



Office of
Research Assurances

LITERATURE SEARCH FOR ALTERNATIVES

INFORMATION REQUIREMENTS OF THE AWA

9 CFR 2.31 (D)

[The] IACUC shall determine that...

- (i) Procedures involving animals will avoid or minimize discomfort, distress, and pain to the animals;
- (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

(9 CFR, Section 2.31(d)(1)(i) & (ii))

PROVISION OF ANALGESICS & ANESTHETICS WHERE POSSIBLE

9 CFR 2.31 (D)

[The] IACUC shall determine that...

- i. The principal investigator has provided written assurance that the activities do not unnecessarily duplicate previous experiments.
- ii. 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

(9 CFR, Section 2.31(d)(1)(iii) & (iv))

WHAT ARE THE INFORMATION REQUIREMENTS?

TITLE 9, CHAPTER 1, SUBCHAPTER A, ANIMAL WELFARE SEC 2.31 (E)

- Rationale for using animals.
- Appropriateness of the animal species.
- Appropriateness of the numbers of animals.
- Complete description of research procedures.
- Description of euthanasia method

Animal Care



Animal Welfare Act and
Animal Welfare Regulations

DATABASE SEARCHES IN WSU IACUC PROTOCOLS



- A database search for alternatives to painful and distressful procedures is required for all WSU IACUC protocols that contain Category D or E activities.
- Protocols using USDA-covered species must conduct two database searches.
- The keywords must include the species used under the protocol and terms that define the category D and/or E activities (e.g., Surgery, Inflammation, etc.)

DATABASE SEARCH – CONTINUING REVIEW

- The database search must be updated at every three-year renewal and whenever a new species or category D/E activity is added.
- It is the IACUC's responsibility to review the database search to ensure that all possible alternatives to potentially painful and/or distressful procedures are considered and justified.



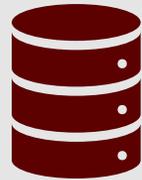
FEDERAL CRITERIA FOR GRANTING IACUC APPROVAL - SUMMARY

- Housing/Health: **Living conditions will be appropriate for the animals' welfare.** Care of Health of the animals will be directed by the attending veterinarian or other trained scientists.
- Alternatives: Must provide **written narrative description of methods and sources used to determine that alternatives were not available.**
- Animals: A proposal...must contain the following: (1) **Identification of the species and approximate number of animals to be used;** (2) **A rationale for involving animals, and for the appropriateness of the species and numbers of animals to be used...**
- Duplication: Must provide assurances that **activities do not unnecessarily duplicate previous efforts**
- Qualifications: Personnel must be appropriately qualified for procedures and species.
- Deviations: Must be **justified for scientific reasons**, in writing.

SUMMARY: HOW SHOULD I SEARCH?



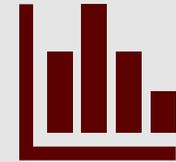
Analyze the protocol to identify areas to potentially implement alternatives



Choose which databases to search – where to go for information



Develop and run a search strategy



Evaluate the results and refine as needed

RESOURCES - ANIMAL WELFARE INFORMATION CENTER (AWIC)



