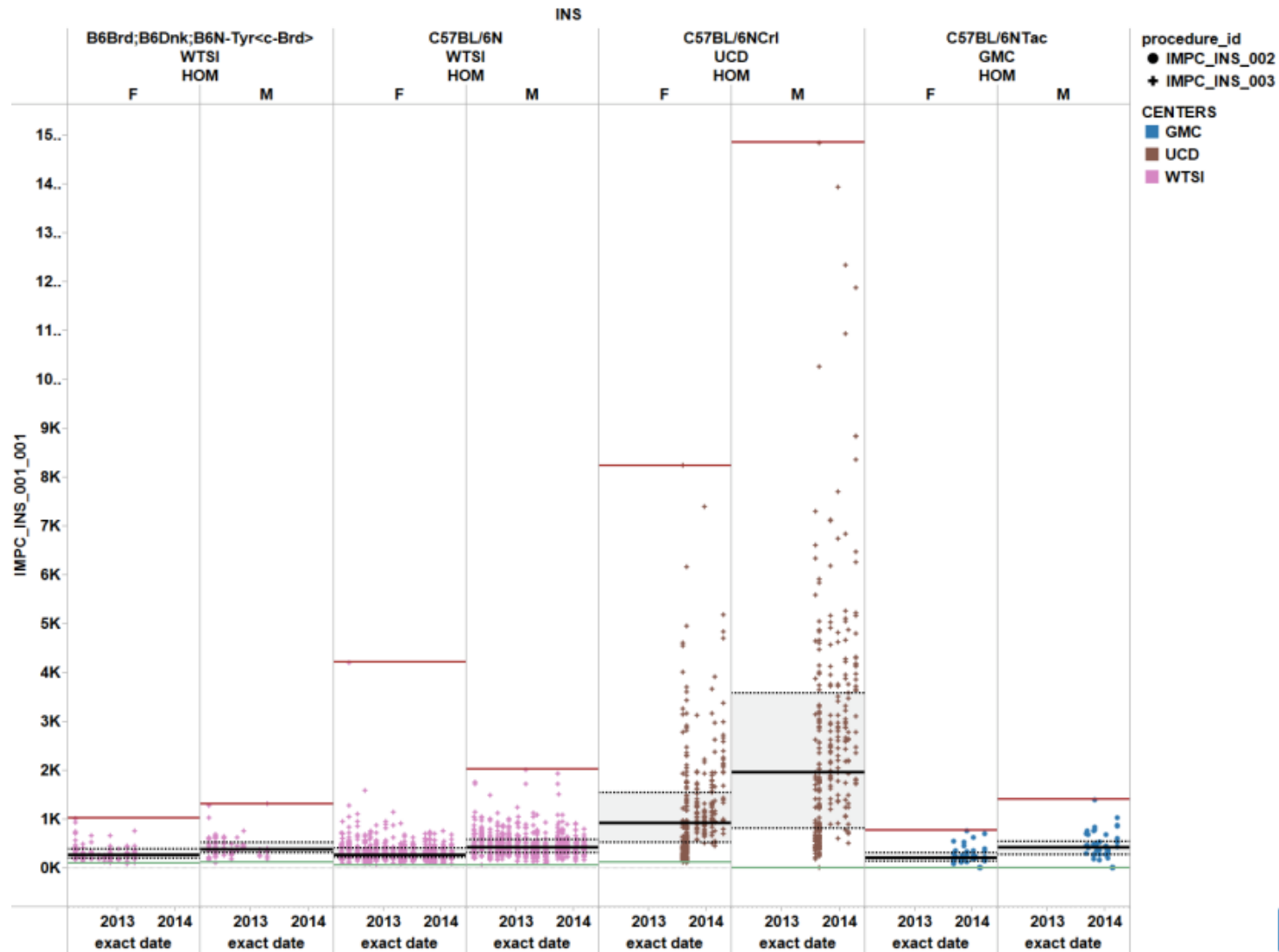


The Adult and Embryonic Phenotype Pipeline



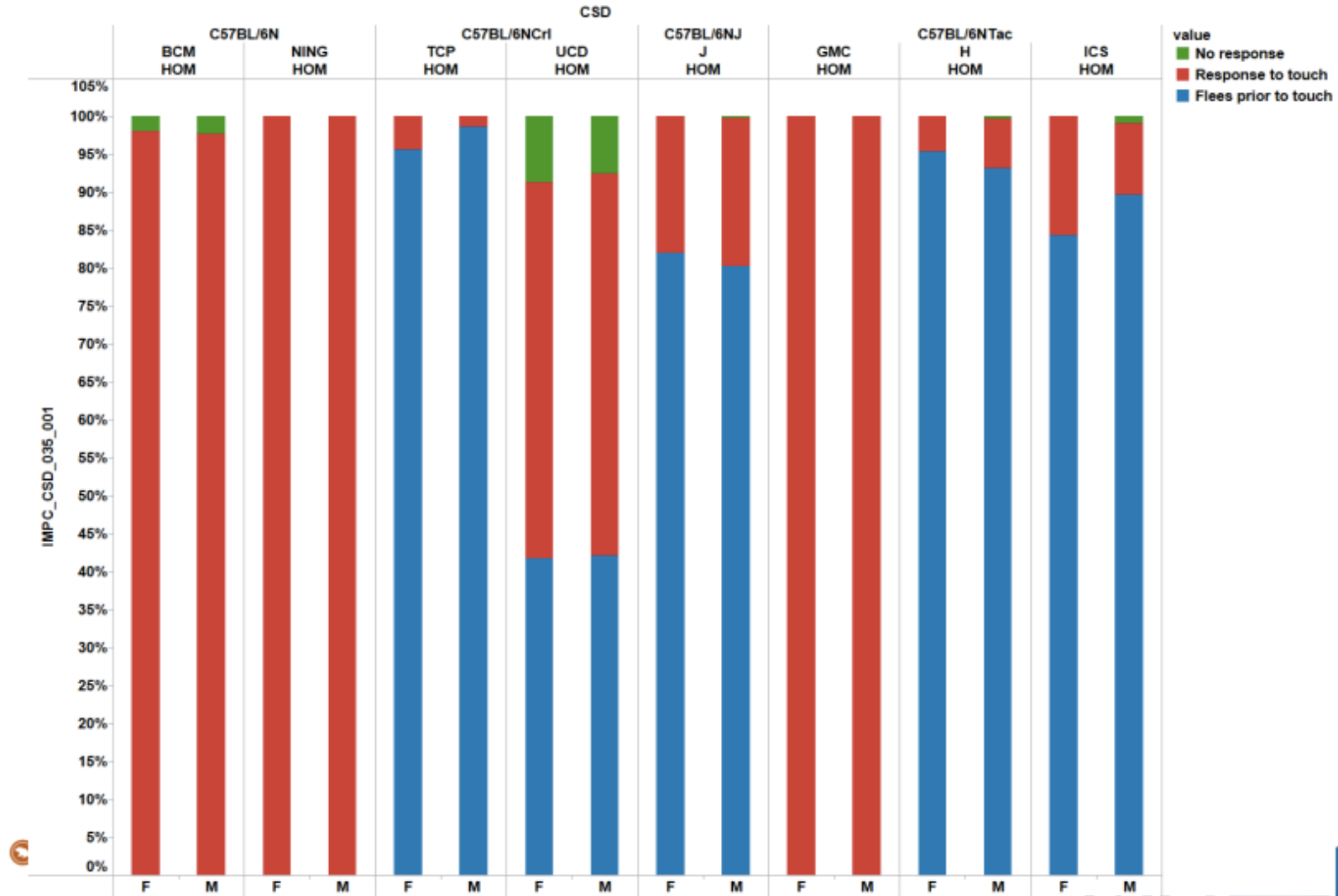
設備校準

Insulin IMPC_INS_001_001



淘汰不適用的 protocol

Touch escape IMPC_CSD_035_001



Search All 8901 Knockout Data...



Phenotype: abnormal circulating glucose level



Definition any anomaly in the concentration in the blood of the major monosaccharide of the body

Synonyms abnormal blood glucose level

8.32% of tested genes **693** significant genes **8329** tested genes



[Significant gene associations](#)



[The way we measure](#)



[Phenotype stats](#)

IMPC Gene variants with abnormal circulating glucose level

Total number of significant genotype-phenotype associations: 844

Search

Gene / Allele	Zygoty	Sex	Life Stage	Phenotype	Parameter	Phenotyping Center	P Value
Agl <i>Agl^{flm1b(EUCOMM)Wtsi}</i>	HOM	♀	Early adult	decreased circulating glucose level	Glucose <i>Clinical Chemistry</i>	MRC Harwell <i>IMPC</i>	0.00
Sfxn5 <i>Sfxn5^{tm1b(EUCOMM)Hmgu}</i>	HET	♂	Early adult	decreased fasting circulating	Fasted blood glucose concentration	JAX <i>IMPC</i>	0.00

Intraperitoneal glucose tolerance test (IPGTT) [MGP_IPG_001]

Home > Pipelines > Intraperitoneal glucose tolerance test (IPGTT)

Jump to:

[Purpose](#)[Experimental Design](#)[Equipment](#)[Procedure](#)[Notes](#)[Parameters & Metadata](#)[Ontologies](#)

Purpose

The glucose tolerance test measures the clearance of an intraperitoneally injected glucose load from the body. It is used to detect disturbances in glucose metabolism that can be linked to human conditions such as diabetes or metabolic syndrome. Animals are fasted for approximately 4 hours, fasted blood glucose levels are determined before a solution of glucose is administered by intra-peritoneal (IP) injection. Subsequently, the blood glucose level is measured at different time points during the following 2 hours.

