Animal Welfare Information Center Bulletin

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CONGRESS IN SESSION

- **H.R.503 To amend the Horse Protection Act to prohibit the shipping, transporting, moving, delivering, receiving, possessing, purchasing, selling, or donation of horses and other equines to be slaughtered for human consumption, and for other purposes.**

Introduced on February 1, 2005, by John Sweeney (R-New York) and referred to the House Committee on Energy and Commerce. Related bill: S.1915

Amends the Horse Protection Act to prohibit the shipping, transporting, moving, delivering, receiving, possessing, purchasing, selling, or donation of horses and other equines to be slaughtered for human consumption.

Authorizes the Secretary of Agriculture to detain for examination, testing,

(Legislation cont'd p. 18)

ALSO IN THIS ISSUE...

Searching Bibliographic Databases for Alternatives

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Introduction

Federal animal welfare regulations require that an investigator performing procedures that are painful or distressful to the animal provide assurance that no alternatives exist to the painful procedure. According to USDA Animal Care Policy 12 (http://www.aphis.usda.gov/ac/policy/policy12.pdf), "We believe that the performance of a database search remains the most effective and efficient method for demonstrating compliance with the requirement to consider alternatives to painful/distressful procedures." To provide this assurance, the investigator must provide, except in unique circumstances, a written narrative that describes the literature databases searched (Medline, EmBase, Biosis Previews, Agricola, etc.), the keywords or strategy used to retrieve information, and a brief description of why alternatives are or are not available.

The first step in conducting a search is to have a clear understanding of the objectives and methods of the proposed study. Too often investigators ask for alternatives to very specific procedures without putting the procedure in the context of an experiment. To properly look for alternatives, you have to know why the procedure is being performed and what the expected outcome is.

If an information specialist is conducting the search, there should be direct communication between the investigator and the information provider. This avoids misinterpretation by third party participants. Once all pertinent information is at hand, the literature search strategy can be developed. It is convenient to conduct a search using the 3Rs as a guide. The first part of the search will examine the literature closely related to the proposed study for refinements to the proposed methods, for methods or models that reduce the number of animals used, and for previously published experiments that the proposed work might duplicate (this is a requirement of the U.S. Animal Welfare Act (http://www.aphis.usda.gov/ac/awa.html#2143). The terminology used in this part of the search will come from the area of study. Depending on the type of research, it might also be important to look for appropriate anesthetics, analgesics, methods of restraint, etc.

In the second part of the strategy, the remaining R—replacement—is considered. There may be some overlap with the first part of the search, in that alternative animal models may already be identified. If not, then alternative animal and nonanimal models should be considered.

In the following tutorial, we will begin with a short introduction to the basic concepts involved in searching electronic databases. We will then discuss development of the search strategy and the terminology that may be useful. As a tie-in to this, we will list resources that can be consulted for appropriate terminology. This will lead us to consider how to analyze a research protocol to extract information and formulate questions that will guide our selection of terminology and development of the strategy. Based on the protocol, we will choose appropriate databases and then execute the search.

General overview of searching concepts

Regardless of the database system used, there are basic searching concepts that remain constant.

What is truncation?

Depending upon the database system being searched, symbols such as the * or ? may be used at the end of a search term to retrieve many word variations to the original term.

Example of truncation at the end of the term:

train* will retrieve *train, training, trainer, trained, trainers, trainees,* etc.

behav? will retrieve *behavior, behaviour, behaving,* etc.

Dangers of Truncation:

Truncation can result in retrieval of irrelevant information. Be cautious when using truncation. For example if you truncate the word *rat** you will receive information containing words such as *rate, ratio, rations, ratification,* etc.

What about spelling?

When searching multiple databases, it is important to include American and British (which generally includes Canadian and European) spellings of English language words to ensure retrieval of all materials. This is especially important in the biomedical sciences.

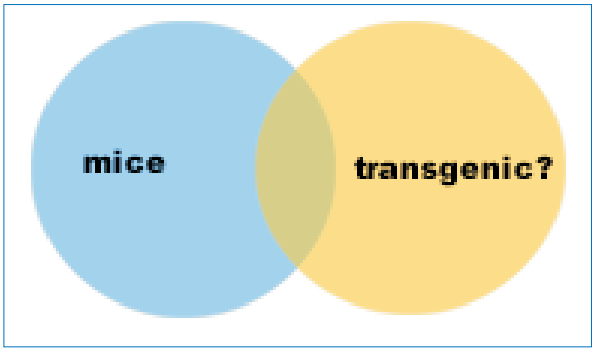
Examples include:

anesthesia, anasthesia, anaesthesia
behavior, behaviour
estrogen, oestrogen
hematology, haematology
pediatric, paediatric
tumor, tumour

What is boolean logic?

Use of connecting words (operators) such as AND, OR, NOT, to either expand or narrow a search.

AND is used to find information containing both search terms linked by the operator. This is a way of narrowing your search results.For example, to find information about use of transgenic mice: Each circle represents the set of documents containing one of the terms. The shaded area indicates the documents retrieved that include both terms —***mice* and *transgenic?***.



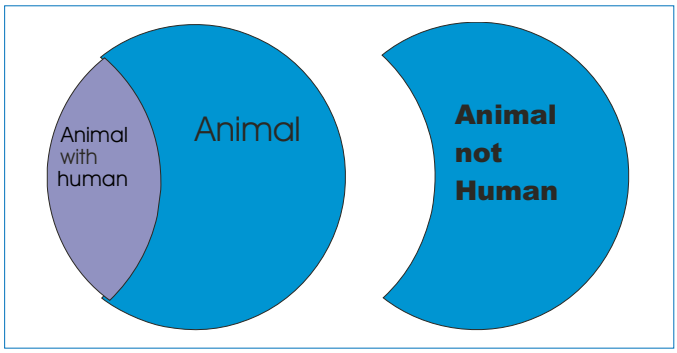
OR is used to find information containing either one or both of the search terms. This is a way of expanding your search results.

For example, to find information referring to *pain*, *distress* or both terms: Each circle and the overlapping area represents the set of documents containing one or both of the terms. As a result this will find all documents that refer to the word ***pain?***, all documents that refer to the word *distress?* and all documents that refer to both terms.

NOT is used to find information that does not contain a term. This is another way of narrowing the search. Be careful, however, because relevant information may be lost.

For example, to find animal studies but not human studies:

animal? not human
This removes citations containing the word human, however, comparative studies of humans and animals will also be removed. Use NOT with plenty of caution!



A Few More Tips

- Determine possible synonyms for each concept and decide where truncation should be used.
  For example: heart, cardiac, cardiovascular
  xylazine, rompun
  blood collection, blood sampling
  euthan? (euthanasia, euthanize)

Searching cont'd on p.9

An Alternative's Search Example for Advanced Trauma Life Support Training

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Trauma training centers use dogs and pigs to teach advanced trauma life support procedures. This training is critical to keeping doctors and nurses skilled in emergency medical procedures that are performed on patients within the first critical hour after traumatic injury.

