MEETING THE INFORMATION REQUIREMENTS OF THE ANIMAL WELFARE ACT

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Objectives

• History of the Animal Welfare Act and the AWIC program

• Define the 3 Rs of Alternatives

• Become familiar with databases and other resources helpful in searching for alternatives

• Design and run a search
June 22, 1965

PEPPER GOES MISSING

_Sports Illustrated_ reports the story about Pepper, the Lakavage family's Dalmatian that was stolen from their farm in Pennsylvania in June 1965 and sold to a research facility in New York City. Pepper's theft and eventual death prompts Rep. Joseph Resnick (D-NY) to introduce a Laboratory Animal Welfare bill in Congress, an early milestone in the history of the Animal Welfare Act.

The dog’s name is Lucky. He is a horn-colored English pointer with a fine head and subtle signs of good, expensive breeding. But when a woman from the Animal Rescue Institute came across Lucky at a Sylmar, Okla., fair three weeks ago, this is what she saw—a pathetic, emaciated hound, emaciated, shrunken and up for auction. The woman bought him for $3 plus a dollar for the chain.

Lucky has his counterparts all over the U.S. Unscrupulous dog “dealers,” taking advantage of the growing demand for dogs for vital medical research, are running a lucrative and lucrative business. Laboratories now need around two million dogs a year. To cash in on this need, the dealers rear the country paying a buck or two to anyone who tunes forward with a dog and an questions asked. Family pets, trained to obedience and easy to handle, are especially prized, and the Humane Society of the U.S. estimates that 10 percent of all breeding pets have been stolen by “dealers,” who in turn sell them to the dealers. Some dealers keep big inventories of dogs in unspeakably filthy compounds that morbidly has tempting than the concentration camps of World War II. Many do not sell directly to labs but simply dispose of their packs at auction where the going rate is 10 a pound. Puppies, often drenched in their own vomit, set for life space. Stored by revolts in a House subcommittee of such outrage and performed by the committee’s raids on these camps by humane societies, Congress already has eight bills pending, any of which would outlaw these shameful conditions.

Pets for sale cheap—no questions asked

CONCENTRATION CAMPS FOR DOGS

Photographed by STAN WAYMAN
August 24, 1966
Laboratory Animal Welfare Act signed into law

“…the farm bill contains legislation dealing with the humane treatment of animals. The main thrust of the bill is to minimize pain and distress suffered by animals used for experiments and tests. In so doing, biomedical research will gain in accuracy and humanity. We owe much to laboratory animals and that debt can best be repaid by good treatment and keeping painful experiments to a minimum.”

Sen. R. Dole
Congressional Record, Senate
18 December 1985
AWA Defines Service at NAL
Animal Welfare Information Center (AWIC)

Provides information—

(1) pertinent to employee training;
(2) which could **prevent unintended duplication** of animal experimentation as determined by the needs of the research facility; and
(3) on **improved methods of animal experimentation** which could--
   (A) **reduce** or **replace** animal use; and
   (B) **minimize pain and distress** to animals, such as anesthetic and analgesic procedures.
Information
Requirements of the
Animal Welfare Act
What are the Information Requirements?

• Rationale for using animals (AWAR, Section 2.31(e)(2))
• Appropriateness of the animal species
• Appropriateness of the numbers of animals
• Complete description of research procedures
• Description of euthanasia method
• Minimization of and consideration of alternatives to painful or distressful procedures (AWAR, Section 2.31(d)(1)(i) & (ii))
• Assurance that the activities do not unnecessarily duplicate previous experiments (AWAR, Section 2.31(d)(1)(iii))
Sec 2.31 (d): [The] IACUC shall determine that...

(ii) The principal investigator has considered alternatives to procedures that may cause more than momentary or slight pain or distress to the animals, and has provided a written narrative description of the methods and sources, e.g., the Animal Welfare Information Center, used to determine that alternatives were not available;

(iii) The principal investigator has provided written assurance that the activities do not unnecessarily duplicate previous experiments.

(iv) Procedures that may cause more than momentary or slight pain or distress to the animals will:

(A) Be performed with appropriate sedatives, analgesics or anesthetics, unless withholding such agents is justified for scientific reason, in writing, by the principal investigator and will continue for only the necessary period;
Alternatives and the 3Rs
Definition of Alternatives: The 3RS

“Alternatives, or alternative methods, as first described by Russell and Burch in 1959, are generally regarded as those that incorporate some aspect of replacement, reduction, or refinement of animal use in pursuit of the minimization of animal pain and distress consistent with the goals of the research.”
Replacement

Substituting conscious living higher animals with non-sentient methods.
Replacement

- Full/Absolute
- Partial/Relative
Full/Absolute Replacement Examples

- TraumaMan simulator
- Microdosing
- Tissue culture
Partial/Relative Replacement Examples