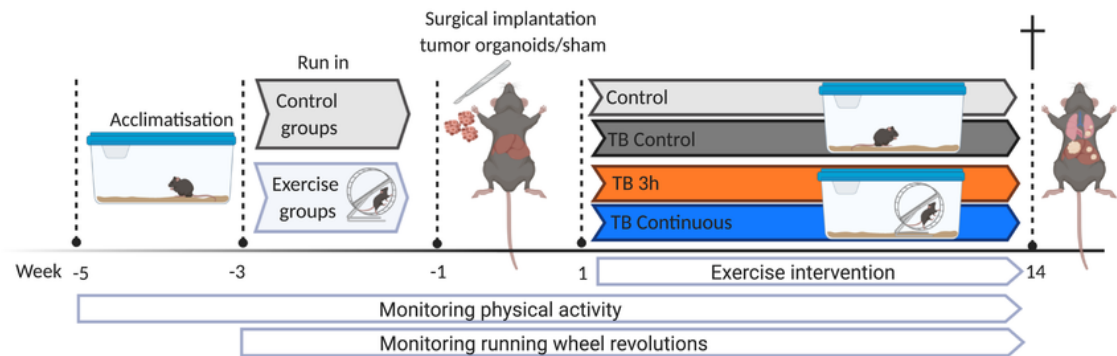
Ontological description: MP:0005559 - increased circulating glucose level, MP:0005560 - decreased circulating glucose level, MP:0005293 - impaired glucose tolerance, MP:0005292 - improved glucose tolerance, MP:0005291 abnormal glucose tolerance, MP:0000188 - abnormal circulating glucose level.

Experimental Design

- **Minimum number of animals** : 7M + 7F
- **Age at test**: Week 13
- **Sex**: We would expect the results of this test to show sexual dimorphism

實驗規劃- STEP4 實驗流程

1. 實驗流程- 從取得動物~ 犧牲動物



JCSM Rapid Communications. 2021, 5. 10.1002/rco2.51.

2. 動物實驗細節

What 實驗項目

How 實驗protocol

When/ how often 操作時序及頻率

Where 動物移動及適應期

Why 量測項目的選擇

3. 重要的前置準備

執行團隊是否具有經驗可以操作動物實驗項目？

動物設施是否可以支持動物移動、設備、動物照護及每日觀察？

實驗規劃- STEP 5 動物實驗管理

繁殖育種
環境豐富化
健康品質
社群行為

動物資源
供應單位

動物運輸

動物實驗
執行單位

檢疫及適應
環境豐富化？
健康品質？
飼育環境？



採樣分析

實驗操作

飼料及營養？
採樣及投藥技術？
每日觀察及疼痛評估？
人道試驗終點？
跨設施合作？

剖檢及採樣序？
病理分析？
樣本納入及排除？
統計方法？

動物健康品質管理

影響實驗動物健康的因素



環境因素

- ❑ 飼料及飲水
- ❑ 籠具及墊料
- ❑ 光及噪音
- ❑ 溫溼度
- ❑ 通風及換氣



動物因素

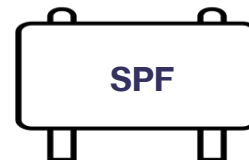
- ❑ 動物來源
- ❑ 病原管制清單
- ❑ 健康監測頻率
- ❑ 檢疫政策

實驗動物健康品質



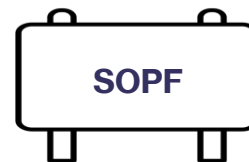
一般品質 (Conventional)

- ❑ 帶有飼育環境中存在但未定義的微生物
- ❑ 不一定會進行監測，也不一定會清除病原



無特定病原品質 (Specific Pathogen Free)

- ❑ 排除特定表列的病原微生物
- ❑ 需要定期監測，若出現表列微生物需要清除



無特定機會性病原品質 (Specific Opportunist Pathogen Free)

- ❑ 排除特定表列的病原微生物 (擴大到機會性病原)
- ❑ 需要定期監測，若出現表列微生物需要清除



無菌品質 (Specific Opportunist Pathogen Free)

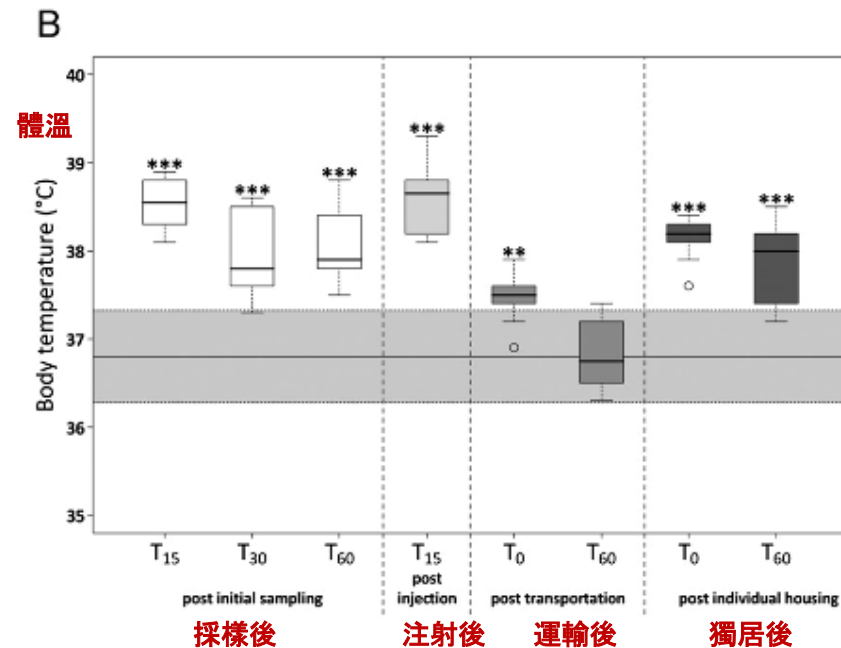
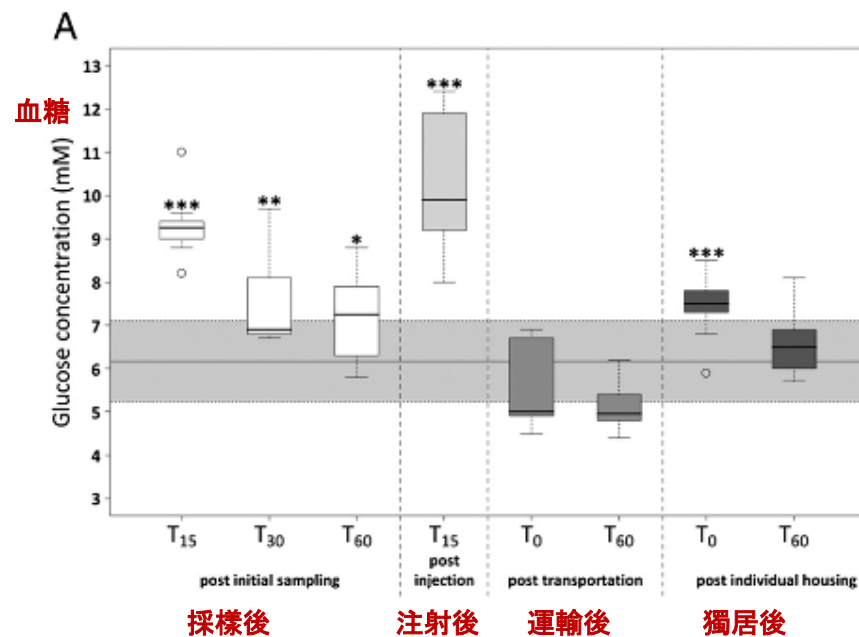
- ❑ 排除所有微生物
- ❑ 需要定期監測，若出現微生物需要清除

動物適應, 換籠及操作

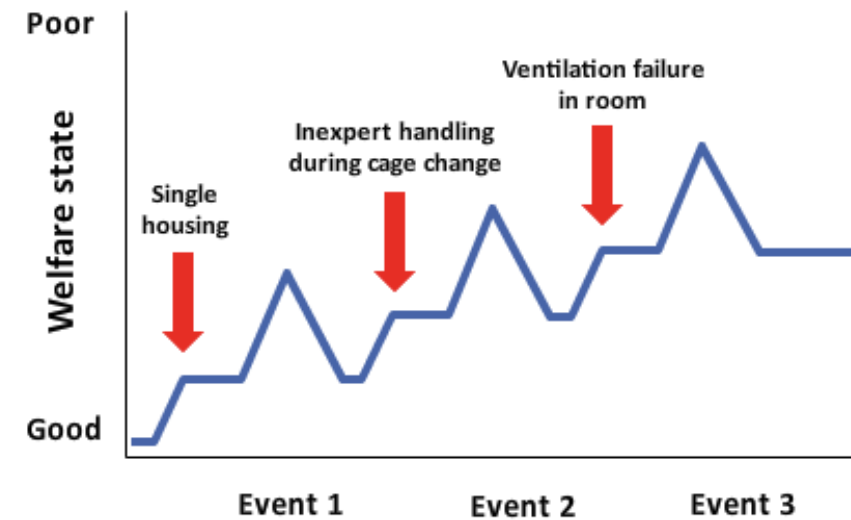
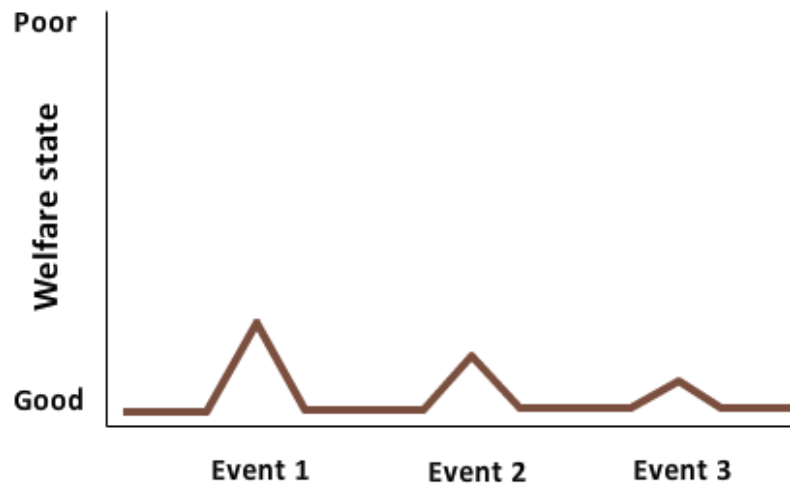
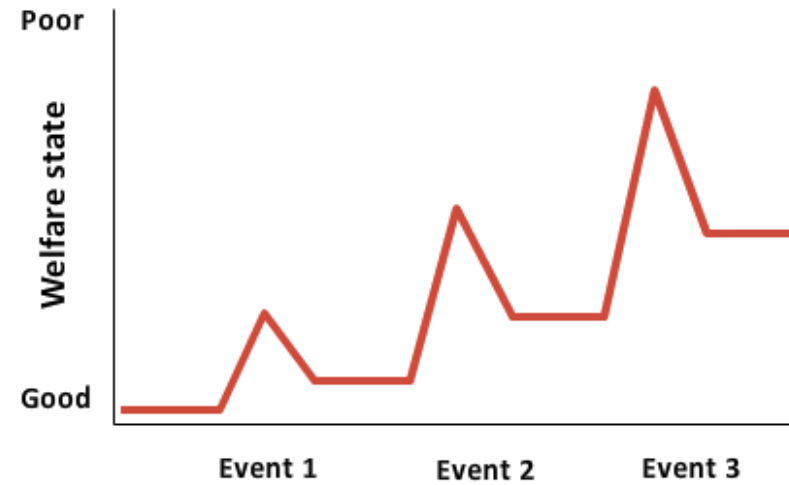
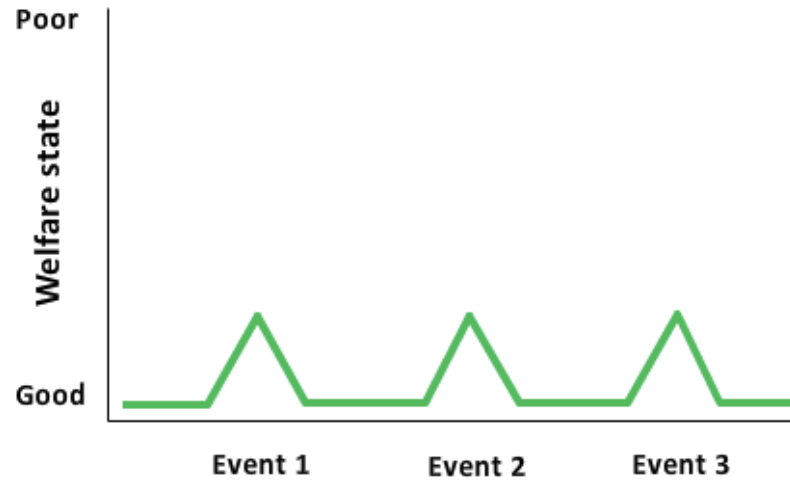
Experimental and husbandry procedures as potential modifiers of the results of phenotyping tests