Dr. S. Breager uses pigs and dogs in his advanced trauma life support training course. All procedures are conducted on anesthetized animals. When the training session is complete, all animals are euthanized.

The Institutional Animal Care and Use Committee has requested Dr. Breager to determine if any nonanimal methods could be used in the class.

DISCUSSION

There is potential for nonanimal methods and models where training is involved. The search for possible alternatives would include models, manikins, simulations, cadavers, virtual reality trainers, etc. Once the search is complete, the scientist/educator must determine whether the alternative is appropriate for use within their particular protocol.

Database Selection

- MEDLINE(R)—years of coverage 1966-2003
- NTIS—years of coverage 1964-2003
- FEDRIP—current up to September 2003
- Biosis Previews—years of coverage 1969-2003
- EMBASE—years of coverage 1974-2003
- Gale Group Health & Wellness —years of coverage 1976-2003
- ELSEVIER BIOBASE—years of coverage 1994-2003
- SciSearch Cited Ref Sci—years of coverage 1990-2003
- Current Contents Search—years of coverage 1990-2003
- Pascal—years of coverage 1973-2003

Developing the Strategy

As described in detail earlier in this training module, the search for alternatives is conducted in a two- phase approach—phase 1, addressing Reduction and Refinement aspects of alternatives and phase 2, addressing Replacement. This teaching protocol would *not* be considered unnecessarily duplicative because there are always new personnel to train and emergency medical skills that need to be maintained and enhanced.

When developing any search strategy, keep different concepts separate as you create search sets. [A search set is a specific term or grouping of terms sent to the database as a query.] Separating concepts into discrete sets allows for flexibility in using terms as the strategy develops. Each concept (in this case, set) will be explained in detail below step by step. All sets will be located in figure 1.

Set 1 (S1)
We start the search by looking for literature concerning the proposed training using animal models. This addresses phase 1 (reduction and refinement) aspects of our alternatives search. Terms for phase 1 of the search come from the protocol. In this case, we will use the terms such as *ATLS*, *trauma*, *emergency medicine* and *life support* in set 1.

In the search strategy on figure 1, *train?* (The *?* is a truncation mark used to retrieve word variations—train, training, etc.) has resulted in the retrieval of 338,276 citations containing synonymous search terms for *ATLS* or *trauma* or *emergency medicine*. The (W) is a With command that connects the terms in the order that they are written, thus resulting in citations that contain *emergency medicine* or *life support*.

Because of the vast amount of information available in the area of ATLS and emergency medicine, another searching feature available on many database systems is used in set 1. Using field limiters, we will now ask the database to limit the terms *ATLS* or *emerg?(w)medic?*, etc. to the title (ti) of the article, or the descriptors (de) or identifiers (id) added by the database vendor. This is another powerful tool that allows us to focus the search to a small subset of a topic.

Set 2 (S2)
In set 2 of the strategy, synonymous terms for training have retrieved 1,236,484 citations. Again, due to the vast amount of information in the area of training, the limiters of /ti,de,id have been applied to limit the terms to the title, descriptors and identifiers. Even so the set is still very large. Further narrowing of the search occurs in subsequent sets.

Set 3 (S3)
Set 3 in figure 1 has results from synonymous terms for different animal models that are known to be used in trauma training and has retrieved 2,096,305 citations. One good way to get a handle on what information is out there and the amount is to conduct a simplified version of the search on just one database. This way, you will know whether it is appropriate to use limiters or not.

Set 4 (S4)
We can now combine the three sets to retrieve only citations that contain all of those concepts. Combining sets 1, 2

and 3 using the AND boolean operator narrows the number of relevant citations to 336 (fig. 1).

Set 5 (S5)

Because we are searching in multiple databases, there will be some duplication of citations. Using a tool found in Dialog, we can remove the duplicates and end up with 34 unique citations that appear in set 5. A few representative citations appear at the end of this article. The results of this set are surprising in that there are so few citations that have information on the use of dogs, pigs, cats, goats or ferrets in trauma training. Intuitively this does not seem to be possible. This may be a topic that is not written about in the manner that it was searched for or indexed in the database. So let's continue on to see what we get.

Set 6 (S6)

We are now ready for phase 2 of the search. We can look for any replacement alternatives that might be useful to the investigator. In this part of the search, we use terminology to look for replacements to the animal model (fig. 1). Again, we add this new concept to our strategy as a discrete set. Not surprisingly, animal models (may allow refinement to the proposed model) will still be retrieved because *model?* was used, but many of the citations will focus on alternative inanimate models and methods to teach trauma training, such as manikins, simulators, and virtual reality.

In this set you will note that the term *alternative?* is used. This term is useful in teaching and toxicology protocols because much research has gone into developing nonanimal teaching and testing methods.

Set 7 (S7)

Now we combine the concepts of trauma (set 1), training (set 2), and alternatives (set 6) to form set 7. We are looking for possible models, manikins, virtual reality or simulation, etc., that may be useful to enhance or modify the methods by which the teaching of trauma training is conducted.

Set	Terms Searched	Items
• S1	(TRAUMA OR EMERG?(W)MEDIC? OR LIFE(W)SUPPORT OR ATLS) / ti,de,id	338,276
• S2	(TRAIN? OR TEACH? OR EDUCAT? OR INSTRUC?) / ti,de,id	1,236,480
• S3	(DOG OR DOGS OR CANINE OR PIG OR PIGS OR PORCINE OR PIGLET? OR GOAT? OR CAPRINE OR CAT OR CATS OR FELINE OR FERRET?) / ti,de,id	2,096,305
• S4	S1 AND S2 AND S3	336
• S5	RD (unique items)	34
• S6	(ALTERNATIVE? OR MODEL? OR SIMULAT? OR CADAV? OR CARCAS? OR SOFTWARE OR VIDEO? OR INTERACT? OR DIGITAL? OR VIRTUAL OR MANNEQUIN? OR MANIKIN? OR COMPUTER?) / ti,de,id	7,835,313
• S7	S1 AND S2 AND S6	2,368
• S8	RD (unique items)	980
• S9	S8 and PY>1995	574

Figure 1—Separate concepts into discrete sets to develop a proper search strategy.

Set 8 (S8)

This set removes the duplicates from set 7. The set is still large.

Set 9 (S9)

Because set 8 is still quite large, another limiter is used to narrow the results. In this case the publication year (PY) limiter is used. By limiting the search to PY>1995, the search system will retrieve publications from the year 1995 to the present. At times your results may contain information that is older than that because of when it was entered into the database. When you are looking for alternatives that include current advances in modeling, computers, or imagery, it is very appropriate to limit by year. In the case of many research protocols that do not include such advances, this may not be true, because you want to see all that has been done. Often times in research protocols, vital information can be obtained from older literature.