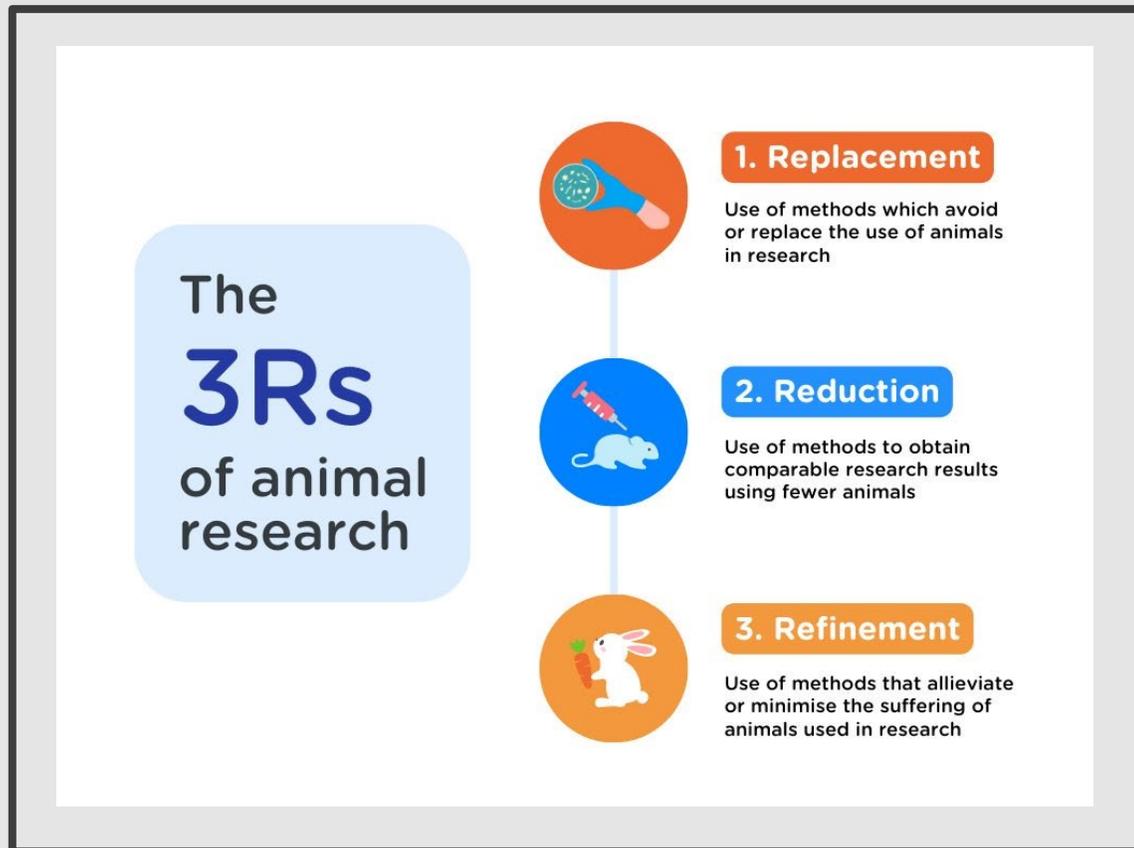
- **The Animal Welfare Information Center (AWIC)** is library service established as a part of USDA's National Agricultural Library (NAL). <https://www.nal.usda.gov/programs/awic>
- As a part of their services, AWIC provides free literature search for alternative services and instructions on best practices when performing literature searches.

HOW TO CONDUCT A LITERATURE/DATABASE SEARCH

■ **Step 1: Identify Areas to Potentially Implement Alternatives**

- The “Three R’s” (replace, refine, reduce) should always be considered when conducting a literature search for alternatives.
- Examples of questions to ask when developing search terms:
 - Is the species of animal appropriate for this type of research? Could it be conducted in a non-animal model?
 - What procedures performed on these animals might cause pain or distress? Are there refinements or alternatives to these procedures?
 - Can anesthesia or analgesia be used to minimize pain or distress? If so, are the drugs used appropriate for the species and procedures?

BENEFITS OF INITIATING THE LITERATURE SEARCH PROCESS EARLY (ADJUSTING YOUR SEARCH AS NEW STRATEGIES ARE IDENTIFIED):



- Choose the appropriate model.
- Determine appropriate numbers.
- Increase research efficiency.
- Learn new approaches.
- Find opportunities for less painful and invasive procedures.
- Reduce animal stress.
- Identify possible collaborators.

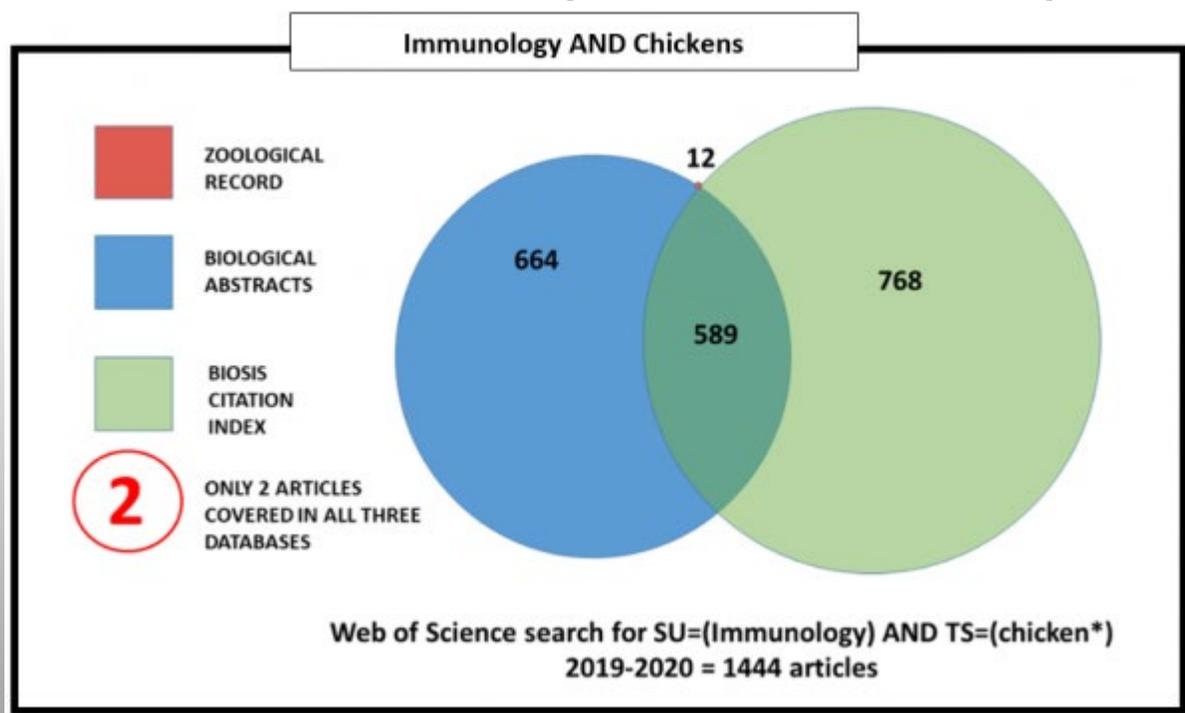
HOW TO CONDUCT A LITERATURE/DATABASE SEARCH