Anna-Karin Gerdin, Natalia Igosheva, Laura-Anne Roberson, Ozama Ismail, Natasha Karp, Mark Sanderson, Emma Cambridge, Carl Shannon, David Sunter, Ramiro Ramirez-Solis, James Bussell, Jacqueline K. White *

Mouse Genetics Project, Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge, CB10 1SA, UK



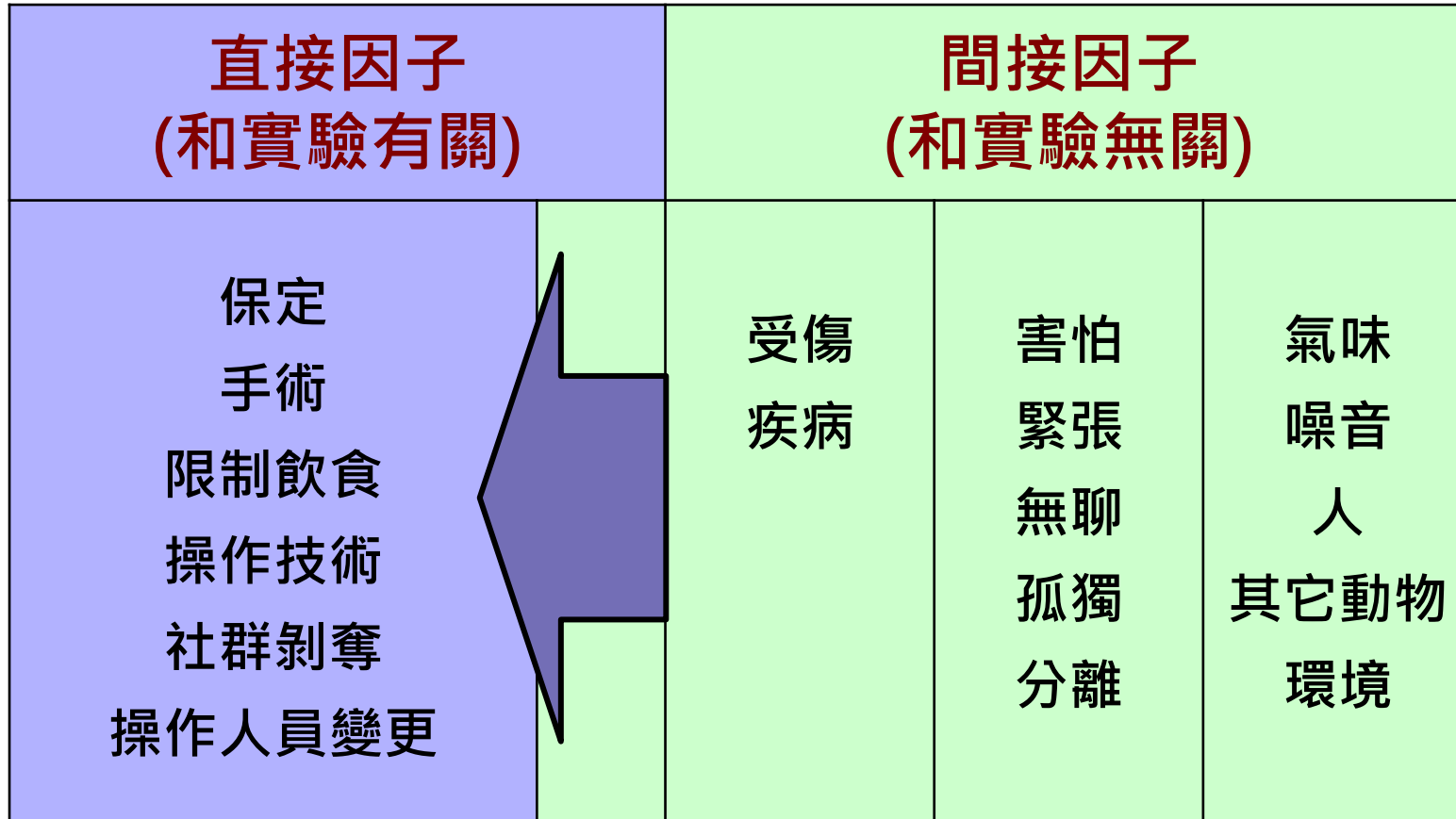
熟練的技術是動物實驗基礎



實驗動物的潛在壓力來源

生理壓力	心理壓力	環境壓力
受傷 手術 疾病 脫水 飢餓	害怕 緊張 無聊 孤獨 分離	保定 氣味 噪音 人 其它動物 環境

實驗優化- 實驗團隊和飼育團隊協力



- ✓ 實驗protocol、流程優化
- ✓ 技術品質優化

- ✓ 飼育環境優化、豐富化
- ✓ 每日觀察照顧品質優化

實驗規劃- STEP6 實驗結果

實驗數據的納入

- ✓ 最重要的實驗結果 (實驗假說)
 - ✓ 用來推估樣本數的那一項重要指標，應優先計算、納入與結論
 - ✓ 例如: 腫瘤藥效測試 vs 腫瘤抑制效果
- ✓ 次要的實驗結果
 - ✓ 列出所有依實驗規劃進行的量測結果 (細胞存活、行為、病理等)
 - ✓ 避免依故事情節挑選結果

實驗結果與討論

- ✓ 基礎值、樣本分析狀況
 - ✓ 報告絕對數值(如10/20)，而不只是處理過的數據 (如 50%)
- ✓ 結果與評估
 - ✓ 此研究可能造成偏移(bias)的任何潛在來源、所使用的動物模式的局限性
 - ✓ 研究結果是否可以應用到其他物種或其他系統，尤其是與人類醫學相關性

小結

- 動物實驗流程需要依循實驗設計嚴謹地執行，在過程中應留意下列項目：
 - 實驗protocol應定期更新，採用可重覆且對動物影響最小的流程
 - 如何減少人為的偏誤- 隨機分組、盲法、樣本的納入及排除
 - 選擇正確的實驗分組與統計方法
 - 運用預試驗或文獻資料，計算合理的樣本數，減少動物使用