The set 9 results contain 574 citations. This may sound like a lot, but it does not take long to browse through and pull out material relevant to trauma training. You may want to impose other limits (such as title only), but please refrain from doing this, because you don't want to narrow your search too much and exclude beneficial information. You will get a few citations that are not relevant, but that is common when conducting comprehensive literature searches. In figure 1b, you will see sample citations from set 9. The citations contain possible replacement alternatives such as computer simulations, 3D simulators, virtual reality, human cadavers, intubation simulators and manikins. Along with the various nonanimal alternatives found in S9, you will also find surveys of trauma training programs that have involved some of the alternative methodologies.

Although all of the results may not be relevant to the protocol at hand it is the responsibility of the principal investigator or trainer to determine what is relevant.

Sample Citations from Set 5 and Set 9

- **Definitive surgical trauma care live porcine session: a technique for training in trauma surgery.**

Jacobs L M; Lorenzo C; Brautigam R T
Connecticut medicine 2001, 65 (5) p265-8.

BACKGROUND: **A new Definitive Surgical Trauma Care course was developed to educate surgeons in operative management of injuries. The course consists of an interactive CD-ROM and a live porcine animal laboratory**.

METHOD: A five-hour session was conducted. Penetrating injuries to stomach, bowel, diaphragm, spleen, pancreas, kidney, ureter, inferior vena cava, liver, and heart were created by the senior surgeon and managed by the junior surgeon. Participants rated their expertise in 26 maneuvers pre- and post-lab. The evaluation scale used was: no prior experience; able to perform skill with assistance; proficient at procedure; able to teach procedure to another surgeon.

RESULTS: In 26 procedures, a maximum score of 78 was possible. There was an increase from pre- to post-session scores of 22.6 for PGY-4 residents (n = 3); 23.3 for PGY-5 residents (n = 4); 11.25 for fellows (n = 4); and 0 for attendings (n = 4).

CONCLUSION: The operative animal session had the greatest educational benefit among surgeons without formal training in trauma surgery. By exposing them to a range of trauma-induced surgical conditions, the DSTC course develops their operative repertoire and should increase their effectiveness in managing trauma patients.

Descriptors: *Education, Medical, Graduate—methods—MT; *Surgery—education—ED; ***Swine** ; Traumatology—education; Wounds, Penetrating—surgery

- **Trauma life support education: a didactic and caprine laboratory course for Nigerian physicians.**

Tortella B J; Swan K G; Donahoo J S; Tischler C; Marangu J A; Orjiako A B; Sharples C; Swan B C; Hill D W
Injury (ENGLAND) Jun 1996, 27 (5) p329-31.

The purpose of this study was to introduce the principles of initial hospital assessment and treatment of injured patients, tailored to the facilities and resources available in Nigeria. A 3-day didactic and laboratory course was presented by four trauma surgeons. The didactic session stressed the initial assessment and treatment of injured patients. **The caprine laboratory taught the performance of common resuscitation manoeuvres: cricothyroidotomy, tube thoracostomy, i.v. cut-down, diagnostic peritoneal lavage, etc.** The mean pre-course test score was 49.3 percent and the mean post-course test score was 69.5 percent; 93.5 percent of the 124 participants increased their test scores.

Descriptors: *Developing Countries; *Education, Medical, Continuing; *Resuscitation —education—ED; *Traumatology—education—ED ; **Goats**; Nigeria; Resuscitation—methods—MT; Traumatology—methods—MT; Triage

- **The use of advanced simulation in the training of anesthesiologists to treat chemical warfare casualties.**

Berkenstadt Haim; Ziv Amitai; Barsuk Daphna; Levine Inbal; Cohen Amir; Vardi Amir
Anesthesia and analgesiaJun 2003, 96 (6) p1739-42.

Training anesthesiologists to treat nerve gas intoxication in a mass casualty scenario is a complicated task. The scenario is an unfamiliar medical situation involving the need to decontaminate patients before providing definitive medical treatment, and the need for physical protection to the medical team before decontamination. We describe the development of a simulation-based training program. In one site of a virtual hospital, anesthesiologists were trained in initial airway and breathing resuscitation before decontamination while wearing full protective gear. In another site, they were trained in the treatment of critically-ill patients with combined conventional and chemical injuries or severe intoxication. **Intubation simulators of newborn, pediatric, and adult patients, advanced full-scale simulators, and actors simulating patients were used**. Initial airway, breathing, and antidotal treatment were performed successfully, with or without full protective gear. The gas mask did not interfere with orotracheal intubation, but limited effective communication within the medical team. Chemical protective gloves were the limiting factor in the performance of medical tasks such as fixing the orotracheal tube. Twenty-two participants (88%) pointed out that the simulated cases represented realistic problems in this scenario, and all 25 participants found the simulated-based training superior to previous traditional training they had in this field. Using advanced simulation, we were able to train anesthesiologists to treat nerve gas intoxication casualties and to learn about the limitations of providing medical care in this setting. IMPLICATIONS: Advanced medical simulation can be used to train anesthesiologists to treat nonconventional warfare casualties. The limitations of medical performance in full protective gear can be learned from this training..

Descriptors: *Anesthesiology—education—ED; *Chemical Warfare; *Chemical Warfare Agents —poisoning—PO; *Patient Simulation ; Antidotes—administration and dosage—AD; Antidotes—therapeutic use—TU; Communication; Emergency Medical Services; Patient Care Team; Poisoning —therapy—TH; Questionnaires; Respiratory Tract Diseases—chemically induced—CI; Respiratory Tract Diseases—therapy—TH

- **Evaluation of a teaching laboratory using a cadaver model for tube thoracostomy(1).**

Proano Lawrence; Jagminas Liudvikas; Homan Clark S; Reinert Steve
Journal of emergency medicine 2002, 23 (1) p89-95.

A prior study evaluated the efficacy of a dog laboratory to teach residents chest tube thoracostomy. This study evaluated a similarly structured program using human cadavers. A prospective repeat measure study of chest tube thoracostomy placement training was performed in a university laboratory setting using human cadavers. Ten Emergency Medicine residents were given a written pretest, followed by training. Resident attempts were then timed. The following day, a repeat test was administered. Three weeks later, a third written post-test was conducted. The written test scores improved for every participant. Mean times for procedure completion improved from 86 sec to 34 sec during the first session, and remained stable over 4 attempts from 30 sec to 32 sec during the second session. This approach to teaching clinical procedures should be considered for Emergency Medicine residency programs and for continuing education courses that emphasize procedural skills.