■ Step 2: Choose Which Databases to Search

- The databases used for literature searches for alternatives may change depending on the topic(s) being searched (biomedical research, biological science, veterinary medicine, animal use alternatives, etc.)
 - AWIC provides a list of bibliographic databases based on subjects they cover:
<https://www.nal.usda.gov/services/literature-searching-animal-use-alternatives>
- Bibliographic databases (AGRICOLA, PubMed, etc.) are not the only resources available to search. Grey literature sources, which is any literature that has not been published through traditional publications, can also be searched.
 - AWIC also provides a list of 3R organizations that publish grey literature sources
<https://www.nal.usda.gov/animal-health-and-welfare/animal-use-alternatives#3RsOrgs>

HOW TO CONDUCT A LITERATURE/DATABASE SEARCH

It is recommended to search multiple databases to obtain the best results as no single database is 100% comprehensive on a topic.



For example, this diagram from AWIC shows the results on a search for “Immunology and Chickens”.

If just the Zoological record database was searched with these keywords, only 12 of the 1400 citations available would be received.

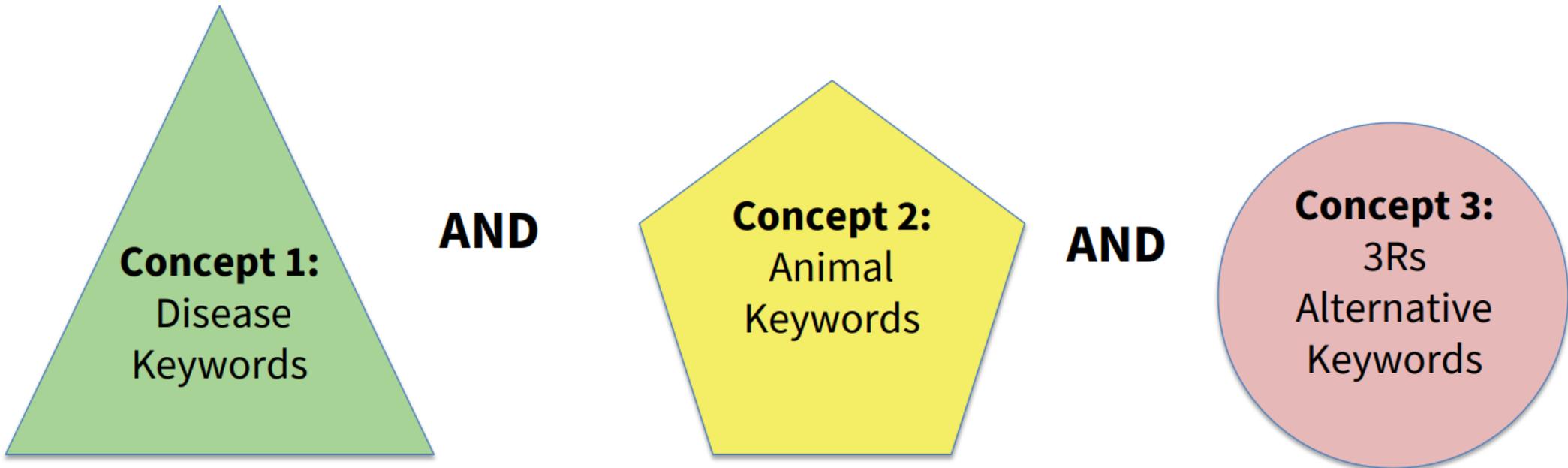
HOW TO CONDUCT A LITERATURE/DATABASE SEARCH