國科會計畫涉及動物實驗之3R文件調整說明

如何做好動物實驗規劃

國家實驗動物中心 秦咸靜主任

NAR Labs
國家實驗研究院



第四部份

動物實驗規劃 (III) – 傷害利益評估

國家實驗動物中心 秦咸靜主任

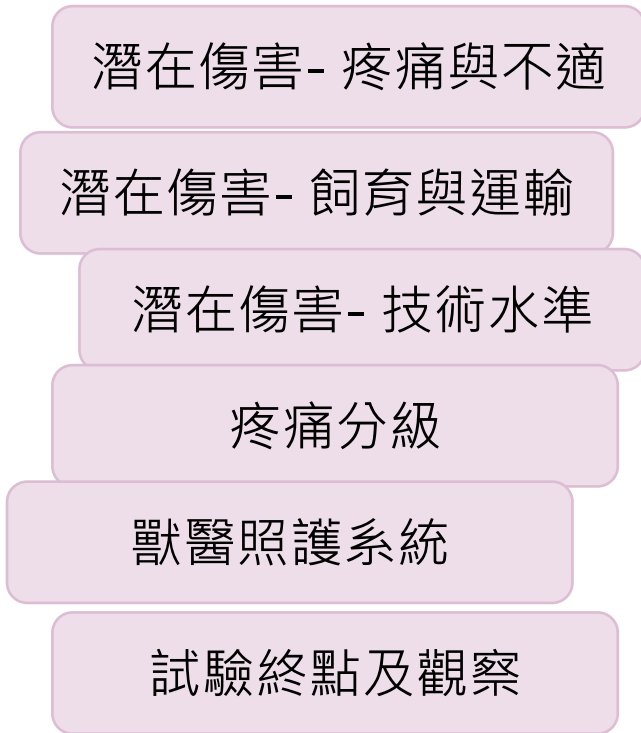
NAR Labs
國家實驗研究院

課程大綱

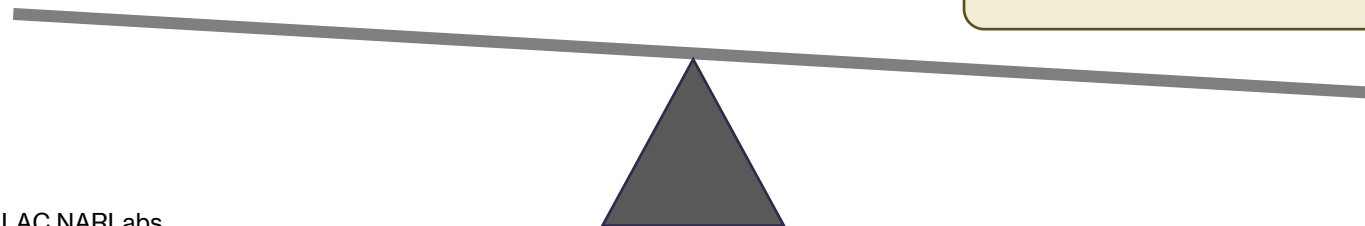
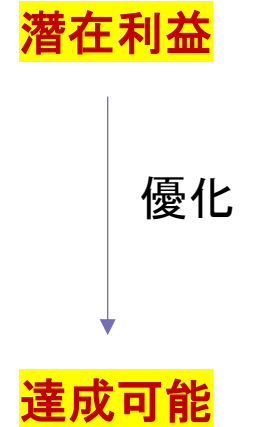
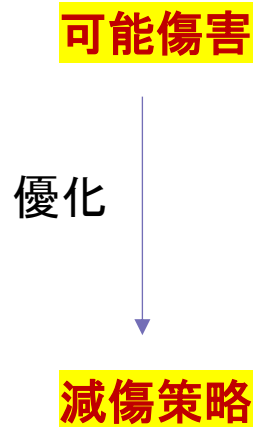
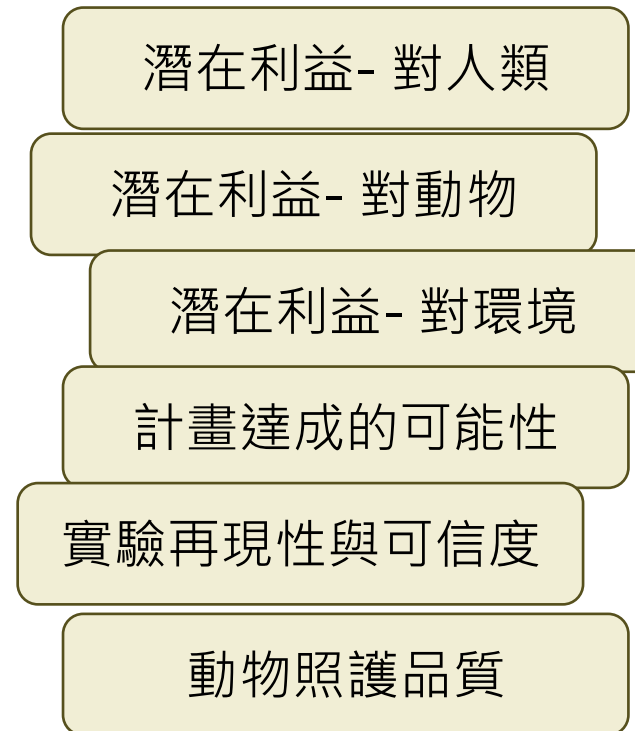
1. 國科會計畫涉及動物實驗之3R文件調整說明
2. 動物實驗規劃 (I) 實驗動物與統計方法
3. 動物實驗規劃 (II) 實驗流程及結果分析
4. 動物實驗規劃 (III) 傷害利益評估

動物實驗優化- 傷害利益評估

Harm



Benefit



傷害評估 HARM ANALYSIS

預測可能的疼痛

- 預試驗 (pilot study)或文獻分析
- 疼痛預測
 - 可能造成疼痛的流程
 - 疼痛的類別及位置
 - 出現的機率及疼痛程度
 - 綜合評估動物感受疼痛的嚴重程度

建立監控疼痛的策略

- 監控疼痛的特殊臨床症狀
- 監控的頻率及止痛的行動
- 人道介入的評估方式
- 負責監控的人員及其教育訓練
- 觀察記錄文件保存方式

臨床觀察能力是必備之技能

籠邊觀察

1. 觀察飼料及飲水
2. 觀察籠邊及墊料
4. 外觀/體態/行為/步伐/活動力



Copyright © Genie Chin, NLAC NARLabs

開籠蓋觀察

1. 抓取動物
2. 觀察動物腹部/背部及反應
3. 觀察動物頭部、尾部、四肢



人道試驗終點線上學習資源

HUMANE ENDPOINTS

G. Chin EN

Humane endpoints in laboratory animal experimentation

What are humane endpoints?

About this website

This website trains you how to monitor welfare in laboratory animals, identify endpoints and define responsibilities. You learn how to apply humane endpoints, which improves the scientific quality of your research. Read more [here](#).

The website is free of charge, but you can contribute to its future by making a voluntary [donation](#).

The Humane Endpoints website is part of the [3Rs Database Programme](#), together with [www.interspeciesinfo.com](#). and [fcs-free.org](#). These websites will help you with the reduction and replacement of animal experiments, respectively.

Open and secured section

The website on humane endpoints has an open and closed section. The open section is accessible to everyone and contains general information on normal behavior of mice and rats. The closed section contains in-depth information and training modules. To register for the closed section, go to [Registration](#).

E-learning and training modules

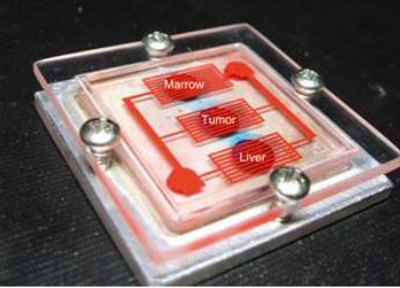

Try the interactive [E-learning module on humane endpoints](#), or one of our other training modules. Training modules are only available after registration. You can test your knowledge by choosing a case or a theme approach and selecting the preferred module. After the test, you get a score and can review results if desirable. Go directly to the [training modules](#).

<https://www.humane-endpoints.info/en>

MENU MODULE HUMANE ENDPOINTS PAG. 8

Basics of humane endpoints | Humane endpoints: Why bother? (1 task)

Laboratory animals have been used for centuries in biomedical sciences as a surrogate model to study human and veterinary medical issues such as infectious diseases or cancer, to monitor environmental changes but also for teaching and training purposes. And although a wide variety of non-animal models have become available (e.g. tissue cultures, in silico models), their applicability is still limited and laboratory animals continue to be used. Statistics show that the annual numbers in the Netherlands are slowly going down, but are still at a level of about 500,000 animals/year.

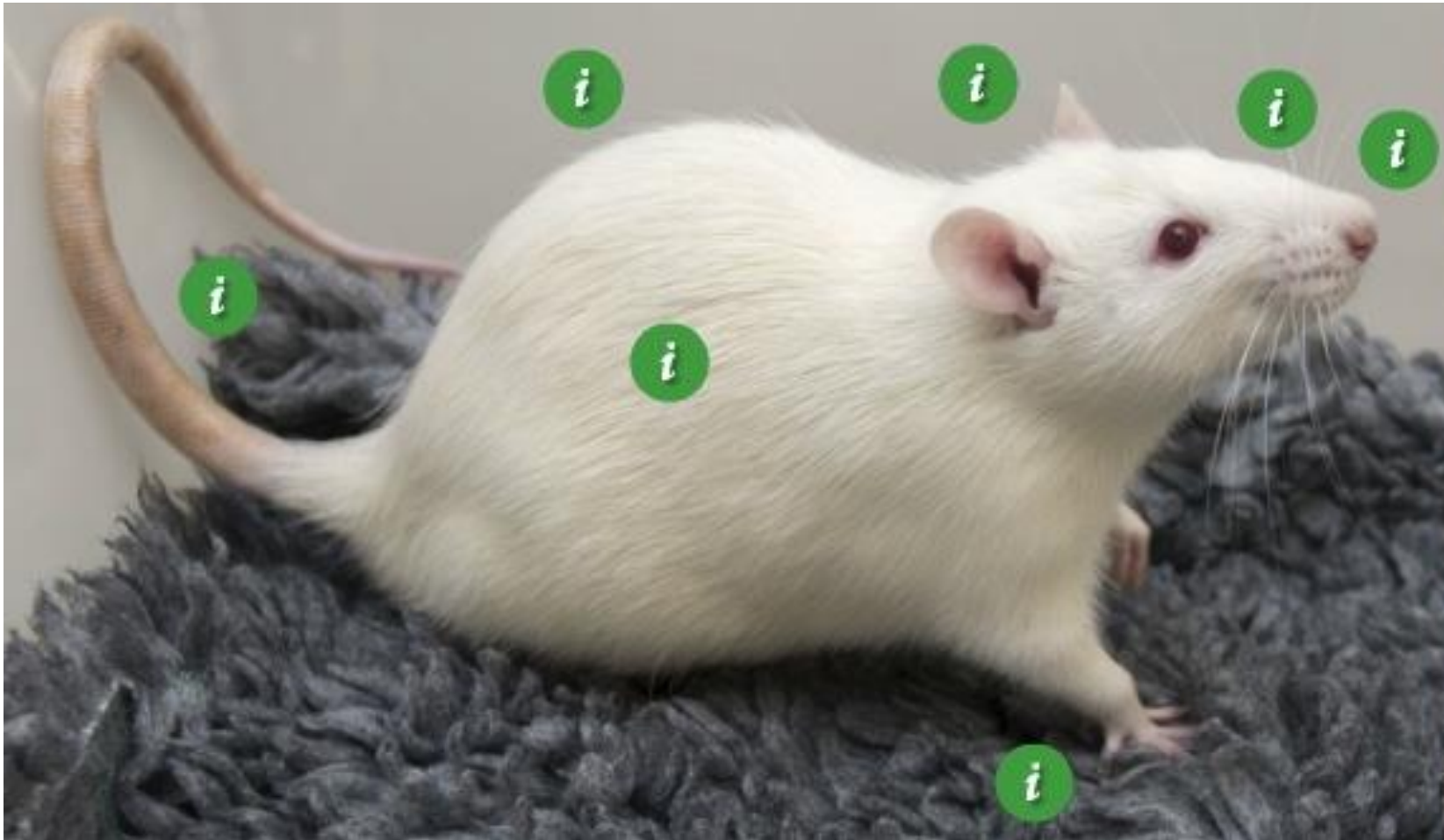


Claude Bernard (1813 - 1878) surrounded by pupils performing an experiment on a rabbit