Descriptors: *Emergency Medicine—education—ED; *Hospitals, Teaching—methods—MT; *Thoracostomy—education—ED ; Cadaver; Internship and Residency; Models, Anatomic; Program Evaluation; Prospective Studies ■

Examples of Reduction, Refinement and Replacement from the British Home Office Animals Inspectorate

This [article] provides some insights into how the Animals (Scientific Procedures) Inspectorate's assessment and inspection processes "add value" to the regulatory system by ensuring that the 3Rs are properly reflected in all licensed work. The 3Rs are widely recognised as the different facets of alternatives to animal use in scientific procedures: refinement of procedures to minimise suffering, reduction in the number of animals used for a particular purpose, and replacement of animal use wherever possible.

A major proportion of Inspectorate resources is dedicated to ensuring that the 3Rs are properly applied during the consideration of applications for project licence authorities, and that opportunities are taken for continuous improvement whilst work is in progress.

The Home Office maintains no central system for quantifying, collating and publishing all of the relevant outcomes. Instead, this appendix offers a sample of ten cases dealt with during 1998. The cases are considered to be typical rather than exceptional.

Only summaries can be provided and, even then, certain details (such as the species involved in some cases) have been omitted. This is for two reasons: the publication of further details would contravene section 24 of the Animals (Scientific Procedures) Act 1986, which prohibits the disclosure of information given in confidence; and some details, when linked with descriptions of the objectives and methodologies, would make the sources and applicants too readily identifiable to close observers. This goes beyond the constraints of Section 24. As described in the following paragraphs, the reputation of individual scientists should not be held up for implied criticism when they have fully engaged with the Inspectorate in applying both the letter and spirit of the law.

These examples demonstrate the value of the breadth and depth of knowledge and expertise within the Inspectorate, and the consultancy and negotiating skills required by inspectors to catalyse the necessary changes to requests for project licence authorities and to work in progress (as new technologies, knowledge and research strategies emerge). They also illustrate the research community's preparedness to adopt more refined research methods. In each case, the improvements were agreed with the scientists; in none was it necessary for the Secretary of State to impose the changes; and no improvement was the subject of representations by the applicants. It is also of note that, in a proportion of cases, the quality of the science was also enhanced as a result of applying the 3Rs.

Applicants and researchers with existing authorities are already aware of the necessary constraints on using protected animals and are alive to the importance and value of the 3Rs - not just in terms of animal welfare but as an adjunct to good science. The cases represented here cannot therefore be construed as critical (in the individual or general case) but as exemplifying the "added value" of a Government body with responsibility for the protection of animals used for experimental or other scientific purposes against unnecessary suffering.

The mandatory local ethical review processes, required at each designated establishment with effect from 1 April 1999, will provide additional resources and assistance to applicants, and licensees, to ensure that the 3Rs are properly reflected in programmes of work.

These cases focus on refinement and reduction. It is more difficult to find good examples of replacement since, when replacement alternatives are known to exist, formal requests are seldom made for project licence authorities. It is not possible to calculate how many animals were spared (or experienced reduced suffering or improved welfare) as a result of the Inspectorate's intervention. Nor is it possible to estimate the total effect of:

- scientists' own considerations;
- local ethical review process and peer reviews;
- the inputs of named persons under the 1986 Act, statisticians or others; or
- the practical insights gained as the research progressed.

Whilst these cases are presented as typical, the numbers in each vary enormously and it is therefore impossible to extrapolate the likely outcomes to the over-1100 new applications considered by the Home Office during 1998.

Case 1 Models of liver disease

The assessment of a project licence application identified newly published knowledge that cast doubt on the scientific validity and relevance of some of the proposed animal models. Although the area of interest was well defined, it was less clear what the specific objectives and hypotheses to be tested were, or whether the use of symptomatic animals could be justified.

Two of the proposed animal models were removed from the proposed plan of work (halving the numbers of animals required, from 240 rats per year to 120). The objectives were clarified and limited to the generation of the fundamental knowledge needed to underpin the development of improved clinical treatments. More humane endpoints were introduced to obviate the need for significant suffering to be produced or tolerated.

Case 2 Development of novel surgical treatments

A proposal was considered for a programme of work to look at a new, minimally invasive surgical treatment in a sheep model of human vascular disease. The proposed endpoint for some animals was death from progression of the induced disease process.

An analysis of the diagnostic technologies used by others in the field identified diagnostic systems that would allow the natural history of the disease to

be imaged non-invasively and allow animals to be humanely killed before significant adverse effects became evident. The collection of serial data was introduced to allow the disease process to be tracked over time in individual animals, rather than requiring that several animals be killed at different time points.

Consequently, when final authorities were negotiated, the number of animals required was reduced by about 30% (a reduction of about 10-15 animals per year) and the endpoints were refined. Initial authorities were restricted to a small-scale pilot study to demonstrate that the proposed new treatment was likely to be efficacious before any large-scale study was approved.

Case 3 Environmental enrichment

During an ongoing programme of work, opportunities were sought to refine the care and housing of surgically-prepared rodents used for long-term studies. In this case, it was the inspection programme, rather than the assessment system, which produced the benefits.

Opportunities were identified for environmental enrichment and improved restraint protocols. Within the establishment, the pre-existing culture of care is now reflected in a welfare group established actively to seek similar improvements in other research programmes.

Case 4 Acute toxicity testing

Various other cases of improvements to project design, leading to improved practices and the refinement of endpoints, resulted from the review of research records. (Again, this was during visits of inspection, rather than the assessment of applications.) For example, examination of records of acute toxicology procedures at a number of establishments was performed to identify refinement opportunities. By adjusting the time of dosing, it was possible to ensure that any signs of toxicity were more likely to be observed and dealt with during the normal working day. Observation schedules were also revised to ensure that adversely affected animals were less likely to escape detection; and consideration was given to the humane killing of animals deemed unlikely to survive until the next scheduled observation.

Case 5 Respiratory disorders

One proposal involved a study of respiratory disorders requiring the use of surgically prepared animals (the surgery having been performed on clinical grounds by veterinary surgeons). Assessment of the application identified scope for improvement in the experimental design and statistical analyses.

A 25% reduction in the maximum number of animals to be used (from 16 to 12) was achieved. Further reductions are expected as a result of an agreement that serial data would be collected: the use of additional animals will not be necessary once the desired effect is confirmed or refuted.

Case 6 In vitro alternatives

The assessment of an application, which in part involved a type of insect feeding and the generation of particular tissues for laboratory use, identified that replacement alternatives had been developed elsewhere (though not widely publicised). The total number of mice, rats and guinea pigs required for use under project licence authority was consequently reduced by 150 per year (from 200 to 50). Material from animals humanely killed by Schedule 1 methods is, however, still required.