■ **Step 3: Develop and Run a Search String**

- Keywords are used to run a database search with the purpose of expressing the main concepts and ideas being searched for.
- In general, keywords should include:
 - Names of species used
 - Names of procedures expected to cause pain or distress (infection, surgery, cancer, etc.)
 - The main concepts/goals of the study (gene expression, metabolism, etc.)
 - “3 R’s” Keywords (animal use alternatives, analgesia, anesthesia, refinement, etc.)
- Examples of keywords can be found in various online resources such as AWIC’s [Examples of 3R Keywords](#) or the [National Agricultural Library Thesaurus](#).

DEVELOPING A SEARCH STRING

Think of a search string as a sentence composed of phrases. Each “concept” contains a set of terms/keywords joined by **OR**. The 3 concepts are joined by **AND** to create your search string.



COMBINING THE SEARCH STRINGS:

- **Disease:** “inflammatory bowel disease” OR IBD OR colitis.
- **Animal:** mice OR mouse OR murine OR mus.
- **3Rs:** “animal welfare” OR “humane endpoint*” OR “non-invasive” OR “noninvasive” OR imag* OR biomarker*.

HOW TO CONDUCT A LITERATURE/DATABASE SEARCH

■ **Step 4: Evaluate the Results and Modify as Needed**

- Searches may have to be modified if the search is producing a lot of irrelevant information or not enough results.
- Below are examples of how a search string may be modified:
 - Increase or decrease publication year range.
 - Remove irrelevant keywords/search terms (e.g., instead of searching “Sprague-Dawley rat” just search “rat”)
 - Add more specific search terms to narrow the search (e.g., instead of just using the term “surgery” use “osmotic pump surgery”)
 - Focus on a specific aspect, based on your results (such as imaging)
 - Adjust the search terms according to the results

SEARCH SYNTAX TOOLS VARY BY DATABASE AND INCLUDE

- Truncation: to pick up variants and variant spelling, eg: behav* = behavior, behaviour, behaves, behave, behaving, behaved OR col*r OR col?r = color, colour, collar) Use where appropriate as can cause unintended results (eg: rat* = rat, rats, ratio, ration, rationing, rate, Rattus)
- Boolean Logic: (AND, OR NOT)
- Parenthesis: to nest Boolean concepts, eg: (dog OR dogs OR canine) AND (pain OR distress); this example will return all results that contain at least one of the words in the first set of parentheses AND at least one of the words in the second set.)
- Proximity Operators (some databases do not interpret proximity) (searches for one word within a certain distance of another word. – blood N3 collect* = blood collection, collection of arterial blood, collecting blood)
- Quotation Marks (to keep phrases together in a search, “animal welfare”)

EVALUATE AND REFINE (PART 2)

- If most of the results are relevant, the search strategy doesn't need another concept added.
- If the results are too broad, consider limits: — Publication year. — Specific fields (e.g., title, keywords, abstract).
- Fix what you can — Add a NOT group of things to exclude. — Fix any false hits, where your language may have been misinterpreted, or “unfortunate” truncations.

“GOOD” VS. “BAD” SEARCH

- Bad or unrefined search:
 - Not including search tools/syntax (i.e., Boolean operators, quotation marks etc.)
 - Throwing keywords into the search with no specific order
 - Using only terms like ‘replacement’, ‘reduction,’ ‘refinement’ or ‘alternatives’
- Good or refined search:
 - Synonymous terms grouped with parentheses
 - Use of search tools/syntax
 - Not only using the procedure/method you’re trying to replace

SEARCH EVALUATION ISSUES

- Only one database searched
- Terms only for painful aspects.
- The term “alternative” or phrase “alternatives to animal use” 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 terms listed with no indication of how they were used in a search string (multiple terms dumped into the keywords list; no further context provided in findings)
- Findings simply indicate: “no findings”
- Search terms weak with strong context provided in findings; OR search terms strong with little context provided in findings
- Search doesn't cover adequate time period (5-10 years)