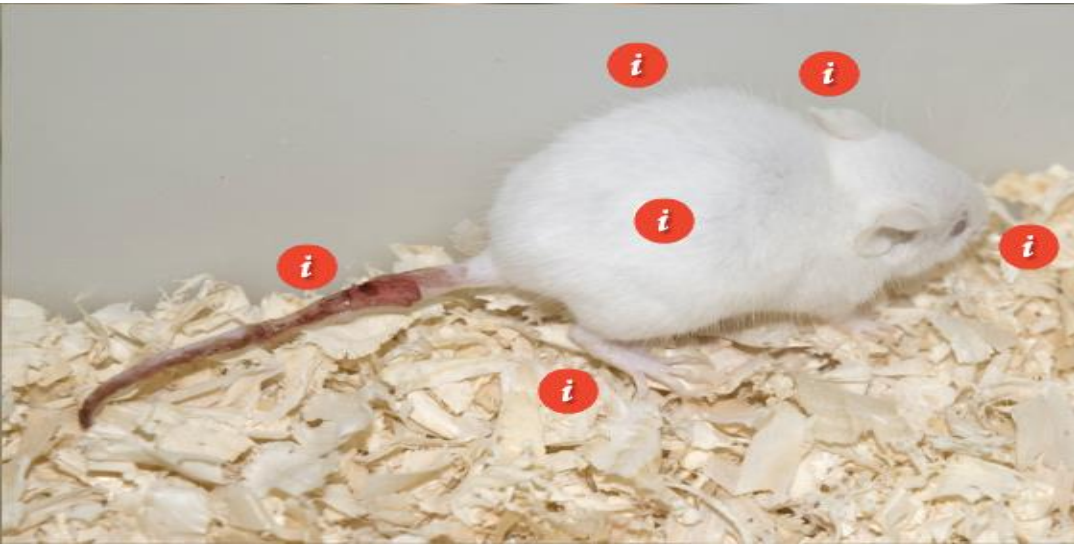
Organs on a chip

Back Task 1 >

臨床觀察與疼痛指標



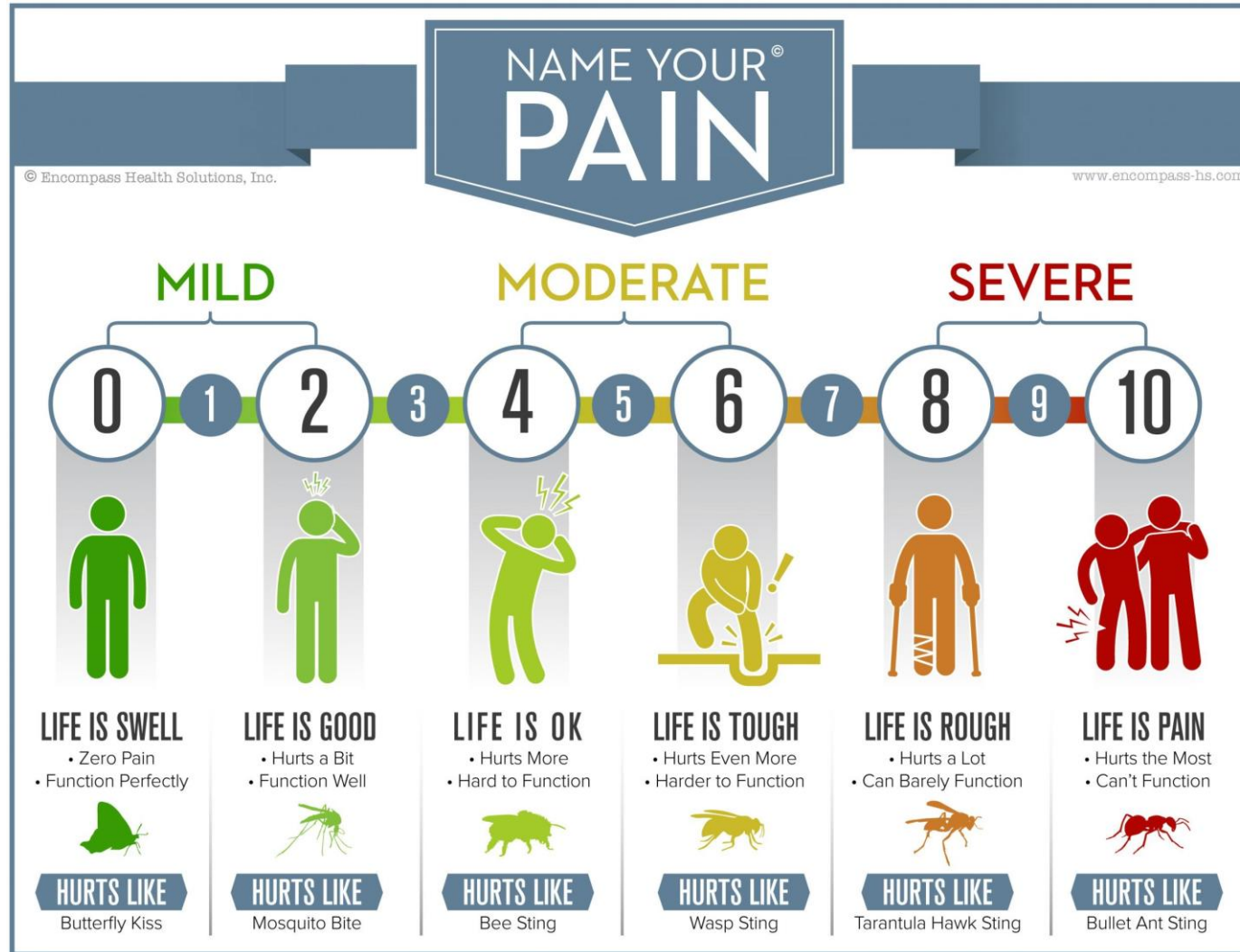
- Decreased activity
- Unkempt fur (not grooming)
- Pilo-erection
- Hunched posture
- Rapid shallow Breathing
- “Red tears” “albino rats”
- Squinting of eyes
- Vocalization
- Feed and/or water refusal
- Weight loss



- Poor body condition
- Poor coat condition
- Poor body posture
- Moving abnormally
- Behaving abnormally

- Appearance of the eyes
- Appearance of the ears
- Appearance of the nose
- Appearance of the tail

疼痛分級評估



<https://carivacare.com/nurse-triage-and-pain-assessment/>

疼痛分級評估- 輕微疼痛

Here are some notes on the classifications. Move the slider to view them.

Mild **Moderate** **Severe** **Non-Recovery**

Mild

Procedures on animals as a result of which the animals are likely to experience **short term mild pain, suffering or distress**. Procedures with **no significant impairment** of the wellbeing or general condition of the animals.

Examples

- 1 Non-invasive imaging of animals (e.g. MRI) with appropriate sedation or anaesthesia.
- 2 Superficial procedures, e.g. ear and tail biopsies.
- 3 Administration of substances by subcutaneous, intramuscular or intraperitoneal routes.

疼痛分級評估- 中度疼痛

Here are some notes on the classifications. Move the slider to view them.

Mild Moderate Severe Non-Recovery

Moderate

Procedures on animals as a result of which the animals are likely to experience **short term moderate pain, suffering or distress, or long-lasting mild pain, suffering or distress.** Procedures that are likely to cause **moderate impairment** of the wellbeing or general condition of the animals.

Examples

- 1 Surgery under general anaesthesia and appropriate analgesia.
- 2 Use of metabolic cages involving moderate restriction of movement over a prolonged period (up to 5 days).
- 3 Models of induction of tumours, or spontaneous tumours, that are expected to cause moderate pain or distress or moderate interference with normal behaviour.

疼痛分級評估- 嚴重疼痛

Here are some notes on the classifications. Move the slider to view them.

Mild Moderate Severe Non-Recovery

Severe

Procedures on animals as a result of which the animals are likely to experience **severe pain, suffering or distress, or long-lasting moderate pain, suffering or distress**. Procedures, that are likely to cause **severe impairment** of the wellbeing or general condition of the animals.

Examples

- 1 Toxicity testing where death is the endpoint.
- 2 Irradiation or chemotherapy with a lethal dose without reconstitution of the immune system.
- 3 Models with induction of tumours, or with spontaneous tumours, that are expected to cause progressive lethal disease associated with long-lasting moderate pain, distress or suffering.

疼痛分級評估- 非存活實驗

Here are some notes on the classifications. Move the slider to view them.

Mild Moderate Severe Non-Recovery

Non-Recovery

Procedures, which are performed **entirely under general anaesthesia** from which the animal shall **not recover consciousness**.