Case 7 Application of new surgical technologies

Two research groups, independently researching different aspects of the application of a new surgical technology for the treatment of the same type of disease process, were identified and persuaded to collaborate by sharing their ideas, resources, expertise and data.

Consequently, a single, common programme of work emerged using only half of the 70 or so animals originally proposed for the separate studies, and generating additional information relevant to the interests of both research groups. This illustrates one of the advantages of having a central Inspectorate to assess proposed programmes of work: it helps to identify related programmes of work and any resulting opportunities for collaboration or other ways of reducing animal use.

Case 8 Drug dependency study

A protocol using rodents to study aspects of drug dependency had been designed to minimise numbers by re-using individual animals on several occasions on a 'mild' protocol. Each animal would have experienced drug withdrawal signs between studies, but there was no scientific need for any animal to experience these adverse effects.

The Inspectorate considered that the suffering would be minimised by not allowing the proposed re-use (and the concomitant withdrawal signs). This did, however, require that a larger number of animals be used (probably up from about 40 to 80 per year). Each animal is now used on a single occasion and then humanely killed, with no animal experiencing withdrawal distress.

This example highlights the fact that reduced suffering sometimes has to be balanced against an increase in the number of animals to be used.

Case 9 Disease control study

An application was considered for an efficacy study of a potential veterinary pharmaceutical. The plan of work and protocol were similar to those used by collaborators of the applicant in related studies overseas. Despite this, the use of untreated controls challenged with micro-organisms was

considered inappropriate (comparison with an established treatment was preferred), as was a request to house animals in conditions in breach of Ministry of Agriculture, Fisheries and Food welfare codes.

The study design was further improved by intensifying the observation schedules and reducing the duration and severity of signs to be tolerated by animals before they were withdrawn from the study.

Case 10 Radiation biology study

The need for some of the control groups requested in a 'fundamental science' study was questioned. The animals would have died from radiation effects or inter-current infection. The use of such groups may have been appropriate for late-stage evaluation of potential novel treatments, but were considered unnecessary in this study.

The control data were not essential to test the main hypotheses and the number of rodents to be used on the programme of work was therefore reduced by about 25% (down by around 500 animals per year). The reductions were in the protocols likely to cause the most suffering.■

New Lancet Offers Painless Bleeding Technique

By Laura McGinnis

For allergy sufferers, the word "goldenrod" may evoke images of discomfort. But for mice and medical researchers, the word may soon be a symbol of relief. "Goldenrod," the name of a new lancet developed by Agricultural Research Service scientists, is being lauded as a humane and painless tool to draw blood from laboratory mice.

Mice are indispensable participants in biomedical research, and their comfort is a priority for those who work with them. But collecting blood samples can be a difficult process.

Traditionally, drawing blood from the mouse's cheek has required a deft and practiced hand. The Goldenrod lancet makes the process much easier. Named for its inventors (ARS microbiologist William Golde, MEDIpoint engineer Peter Gollibin, and ARS research leader Luis Rodriguez), the lancet bypasses the shortcomings of traditional methods.

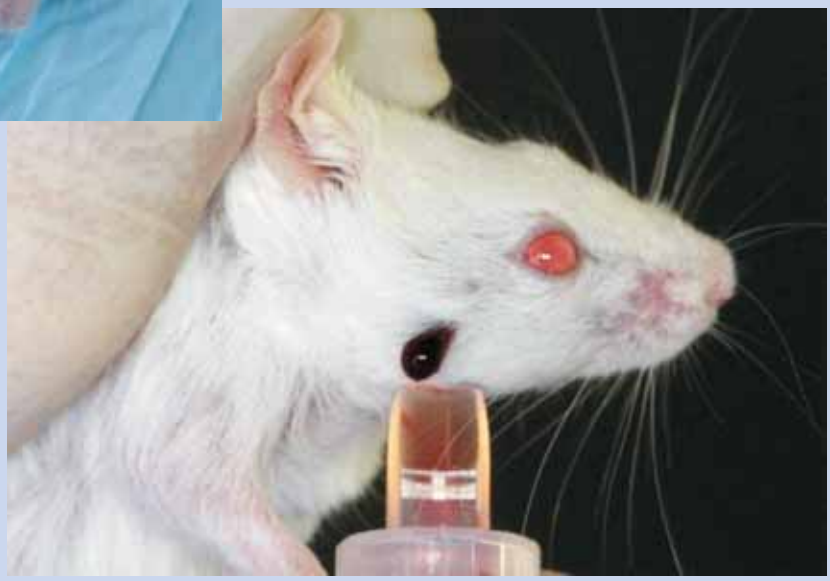
Medical manufacturer MEDIpoint, of Mineola, N.Y. (http://www.medipoint.com/), helped design the product, which is modeled on the lancets used for humans. The Goldenrod draws four to 10 drops of blood from the mouse, while causing minimal discomfort. Golde compares the process to the "thumb sticks" diabetics use to test their blood sugar levels.

Repeated tests show that mice experience greater ease with the Goldenrod lancet than with alternative methods. In addition, the Goldenrod is safe, inexpensive and easy to use. Its many advantages have won praise from the medical community for the ARS scientists at the Plum Island Animal Disease Center, Orient Point, N.Y.

The Federal Laboratory Consortium honored the team with an Award for Excellence in Technology Transfer in a Sept. 15, 2005, ceremony. This award recognizes researchers who bring their federally developed technology to the market.

ARS is the U.S. Department of Agriculture's chief in-house scientific research agency.

More information, including demonstration videos, is available at **http://www.medipoint.com/html/animal_lancets.html**



Veins draining the eye and submandibular area meet at the rear end of the cheek pouch providing a convenient and consistent source of blood

Searching cont'd from p.2

- Pay attention to descriptors or other terminology from relevant citations that might improve the search.
- For new, recently developed, or rapidly changing technologies (for example, virtual simulators, laboratory equipment, transgenics), consider limiting the search by article publication year. This will weed out references to computer software/hardware that is obsolete, outdated transgenic techniques, etc.
- If you are having difficulty in paring down the amount of information retrieved, consider limiting search terms to the title or to fields used to add indexing or thesaurus terms such as descriptors, keywords, or identifiers. But, be aware that while this will ensure a more targeted search it might exclude useful information.

  For example: (dog or dogs or cani?)/ti,de,id
  This will search the database for the terms dog, dogs, canine, canines, canid, canids, canis, etc. but only if they appear in the article title field, descriptors or identifiers fields.

The Alternatives Search Strategy

When preparing to conduct a literature search, certain information must be known. This can come from a protocol form or discussion with the investigator. As mentioned before, direct dialogue between the information specialist and the investigator is preferred to avoid any misinterpretation of the proposed research.