Rat Skin Transcutaneous Electrical Resistance Test
Emerging Technologies

– Artificial Organs/Tissue Engineering
– Organ-on-a-chip technology

Animal-free skin allergy testing

With the recent approval of the human Cell Line Activation Test (h-CLAT) for skin sensitization (allergy), toxicologists now have a battery of methods that allows... Read More

Human Cell Activation Test

“Blood-brain barrier on-a-chip”

Scientists at the Wyss Institute have created a 3-dimensional in vitro model of the human blood-brain-barrier (BBB) “on-a-chip.” The device will make it possible for researchers... Read More

Blood-Brain Barrier on a chip
Reduction in the numbers of animals used to obtain information of a given amount and precision.

Choose the right strategy in the planning and performance phase.
3Rs Alternatives: Reduction

• Appropriate experimental design and statistical evaluation of sample sizes
• Animals serving as their own control
• Pilot studies
• Sharing data and resources, including animals, tissues, or organs
• Imaging technologies
Refinement

Modifying procedures to minimize pain and distress experienced by animals.
3Rs Alternatives: Refinement

- Use of anesthetics and analgesics
- Modifications in capture, handling, restraint
- Noninvasive methods of sampling
- Humane endpoints
- Telemetry
- Imaging technology
- Knowledge of species physiology and recognition of normal/abnormal behavior
Use of Analgesics

“They all look like this after surgery”

“They all look like this after surgery with post-operative analgesia.”
WHERE Can I Search for Information?
Isn’t there one mega-database that I can search?

Isn’t Medline (or PubMed) enough?
Searching Multiple Databases

Pharmacokinetics
pharmacokinetics and pain

BIOSIS

1464

35

551

449

MEDLINE

332

EMBASE

989

Total: 3,939

Without BIOSIS Previews, you would be missing 1,464 unique citations.

In addition to hundreds of journal article records, BIOSIS Unique records contain 415 Meeting records.
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Alternatives Literature Searching

"APHIS continues to recommend a database search as the most effective and efficient method for demonstrating compliance with the requirement to consider alternatives to painful/distressful procedures." (USDA, APHIS, Animal Care Policy #12: Consideration of Alternatives to Painful/Distressful Procedures)
How about Google Scholar??
Google Scholar is NOT a database

- It is an internet search engine, not an organized database
- Not limited to scholarly publications
- The journal titles and time frame of coverage are not specified
- It has not been structured or indexed by humans
- Retrieves publications that are not included in standard bibliographic databases

**No citation metric is an exact measure of research impact. Still it’s important to remember that the number of citing publications listed by GS is likely an inflated number and should not be relied on**
Pros & Cons to Google Scholar

**Pros:**
- Indexed a wide range of scholarly literature
- Searching is free
- Easy to use if you’re familiar with Google
- Google algorithm ranks relevance for you
- Can set up library access links in settings

**Cons:**
- Can’t search by subject area or material type
- No full-text access to most articles
- Very limited filters
- Content not organized by experts
- No easy way to identify ‘peer reviewed’ source
How Should I Search?
AWIC’s Approach

• Analyze the protocol to determine what questions to address

• Decide where to go for the information
  – Databases
  – Websites

• Link terminology appropriately for best search results

• Evaluate the search results and refine as needed
General Searching Tips

• Search beyond your usual database(s)

• Use complex search statements
  – Controlled vocabulary
  – Natural language (text words)
  – Boolean operators

• Contact your institution’s librarian or Animal Welfare Information Center (AWIC)
Search Terminology: Truncation

• A symbol added to the end of the root of a word that searches for all forms of a word.

  behav* = behavior, behaviour, behaves, behave, behaving, behaved, etc.

• BEWARE Unintended results!

  gene* = genes, genetics, general, generation, generic, generous, etc.

  rat* = rat, rats, ratio, ration, rationing, rate, Rattus
Search Terminology: Boolean Operators

- **AND** - All terms are present
  - Example - swine and euthan*

- **OR** - Any one of the terms are present (more than one term may be present)
  - Example - swine or pig or pigs or porcine

- **NOT** - The first term but not the second is present.
  - Example -(pig or pigs or swine or porcine) NOT guinea

- **Use of Parentheses** - When combining terms, an AND operation will be performed before an OR operation if both operations are included in a query.