針對嚴重程度的疼痛建立臨床觀察評分表

肝病臨床觀察評分表

Characteristic	Score			
	1	2	3	4
Coat - general	Normal	Slight lack of grooming	Starey	-
Skin tone	Normal	Mildly dehydrated	Moderately dehydrated	Severely dehydrated
Behaviour	Normal	Slightly dull or lethargic	Aggressive or apathetic and inactive	Very aggressive or immobile and unresponsive
Abdominal distension	None	Mild ascites	Obvious ascites	-
Jaundice	None	Slightly jaundiced appearance	Mild jaundice present	Moderate jaundice present
Body weight	Normal weight gain or weight loss less than 5%	Weight loss $\leq 10\%$	Weight loss $\leq 15\%$	Weight loss $\leq 20\%$

1. 挑選指標

- 一般性指標
- 實驗的特殊指標

2. 決定評量模式

- 0-4分
- 0-10分
- Yes/No
- 量測數值

3. 決定分數級距的意義

- 0-6 正常
- 7-9 輕微，多觀察
- 10-14 介入治療
- 15-22 人道安樂死



腫瘤臨床觀察評分表

Characteristic	Score			
	1	2	3	4
Coat - general	Normal	Slight lack of grooming	Starey	-
Skin tone	Normal	Mildly dehydrated	Moderately dehydrated	Severely dehydrated
Behaviour	Normal	Slightly dull or lethargic	Apathetic and inactive	Immobile and unresponsive (for tumour interfering with normal behaviour and activities)
Tumour size and appearance	Very small (<3mm)	Tumour small (<=5mm) with no necrosis or ulceration	Tumour intermediate size (<=8mm) with no necrosis or ulceration	Tumour large (>=12mm) Ulceration of tumour of any size
Body weight	Normal weight gain or weight loss less than 5%	Weight loss <=10%	Weight loss <=15%	Weight loss <=20%

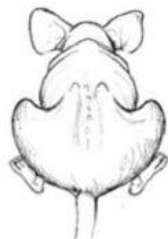
體重是評估動物福祉的重要指標

Body Condition Scoring (BC)



BC1 – Mouse is emaciated

- Skeletal structure extremely prominent; little or no flesh cover.
- Vertebrae distinctly segmented



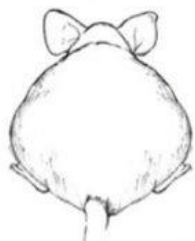
BC2 – Mouse is under-conditioned

- Segmentation of the vertebral column evident
- Dorsal pelvic bones are readily palpable



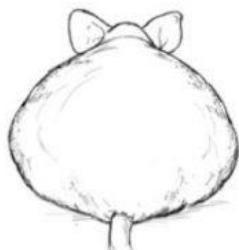
BC3 – Mouse is well-conditioned

- Vertebrae and dorsal pelvis not prominent, palpable with slight pressure



BC4 – Mouse is over-conditioned

- Spine is a continuous column
- Vertebrae palpable with only firm pressure

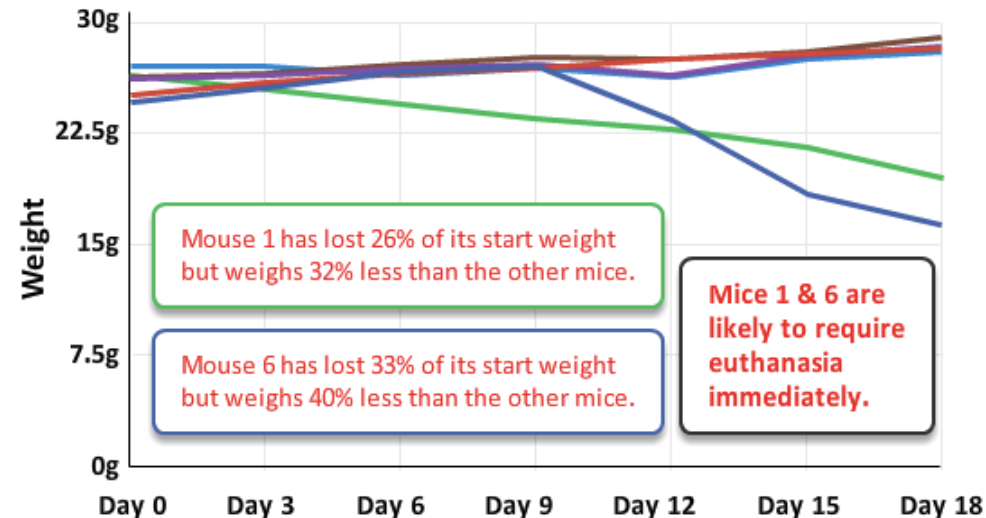


BC5 – Mouse is obese

- Mouse is smooth and bulky
- Bone structure disappears under flesh and subcutaneous fat

<https://www.clearh2o.com/>

Body weight (體重變化)

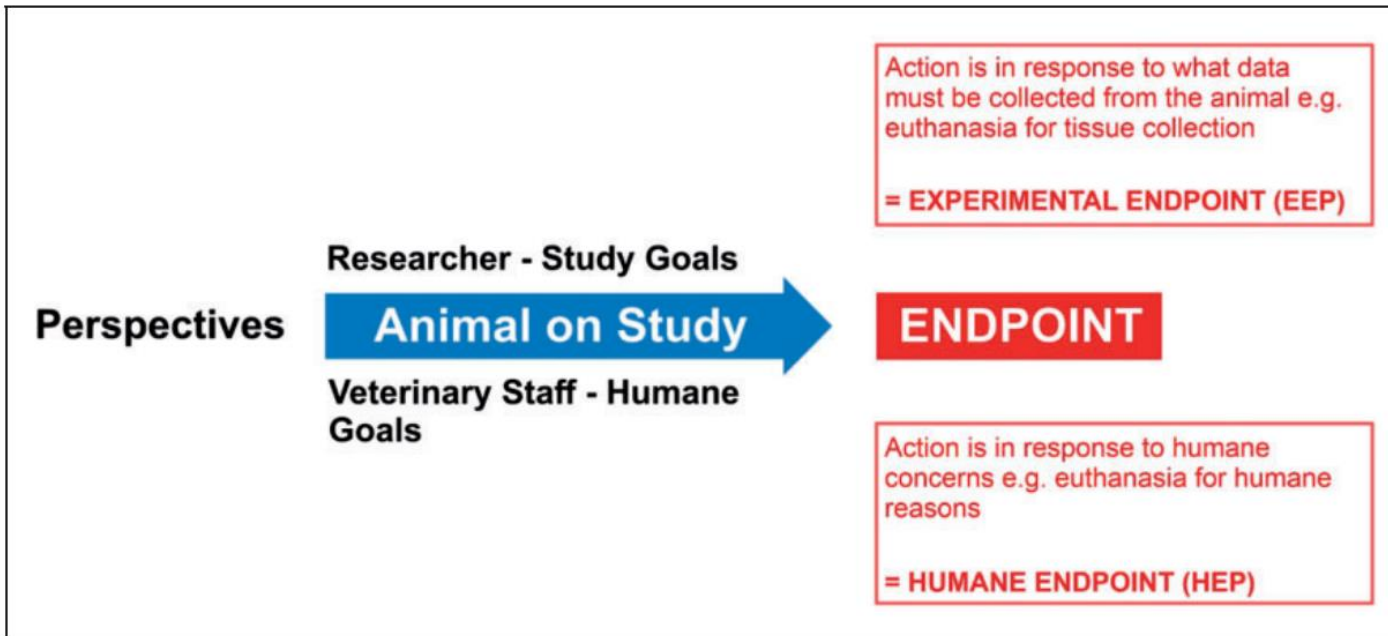


體重變化之注意事項

- 逐漸喪失體重 vs 快速喪失體重
- 損失?%體重

人道介入與人道終點

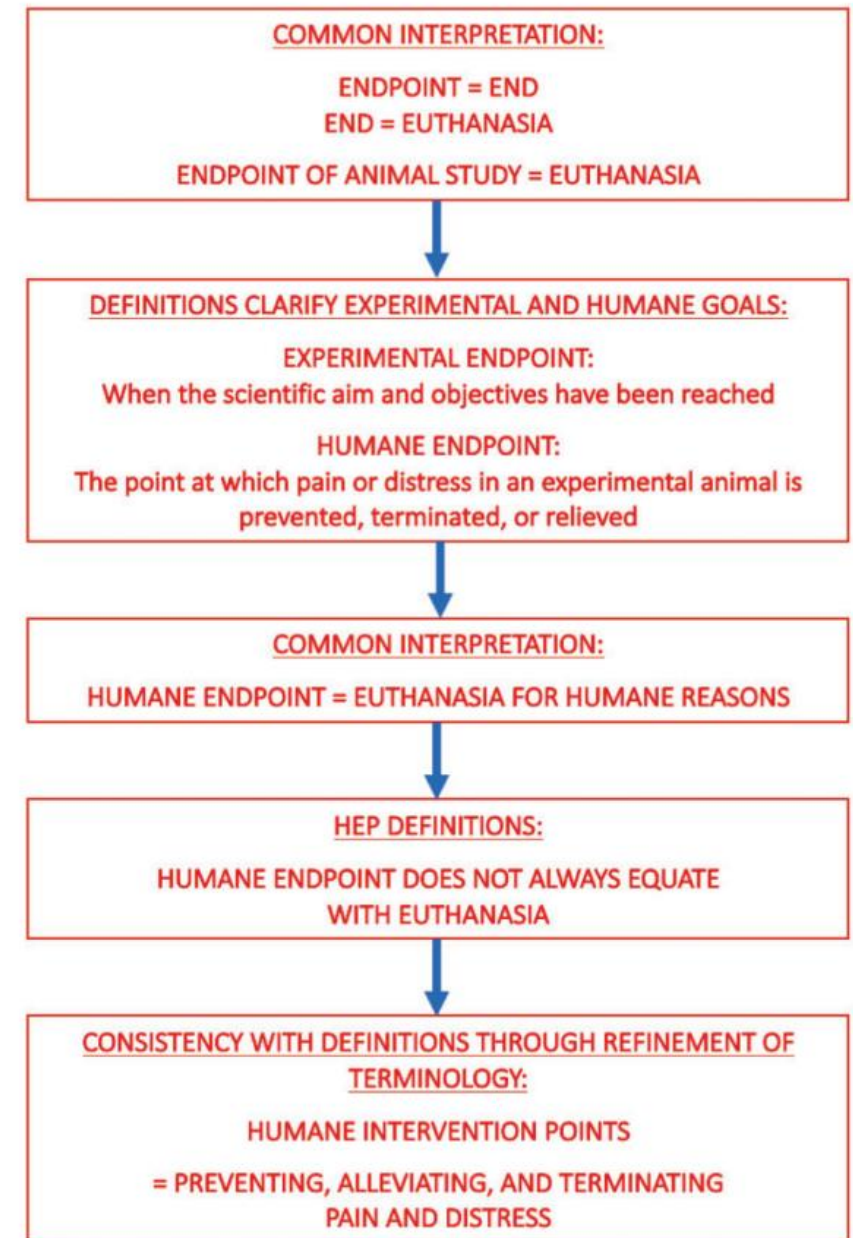
- 試驗終點：實驗取得到足夠的資料，可結束實驗
- 人道終點：動物可忍受疼痛程度的上限
- 人道介入 = 預防、減輕、終結疼痛及不適