TERMINOLOGY FOR REFINEMENT ALTERNATIVES

- analgesic or analgesia or pain reduction
- anesthetic or anasthetic or anaesthetic
- animal welfare or well-being or wellness or colony management
- assay or technique or method or procedure
- bedding or substrate
- behavior or behaviour or ethology
- blood draw or blood sampling or sample sites (intravenous, tail vein, saphenous vein, etc.)
- challenge method or infection
- environmental enrichment
- euthanasia or humane endpoint
- grimace scales (for pain monitoring)
- handling or humane handling or humane restraint or humane treatment
- husbandry or housing or caging
- imaging or scanning (MRI, magnetic resonance imagery, PET scans, positron emission tomography, CAT scans, bioluminescent scanning)
- injection or injection site
- non-invasive or less-invasive
- pain or stress or distress
- positive reinforcement training or animal training
- refinement
- social housing or group housing
- telemetry device, monitoring device, biotelemetry

TERMINOLOGY FOR REDUCTION ALTERNATIVES

- animal model
- animal study registries
- auto control (using animal as its own control)
- biomarker or biological marker
- computational methods, computational models, in silico
- data repositories or reuse data
- experimental or statistical design (pilot study, variation, sample size, etc.)
- imaging or scanning (MRI, magnetic resonance imagery, PET scans, positron emission tomography, CAT scans, bioluminescent scanning)
- microsampling
- monitoring device or telemetry device, biotelemetry
- pilot study
- reduce or reduction or minimize or “use fewer animals”
- reusing or sharing or repurposing animals (between studies)
- sample size or “number of animals”
- tissue banks
- variation (i.e. minimizing variation among animals in study)

TERMINOLOGY FOR REPLACEMENT ALTERNATIVES

- animal testing alternative or animal use alternative or alternative (useful primarily in toxicology and education)
- cadaver or carcass
- cell culture, cell line
- computer aided instruction, computer assisted instruction
- computational methods or models (in silico)
- computer (simulation or application or model)
- digital imaging
- interactive
- in vitro
- isolated (cell, tissue, organ)
- mannequin or manikin or model (non-animal)
- mathematical (computational biology or model or simulation)
- model (animal, cadaveric, interactive, mathematical, statistical, theoretical), modeling (US spelling or modelling (UK spelling)
- non-animal model
- organ-on-a-Chip or microfluidic device
- organoids or 3-D organoids
- platinated or platinated
- replacement alternatives
- simulation or simulator or trainer • structure evaluated system
- tissue culture or organ culture
- tissue engineering •
- software or video (disc, display)
- virtual (reality)

WSU LIBRARIES RESOURCES: BIOMEDICAL DATABASES

CAB Direct

EMBASE

BIOSIS

PsycInfo

Zoological Record

WSU LIBRARIES DATABASES: BIOMEDICAL DATABASES INCLUDE:

Web of Science

PubMed

Fish, Fisheries and
Aquatic
Biodiversity
Worldwide

CINAHL

Agricola and
PubAg

Oldest citation index for sciences – also tracks number of times other authors have cited the research

Agricola is the largest online database of agricultural literature in the world. Strong focus in the 3Rs.

Subject Coverage of Selected Databases

AGRICOLA	CAB	BIOSIS	EMBASE	MEDLINE
General agriculture	Agriculture	Agriculture	Clinical medicine	Clinical medicine
Animal science	Animal science & production	Aerospace biology	Experimental medicine	Experimental medicine
Chemistry & biochemistry	Crop science	Biochemistry & anatomy	Pharmacology, drugs, potential drugs	Pharmacology
Microbiology	Forestry	Bacteriology (microbiology)	Biochemistry	Microbiology
Cytology	Pest control	Cell biology	Developmental biology	Administration
Human & animal nutrition	Human nutrition	Botany	Forensic medicine	Nutrition
Biotechnology	Biotechnology	Anatomy	Health economics	Nutrition
Physiology	Pesticides	Physiology	Occupational health	Anatomy & physiology
Veterinary Medicine	Veterinary Medicine	Clinical med.	Toxicology	Veterinary Medicine
Wildlife	Machinery and buildings	Pathology		Occupational medicine
Zoology	Economics	Biophysics		Toxicology
Entomology		Toxicology		Other medical topics
Other topics		Other topics		



Google Scholar

	Pros	Cons
Access	<ul style="list-style-type: none">• Free to use• Can set up library access links in settings	<ul style="list-style-type: none">• No full-text access to most articles
Content	<ul style="list-style-type: none">• Indexes wide range of literature• Grey literature	<ul style="list-style-type: none">• Not organized by experts• No easy way to identify 'peer-reviewed' source
Searching	<ul style="list-style-type: none">• Easy to use if you're familiar with Google• Google algorithm ranks relevance to you	<ul style="list-style-type: none">• Can't search by material type or subject area• Very limited filters• Google algorithm ranks relevance to you