Information needed by information specialist or searcher

No matter how it is obtained, the information should include:

- Title of animal study protocol Providing the title of the protocol may provide some keywords.
- General area of study (drug testing, cardiology, toxicology, fetal alcohol syndrome, lipid metabolism, etc.).
- Type of protocol Is the proposed study a research, teaching, or testing protocol?
- Proposed animal species The animal model may be used as a keyword in the reduction and refinement phase of the search. At times the animal species is not initially used in the search in order to determine whether the study can be done in alternate models. Is there a unique quality or usefulness about your chosen species that warrants its selection? Providing this may provide additional keywords or eliminate the need to search for other possible models being used.
- Describe your experimental protocol including objectives and endpoints This section should succinctly outline the scientific plan and direction of the experiment.
- Identify the systems or anatomy involved in the study (lung, central nervous system, kidney, etc.).
- List any drugs or compounds used in procedures (anesthetics, analgesics, test compounds, etc.).
- Describe the methods and procedures using animals and the relevance to the study, paying particular attention to those procedures that may cause pain or distress to the animal.
- List any potential alternatives (3Rs of Reduction, Refinement and Replacement) (alternate models, modified techniques, housing modifications, modified restraint, in vitro methods, computer simulations, etc.).

Developing the search strategy

It is convenient to develop the search using the 3Rs as a guide. Search strategies for alternatives may be divided into two phases reduction and refinement and replacement.

Phase I: Reduction and refinement–citations pertinent to the field of study or the animal procedure

The first part of the search will examine the literature closely related to the proposed study for refinements to the proposed methods, information on methods, models, or background material that might reduce the number of animals used, and to see if the proposed work duplicates previously published research. If the investigator has published previous literature, this is a good time to read abstracts of his or her previous work and become familiar with terminology used to describe the study and to note what terms were used by database vendors to index the abstract. Upon completion of Phase I, the information specialist should have a basic understanding of the research area including: (1) the literature published in the particular field, (2) the techniques used, and (3) the commonly used species. The information specialist is now ready to search for possible replacement alternatives.

Phase II: Replacement-use of nonanimal or alternative animal models

In the second part of the strategy, the remaining R—replacement—is considered. There may be some overlap with the first part of the search, in that alternative animal models may already be identified. If not, then alternative mammalian and nonmammalian models should be considered, as well as nonanimal models. The following questions may be used to assist in the search for replacement alternatives:

- Are there in vitro techniques that may reduce or replace the number of animals used (for example, chorioallantoic membrane assay, use of primary cultured hepatocytes)?
- Are there any alternative animal models (invertebrates, fish, protozoa, etc.)?
- Have any computer simulations or statistical models been developed that relate to the study?

Terminology

Alternative Terms: Refine and Reduce

The phrase animal testing alternatives is used as an indexing term by AGRICOLA, MEDLINE, and other databases but fails to retrieve much useful information. Using the term alternative? as part of the strategy, especially for research protocols, is, by and large, useless.

In general, the terminology used in this part of the search will come from the area of study and from the literature describing a proposed technique or approach. For example, killing rats to obtain bone samples for determination of bacterial infections might be refined by using a noninvasive imaging method to detect lesions. This would also allow for a reduction in the number of animals. Important terms would be lesion, bone infection, (*assess?* or *monitor?* or *diagnos?*), *imaging*, etc.

Depending on the type of research, it might also be important to look for appropriate anesthetics, analgesics, methods of restraint, etc. Also remember to include both American and British spelling of words—for example, anesthesia, anaesthesia, anasthesia. It is also useful to determine that any anesthetics or analgesics that are going to be administered do not interfere with any of the physiological variables that are being measured.

Remember to consult with the database help screen for information on how to search phrases on your specific platform.

A sampling of other useful terms (? indicates truncated word stem) includes:

analgesi? anestheti? anasthe? anaesthe?
tranquiliz? sedative
euthan?
pain? distress?
monitor? assess? diagnos?
restrain? immobil?
endpoint? biomarker?
train? (positive reinforce?)
animal welfare
assay? technique? method? proced?
environ? enrich? toy toys play?
behav? well-being
model?
statistic? (experimental design)
model models (animal model)
pain (control relief recogni? assess?)

Alternative Terms: Replacement

Below is a short list of useful terms/phrases for finding replacement alternatives. Add your own!

model? or isolated or vitro or culture? or cell line
fish or cephalopod?
simulat? or digital or interact? or virtual
animal testing alternative?
invertebrate?
fish or cephalopod?
simulat?
software
virtual (surger? or reality)
mannequin? or manikin? or cadaver?
plastinat?

When in doubt, check a thesaurus!!

AGRICOLA Thesaurus for Animal Use Alternatives
http://www.nal.usda.gov/awic/alternatives/altfact.htm

MeSH Browser (from Medline/PubMed) is designed to help quickly locate descriptors of possible interest and to show the hierarchy in which descriptors of interest appear.

http://www.nlm.nih.gov/mesh/MBrowser.html

Protocol Analysis

In this section, we will look at the analysis and search strategy development for two very different types of protocols. The research protocol examines the use of rats for developing osteomyelitis prevention strategies.

Analyze a protocol to determine the information needed to conduct a literature search.

This section presents an abridged version of a research protocol containing crucial elements of the proposed activity. The protocol will be analyzed for relevant concepts that may allow for the implementation of the 3Rs—reduction of animal numbers, refinement of painful/distressful procedures, and replacement with nonanimal/cell culture methods.

Protocol Title

Development of an animal model of acute osteomyelitis to test prevention strategies

Objective/Hypothesis

To develop a method to prevent trauma-induced osteomyelitis.

The environment of an open fracture can be manipulated in both a salutary and degratory fashion with respect to the establishment of acute osteomyelitis. In this study, two compounds will be tested for their abilities to affect the development of *Staphylococcus aureus* osteomyelitis in a rat model. L-fucose should decrease and arachidonic acid should increase the propensity toward infection in comparison with controls.

Materials and Methods

1. Animals. Albino Sprague-Dawley rats will be used.
2. Bacteria. Strain SMH of *Staphylococcus aureus*

Pain Alleviation

The rats will be anesthetized with a cocktail of 1.5 ml ketamine and 1.5 ml xylazine and 0.5 ml acepromazine given at a dosage of 0.5 to 0.7 ml/kg. If the plane of anesthesia is too light as determined by a positive toe pinch reflex, one half the original cocktail dose or isoflurane may be given. Yohimbine may be given to hasten recovery. Buprenorphine will be given up to 3x/day if an animal shows signs of pain.

Establishment of infection

The tibia is exposed and a wound is created in the bone with a dental burr. The wound is inoculated with *S. aureus* or *S. aureus* with L-fucose or arachidonic acid, allowed to incubate, and rinsed with sterile saline. The wound is sutured closed. The animals are killed at various times over several weeks, tibias removed, and examined to track development of osteomyelitic lesions.