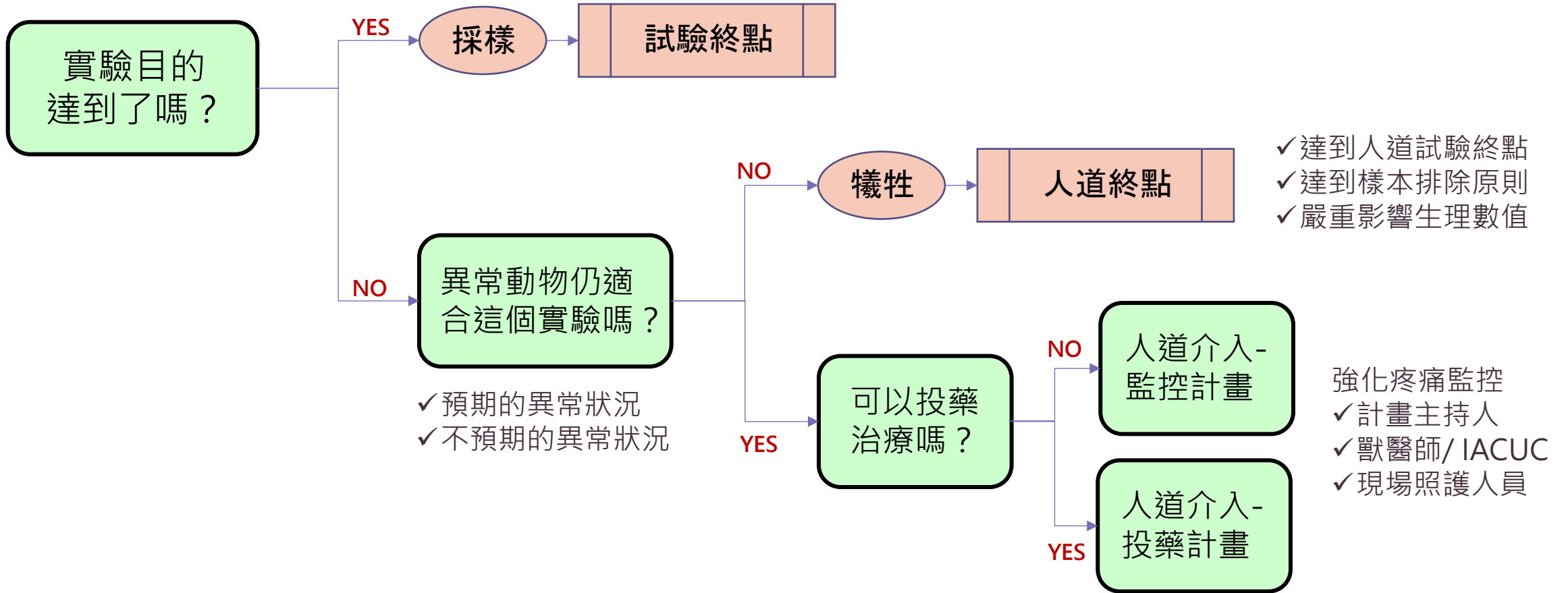
Laboratory Animals 2022, Vol. 56(5) 482-489

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The Evolution of Endpoint and Intervention Terminology




發現異常動物之流程



利益評估 BENEFIT ANALYSIS

動物實驗的BENEFIT- 重要的不是你在計畫書上承諾了什麼，而是你能做到什麼

PREPARE 

The PREPARE Guidelines Checklist
Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

Adrian J. Smith¹, Eddie Clutton², Elliot Lillyer³, Kristine E. Aa. Hansen⁴ & Torodd Strathairn⁵

¹Norecopa, c/o Norwegian Veterinary Institute, P.O. Box 730 Sentrum, 0166 Oslo, Norway; ²Royal (Dick) School of Veterinary Studies, Easter Bush, Midlothian, EH25 9RG, U.K.; ³Research Animals Department, Science Group, RSPCA, Wiltshire Way, Southwater, Merton, West Sussex, RH13 9RS, U.K.; ⁴Section of Experimental Biomedicine, Department of Production Animal Clinical Science, Faculty of Veterinary Medicine, Norwegian University of Life Sciences, P.O. Box 4140 Elve, 0203 Oslo, Norway; ⁵Division for Research Management and Science Funding, Western Norway University of Applied Sciences, 5059 Bergen, Norway

PREPARE consists of planning guidelines which are complementary to reporting guidelines such as ARRIVE. PREPARE covers the three broad areas which determine the quality of the preparation for animal studies:

1. Formulation of the study
2. Dialogue between scientists and the animal facility
3. Quality control of the components in the study

The topics will not always be addressed in the order in which they are presented here, and some topics overlap. The PREPARE checklist can be adapted to meet special needs, such as field studies. PREPARE includes guidance on the management of animal facilities, since in-house experiments are dependent upon their quality. The full version of the guidelines is available on the Norecopa website, with links to global resources, at <https://norecopa.no/PREPARE>. The PREPARE guidelines are a dynamic set which will evolve as more species- and situation-specific guidelines are produced, and as best practice within Laboratory Animal Science progresses.

Topic	Recommendation
(A) Formulation of the study	
1. Literature searches	<input type="checkbox"/> Form a clear hypothesis, with primary and secondary outcomes. <input type="checkbox"/> Consider the use of systematic reviews. <input type="checkbox"/> Decide upon databases and information specialists to be consulted, and construct search terms. <input type="checkbox"/> Assess the relevance of the species to be used, its biology and suitability to answer the experimental questions with the least suffering, and its welfare needs. <input type="checkbox"/> Assess the reproducibility and translatability of the project.
2. Legal issues	<input type="checkbox"/> Consider how the research is affected by relevant legislation for animal research and other areas, e.g. animal transport, occupational health and safety. <input type="checkbox"/> Locate relevant guidance documents (e.g. EU guidance on project evaluation).
3. Ethical issues, Harm-Benefit Assessment and humane endpoints	<input type="checkbox"/> Construct a lay summary. <input type="checkbox"/> In dialogue with ethics committees, consider whether statements about this type of research have already been produced. <input type="checkbox"/> Address the 3Rs (Replacement, Reduction, Refinement) and the 3Gs (Good Science, Good Sense, Good Sensibilities). <input type="checkbox"/> Consider pre-registration and the publication of negative results. <input type="checkbox"/> Perform a Harm-Benefit Assessment and justify any likely animal harm. <input type="checkbox"/> Discuss the learning objectives, if the animal use is for educational or training purposes. <input type="checkbox"/> Allocate a severity classification to the project. <input type="checkbox"/> Define objective, easily measurable and unambiguous humane endpoints. <input type="checkbox"/> Discuss the justification, if any, for death as an end-point.
4. Experimental design and statistical analysis	<input type="checkbox"/> Consider pilot studies, statistical power and significance levels. <input type="checkbox"/> Define the experimental unit and decide upon animal numbers. <input type="checkbox"/> Choose methods of randomisation, prevent observer bias, and decide upon inclusion and exclusion criteria.



ARRIVE

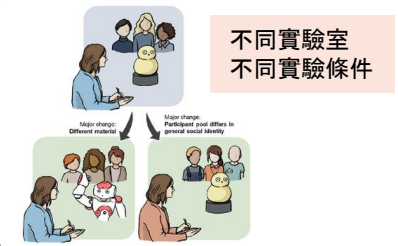
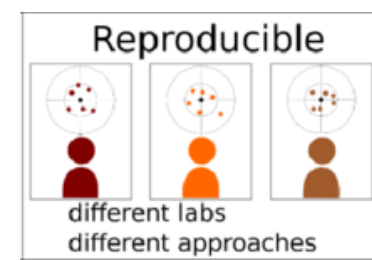
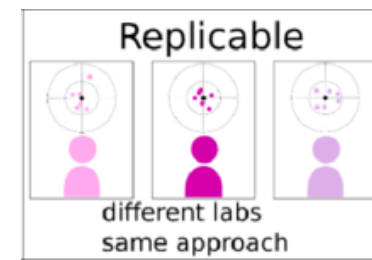
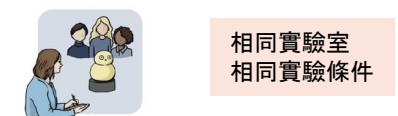
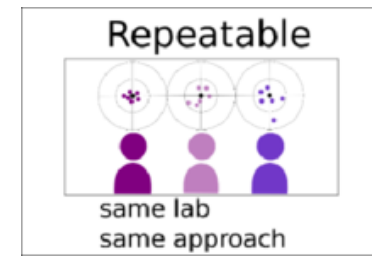
The ARRIVE Guidelines Checklist
Animal Research: Reporting In Vivo Experiments

Carol Kirkenny¹, William J. Browne², Innes C. Cuthill³, Michael Emerson⁴ and Douglas G. Altman⁵