  (dog or dogs or canine) AND (pain or distress)
Search Terminology: Proximity Operators

• Search for one word within a certain distance of another word.
  – blood NEAR/3 collect* = blood collection, collection of arterial blood, collecting blood
  – cardiovascular NEAR/3 dis*= cardiovascular disease, cardiovascular diseases, cardiovascular disorder, cardiovascular disorders

• Search for phrases using quotation marks. (If double quotations are not used, words are searched individually using AND.)
  – “animal welfare”
Building Your Search Pyramid

Steps to completing a search
Step 1: Form the research statement

Understand the question so that you can better frame the topic/concept areas
Step 1: Form the research statement

– Identify the major subject(s) or topic(s) you will be investigating

– Clarify the relationship(s) between topics

– Example: Dr. Dana Scully plans to evaluate the effects of a nutritional supplement on colitis in mice. In order to monitor the effects of the supplement, she plans to euthanize animals at specified time points to examine colon length and look for histomorphological changes.
Step 2: Identify Key Concepts

Break the statement or query into concept groups

Example:
1. Inflammatory Bowel Disease
2. Animal
3. Alternative terminology
Step 3: Generate a List of Alternate Terms for Each Concept

Consider:
- Clarification of concepts
- Related terms or phrases
- Synonymous words
- Alternate spellings
- Acronyms
Step 3: Generate a List of Alternate Terms for Each Concept

1. “inflammatory bowel disease” OR “IBD” OR “colitis”

1. “mouse” OR “mice” OR “murine*” OR “rat” OR “rats” OR “rattus”

2. “Animal Welfare” OR “humane or endpoint*” OR “noninvasive” OR “imag*” OR “biomarker”
Search Terminology:
Scientific Terms Related to the Research

- Description of protocol and area of study
- Species being used
- Organ systems involved
- Acronyms (ex. CNS, WNV, Mab)
- Spelling (behavior, behaviour)
- Names of hormones, enzymes, trade names (xylazine=rompun)
Step 4: Combine Key Concepts in Search Sets
## Combing Sets in PubMed

### History

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<td>Search (((“inflammatory bowel disease” OR “IBD” OR “colitis”))) AND (((“mouse” OR “mice” OR “murine” OR “rat” OR “rats” OR “rattus”)) AND ((“Animal Welfare” OR “humane or endpoint” OR “noninvasive” OR “imag” OR “biomarker”))</td>
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<td>Search (“inflammatory bowel disease” OR “IBD” OR “colitis”)</td>
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### Builder

- **All Fields**
  - (“inflammatory bowel disease” OR “IBD” OR “colitis”)
  - (“mouse” OR “mice” OR “murine” OR “rat” OR “rats” OR “rattus”)
  - (“Animal Welfare” OR “humane or endpoint” OR “noninvasive” OR “imag” OR “biomarker”)

**Search**
Step 4: Evaluate and Refine the Search Based on Results

1. If most of the results are relevant the search strategy doesn’t need another set to be added to narrow

2. If the results are too broad, consider limits:
   - Narrower concepts
   - Publication year
   - Specific fields (e.g., title, keywords, abstract)

3. Fix what you can
   - Add a NOT group of things to exclude
   - Fix any “unfortunate” truncations
Step 5: Save the Search Results and Strategy

- Keep records of your searches and results using ALERTS.
  - Email
  - RSS Feeds

- Maintain citation lists.
  - Endnote
  - Refworks
  - Mendeley
  - Zotero
Bianchi, A.; Bluhmki, T.; Schönberger, T.; Kaaru, E.; Beltzer, A.; Raymond, E.; Wunder, A.; Thakker, P.; Stierstorfer, B.; Stiller, D. Noninvasive Longitudinal Study of a Magnetic Resonance Imaging Biomarker for the Quantification of Colon Inflammation in a Mouse Model of Colitis. *Inflammatory bowel diseases*; 2016; 22 (6); 1286-95

The aim of this work was to evaluate the potential of colon wall thickness measured using MRI as an in vivo imaging biomarker of inflammation for inflammatory bowel disease in an animal model of this disease.
To monitor the course of colitis, to the present day, classical parameters like histological tissue alterations or analysis of mucosal cytokine/chemokine expression often require euthanasia of animals. Recent advances mean revolutionary non-invasive imaging techniques for in vivo murine colitis diagnostics are increasingly available. … For the first time, in vivo imaging techniques allow for longitudinal examinations and evaluation of intra-individual therapeutic response.
Search Evaluation
Red Flags

• Search completed at the last minute.
• Only one database searched.
• Terms only for painful aspects.
• The term “alternative” used alone with no other 3Rs terms.
• Keywords listed not relevant to protocol.
• Keywords and concepts linked in an incorrect manner (e.g. wrong Boolean operators).
• Search doesn’t cover adequate time period (5-10 years).
Summary

- History of the Animal Welfare Act and the AWIC program
- Define the 3 Rs of Alternatives
- Become familiar with databases and other resources helpful in searching for alternatives
- Design and run a search
Contacting AWIC

https://www.nal.usda.gov/awic
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