Discussion

The search strategy will be developed to find answers to questions posed by the protocol.

What are the main concepts to be considered in the search strategy?

★ animal models of osteomyelitis
★ in vitro models
★ noninvasive diagnostic techniques
★ confounding effects, if any, of anesthetics and related drugs

The purpose of this protocol is to develop a model that can be used to test chemicals for their ability to prevent osteomyelitic lesions from developing in bones following trauma. The first question then is: Are there other animal models that may be more suitable for testing potential therapeutics or that more closely resemble the human condition? A corollary to this is: **Is there useful information on the proposed model that might allow the use of fewer animals or might reduce the pain suffered by the animals?** A different model might allow the investigator to use fewer animals or reduce pain, while refinements made to the proposed model, if available, might reduce animal pain or animal numbers.

The logical next question is: **Are there any in vitro methods that might allow for early screening of potential therapeutics**? While animals will have to be used at some point in the drug development scheme, a validated in vitro assay will allow the investigator to quickly screen numerous chemical moieties for therapeutic potential using few or no animals. Screening assays allow the testing of tens to thousands of compounds using cells grown in culture or tissues harvested from humanely killed animals.

In the proposed experimental design, animals will be killed at predetermined time points and examined for development of lesions. While this approach provides definitive assessment of the bones, noninvasive diagnostic techniques may be available that will provide equally definitive data. The third question then is: **Are noninvasive diagnostic techniques available?** This approach allows far fewer animals to be used over the course of the experiment.

Finally, it is always useful to determine if the anesthetics, analgesics, or compounds used to hasten recovery from a sedative (in this case, yohimbine), might exert their own influence on the experimental outcomes. So our final question is: **Do the proposed anesthetics, analgesics, or ά 2-adrenergic antagonist (yohimbine) pose a confounding influence on the outcome?**

Databases

Because we will be looking for biomedical (related to the research) and veterinary (related to the animals being used) information, we will include Medline, EmBase, Agricola, CAB, and Biosis.

Developing the Strategy

While we could certainly begin the search with any of our questions, a good place to start the search will be to look in the literature for information concerning the proposed experiment, in this case the use of arachidonic acid or L-fucose as agents to facilitate or inhibit the development of osteomyelitic lesions in rats. This allows us to determine if the experiment is duplicative (remember, unnecessary duplication is not allowed under the U.S. Animal Welfare Act) and also to provide the investigator with any additional background information on the chosen model. This may give the investigator a better idea of the variablity to expect in the model and choose appropriate animal numbers. Terms for this part of the search will come from the protocol. In this case, we will use the terms *osteomyelitis*, *arachidonic acid*, and *L-fucose*.

The Search Strategy

Set	Terms Searched	Items
S1	OSTEOMYELIT?	37,339
S2	L-FUCOSE OR ARACHIDONIC ACID	128,060
S3	S1 AND S2	27
S4	RD (unique items)	15

Figure 1. Separate concepts into discrete sets

When developing any search strategy, it is always a good idea to keep different concepts separate as you create search sets. [A search set is a specific term or grouping of terms sent to the database as a query.] Separating concepts into discrete sets allows for flexibility in using terms as the strategy develops. In figure 1, *osteomyelit?* (The ? is a truncation mark used to retrieve word variations–osteomyelitis, osteomyelitic, etc.) is set 1 (S1) and has resulted in the retrieval of 37,339 citations containing our search term; *L-Fucose or arachidonic acid* is set 2 and has retrieved 128,060 citations. We can now combine these two sets to retrieve only those citations that contain both of our concepts. Combining set 1 with set 2 winnows the number of relevant citations to 27 found in set 3. Because we are searching in multiple databases, there will be some duplication of citations. Using a tool found in Dialog, we can remove the duplicates and end up with 15 unique citations that appear in set 4. A few representative citations appear at the end of this article.

In this case, it appears that the use of arachidonic acid in facilitating the establishment of disease is already an established protocol. But, this does not mean that the investigator is unnecessarily duplicating earlier research. It may be justified by the need to establish or validate the model in this particular laboratory. This information might still prove useful to the investiga-

The Search Strategy

Set	Terms Searched	Items
S5	ACUTE (3N) S1	2346
S6	STAPH? (W) AUREUS	168,795
S7	S5 AND S6	489
S8	RD (unique items)	291
S9	TRAUMA? OR POSTTRAUMA?	448,998
S10	S1 AND S6 AND S9	269
S11	RD (unique items)	174

Figure 2. Developing the search strategy

tor in properly designing the experiment. For the information specialist, the descriptors assigned to these citations allow us to become more familiar with the terminology that will allow us to pick appropriate search terms. This is especially important if the searcher is unfamiliar with the topic.

The next phase of the search (figure 2) will look for general information related to models of acute osteomyelitis. In this part of the search, we will not include the facilitating agents as we want to broaden the scope of the search. In this way, models using a different approach will be retrieved. This might allow a more appropriate model to be uncovered in the literature or might provide other information that will allow the investigator to refine the proposed model. But, terms related to the type of osteomyelitis will be included. In this case, the investigator is interested in trauma-induced acute osteomyelitis caused by *Staphylococcal aureus (S. aureus)*. Again, we will add these new concepts to our strategy as discrete sets. Set 5 shows why this is useful. In set 1 (see figure 1), we searched for any information related to osteomyelitis and found 37,339 citations; in set 5 we now want to limit our search to acute osteomyelitis. This is done by simply telling the database system to look at set 1 and cull articles in which the word *acute* appears within 3 words of the term *osteomyelitis*. This will retrieve phrases such as *acute osteomyelitis* and *acute models of osteomyelitis*. We have now pared the relevant information to 2,346 citations that appear in set 5. Because this particular research is interested in lesions caused by *S. aureus*, we add set 6 and retrieve 168,795 citations. In set 7, we combine set 5 and set 6 to retrieve 489 citations that contain information on *S. aureus*-induced acute osteomyelitis. Removal of duplicate citations in set 8 reduces this number to 291. In general, the information found includes a mix of both animal and a few in vitro models. Not surprisingly, articles on diagnostic techniques were also found. Remember, the purpose of this section is to retrieve information that will give background information on the proposed model or uncover better models. Sample citations are found at the end of this article.

In the previous sets, we focused on general models of osteomyelitis, now we will narrow our focus to osteomyelitis caused by trauma or posttrauma events. We create set 9 by searching the databases for the terms *trauma?* or *posttrauma?*. As before, the terms are truncated to allow retrieval of all variations of the words–*traumatic*, *posttraumatic*, etc. We now combine set 9, our trauma terms, with set 6 (*S. aureus*) and set 1 (*osteomyelitis*). This will retrieve citations on *S. aureus* and its implications in trauma-induced osteomyelitis (set 10 and set 11 (duplicates removed). Because we are trying to find information that might help refine the proposed model, we will allow the retrieval of citations that concern chronic models or acute hematogenous osteomyelitis (osteomyelitis caused by a blood-borne infection). Sample citations can be found at the end of this article.