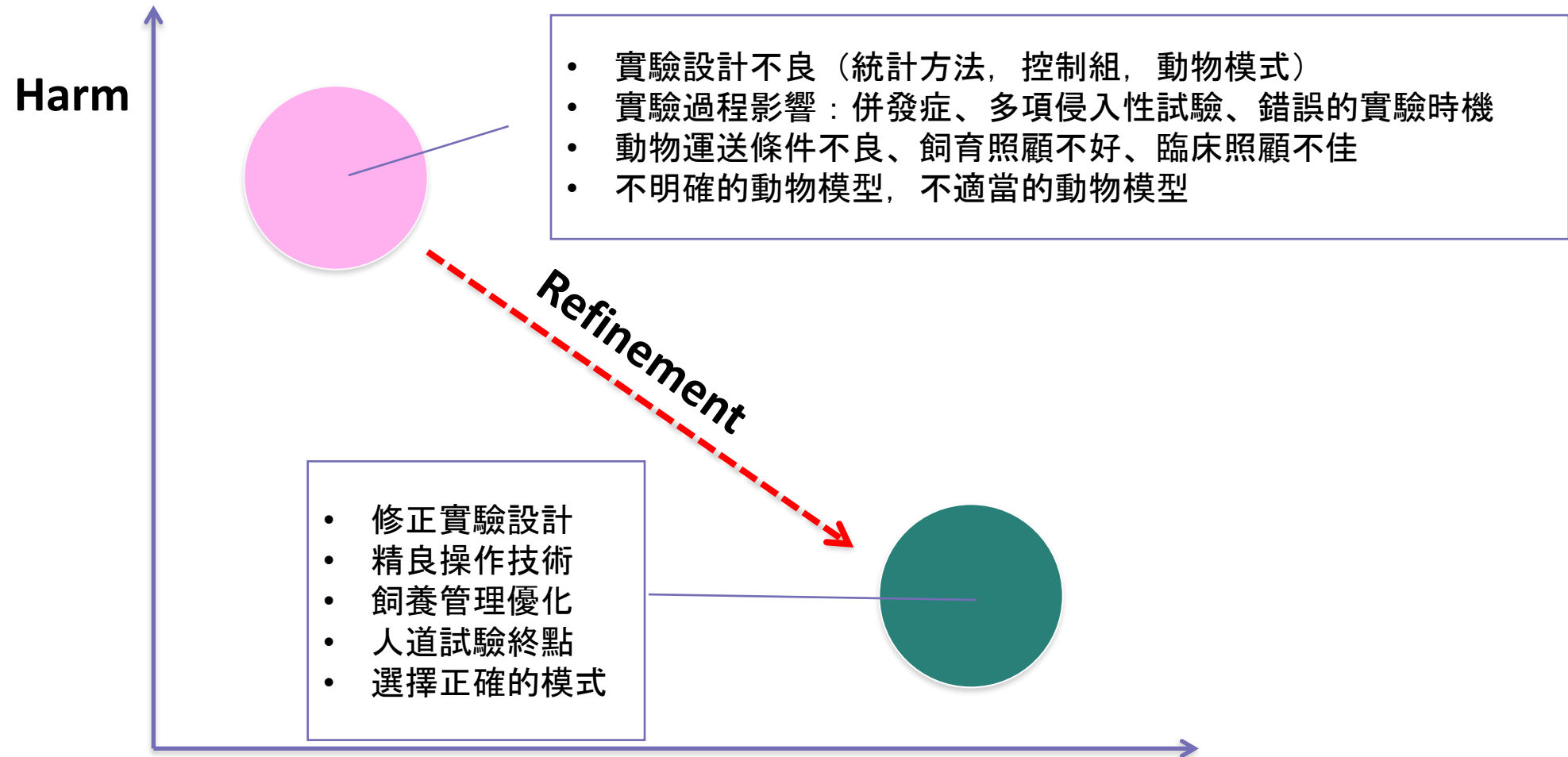
¹The National Centre for the Replacement, Refinement and Reduction of Animals in Research, London, UK; ²School of Veterinary Science, University of Bristol, Bristol, UK; ³School of Biological Sciences, University of Bristol, Bristol, UK; ⁴National Heart and Lung Institute, Imperial College London, UK; ⁵Centre for Statistics in Medicine, University of Oxford, Oxford, UK.

ITEM	RECOMMENDATION	Section Paragraph
Title	1 Provide as accurate and concise a description of the content of the article as possible.	
Abstract	2 Provide an accurate summary of the background, research objectives, including details of the species or strain of animal used, key methods, principal findings and conclusions of the study.	
INTRODUCTION		
Background	3 a. include sufficient scientific background (including relevant references to previous work) to understand the motivation and context for the study, and explain the experimental approach and rationale. b. Explain how and why the animal species and model being used can address the scientific objectives and, where appropriate, the study's relevance to human biology.	
Objectives	4 Clearly describe the primary and any secondary objectives of the study, or specific hypotheses being tested.	
METHODS		
Ethical statement	5 Indicate the nature of the ethical review permissions, relevant sciences (e.g. Animal (Scientific Procedures) Act 1986), and national or institutional guidelines for the care and use of animals, that cover the research.	
Study design	6 For each experiment, give brief details of the study design including: a. The number of experimental and control groups. b. Any steps taken to minimise the effects of subjective bias when allocating animals to treatment (e.g. randomisation procedure) and when assessing results (e.g. if done, describe who was blinded and when). c. The experimental unit (e.g. a single animal, group or cage of animals). A time-line diagram or flow chart can be useful to illustrate how complex study designs were carried out.	
Experimental procedures	7 For each experiment and each experimental group, including controls, provide precise details of all procedures carried out. For example: a. How (e.g. drug formulation and dose, site and route of administration, anaesthetics and analgesics used (including monitoring), surgical procedure, method of euthanasia). Provide details of any specialist equipment used, including suppliers. b. When (e.g. time of day). c. Where (e.g. home cage, laboratory, water maze). d. Why (e.g. rationale for choice of specific anaesthetic, route of administration, drug dose used).	
Experimental animals	8 a. Provide details of the animals used, including species, strain, sex, developmental stage (e.g. mean or median age plus age range) and weight (e.g. mean or median weight plus weight range). b. Provide further relevant information such as the source of animals, international strain nomenclature, genetic modification status (e.g. knock-out or transgenic), genotype, health/screening status, drug or test naïve, previous procedures, etc.	

The ARRIVE guidelines. Originally published in *PLoS Biology*, June 2010¹



透過HBA進行實驗優化



小結

科學

實驗動物科學

實驗動物的科學應用

動物設施管理

動物房設計及維運

經營管理

醫學

實驗動物醫學

實驗動物疾病預防及診斷

實驗動物福祉

動物福祉及人道管理

人文素養

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NLAC 動知識 <https://nlac-course.narlabs.org.tw/>



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的動物實驗 ARRIVE & PREPARE

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課程3
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義與現實權衡的溝通技巧
&
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[實體課程] 和研究團隊進行專業、正義



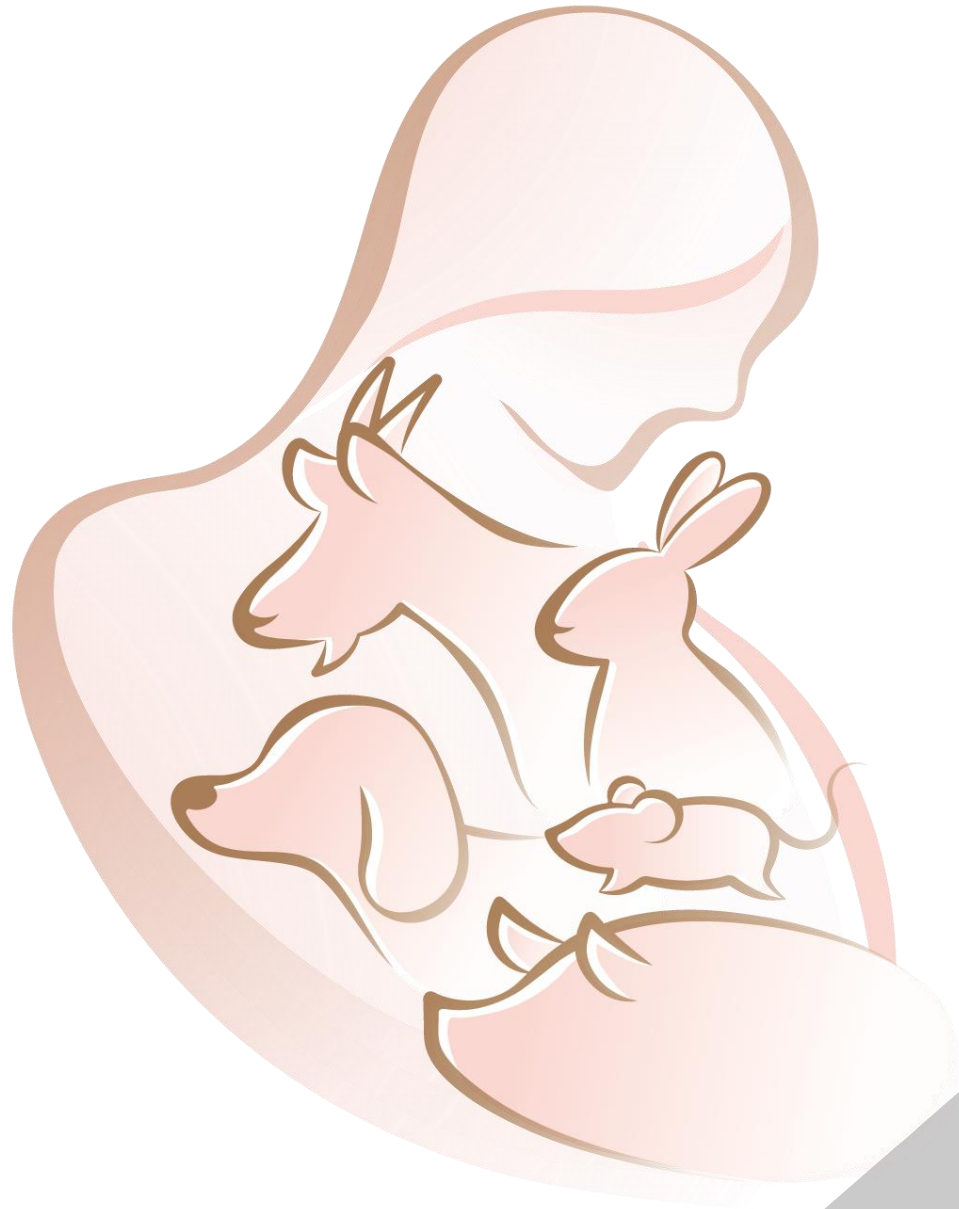
NLAC 系列課程一
**實驗動物模式
基因改造鼠**



NLAC 系列課程一
**實驗動物模式
實驗大小鼠
表現型觀察**



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Thank You