We are now ready to look for any in vitro or nonanimal models that might be useful to the investigator (fig. 3). In this part of the search, we now use terminology to look for replacements to the animal model. Not surprisingly, animal models will still be retrieved, but most citations will focus on minimal animal use (animals needed to harvest cells or tissue) or no animal use. The term *vitro* will look for in vitro techniques, but we will also include the term *culture* to retrieve tissue or cell culture methods. Finally, we will use various operators to look for methods using isolated bone or tibias (another culture technique). This string is found in set 12.

The Search Strategy

Set	Terms Searched	Items
S12	VITRO OR CULTURE OR ISOLATE? (4N) (BONE OR TIBIA)	3,554,863
S13	S1 AND S12	2,545
S14	S6 AND S13	696
S15	RD (unique items)	477
S16	S9 AND S15	27
S17	S15 AND (VITRO OR CULURE)/TI,DE,ID OR ISOLATE?(4N)(BONE OR TIBIA))	233

Figure 3. Developing the search strategy

As we did before, we narrow set 12 by combining it with set 1 (*osteomyelitis*) and find 2,545 citations in set 13. We narrow again with set 6 and find 696 citations in set 14; duplicate removal creates set 15 containing 477 unique citations. This is actually not a difficult number of titles to peruse but we will see if any papers in this area include trauma (set 9). Including set 9 substantially narrows the field to 27 records (set 16). However, none of these records were useful and generally included our search term "culture" in relation to cultures of *S. aureus* and not cell or tissue culture techniques. This is one of the pitfalls of this kind of searching.

To circumvent this, we will now introduce another searching feature that is available on many database systems. Using field limiters, we will now instruct the database to limit the terms *vitro* and *culture* to the title (ti) of the article, or the descriptors (de) or identifiers (id) added by the database vendor. This is another powerful tool that allows us to focus our search to a small subset of a topic. We will continue to allow

the *isolated bone or tibia* search string to appear anywhere in a record, that is, title, abstract, or descriptors. When we reexamine set 15 (in vitro models of *S. aureus*-induced osteomyelitis-477 citations), we now reduce the number of records to 233 (set 17). Sample citations are found after this article.

Now we can look for information on osteomyelitis diagnostic methods (fig. 4).The protocol calls for animals to be killed at various timepoints and necropsied. However, the use of imaging techniques or physiological biomarkers could lead to the use of fewer animals. In set 18, we use a variety of terms commonly used to index this literature. These include: *imag?* that will retrieve information on *imaging*, *imaged* or *image*; *marker?* and *biomarker?* to include plurals; *noninvasive*; *MRI* to pick up articles using the abbreviation for *Magnetic Resonance Imaging* (our term *imag?* will pick up the phrase); and *tomograph?* to retrieve information on various types of tomography. We will also include terms for the type of procedure being performed–in this case diagnostics. The terms will include the truncated form of *diagno?* to retrieve *diagnostic*, *diagnostics*, *diagnose*, etc. The term *assess?* is also used to retrieve articles using *assess*, *assessment*, *assessed*, etc. Finally, these are linked to our other concepts of osteomyelitis (set 1) and *S. aureus* (set 6) with the AND operator. This tells the databases that relevant citations must contain all of these concepts to be retrieved. This set retrieves 75 citations; sample citations are at the end of this article.

In the last question to be examined, we will determine whether any of the preanesthetics, anesthetics, analgesics or anesthetic antagonists might confound the expected outcome (fig. 4). The drugs are listed in set 19 and are combined first with the osteomyelitis set (set 1). Nothing useful was found in set 20. Next we determine if the drugs might interact with the treatment drugs–arachidonic acid or L-fucose. The results are 153 citations in set 22. Sample citations are found at the end of this article.

In this tutorial, the number of sample citations is small. In reality, the information specialist would provide all pertinent citations to the investigator. By discussing the protocol with the investigator, the information provider can examine all the citations retrieved at each stage of the search and download those that will be most useful to the investigator. The idea is not to overwhelm the scientist with so much information as to render it useless, but to provide a good review of the literature on all aspects of the proposed experiment.

The Search Strategy

Set	Terms Searched	Items
S18	(IMAG? OR MARKER? OR BIOMARKER? OR NONINVASIVE OR MRI OR TOMOGRAPH?) AND (DIAGNO? OR ASSESS?) AND S1 AND S6	75
S19	KETAMINE OR XYLAZINE OR ISOFLURANE OR ACEPROMAZINE OR BUPRENORPHINE OR YOHIMBINE	72,600
S20	S1 AND S19	7
S21	S2 AND S19	234
S22	RD (unique items)	153

Figure 4. Developing the search strategy

Sample citations from Set 4

Arachidonic acid facilitates experimental chronic osteomyelitis in rats.
Rissing JP; Buxton TB; Fisher J; Harris R; Shockley RK
Infect Immun 1985, 49 (1) p141-4.
Arachidonic acid was used as a facilitating agent in experimental rat Staphylococcus aureus osteomyelitis and compared with the more commonly used agent, sodium morrhuate. The injection of arachidonic acid or sodium morrhuate and S. aureus into rat tibiae caused increased quantitative bacterial bone counts, gross bone pathology, roentgenographic changes, and weight loss. The doses required to produce these changes appeared to be lower for arachidonic acid.
Descriptors: *Arachidonic Acids—Toxicity—TO; *Osteomyelitis—Etiology—ET ; Disease Models, Animal; Osteomyelitis—Pathology—PA; Osteomyelitis —Radiography—RA; Rats; Sodium Morrhuate—Toxicity—TO; Staphylococcal Infections—Complications—CO; Staphylococcus aureus—Pathogenicity—PY; Tissue Culture

Study on experimental osteomyelitis in mice.
YOKOYAMA TAKASHI (1)
Journal of Tokyo Medical College, 1989, 47(1), .91-104.
Abstract: Osteomyelitis, a representative refractory infectious disease in the field of orthopedics, is liable to develop into a prolonged and chronic disease. In order to investigate the pathogenesis of osteomyelitis, attempts have been made to produce experimental animal model of the purulent osteomyelitis, however ideal model has not been developed. The present paper reports that a mouse model of experimental osteomyelitis was established successfully by injection of Staphylococcus aureus with arachidonic acid as a sclerosing agent directly into the medullary cavity of the tibia of mice with a microsyringe. By injecting both 105.6 CFU of Staphylococcus aureus No.28 and 31.5ng of sodium salt of arachidonic acid, the optimal condition for the formation of osteomyelitis in this model, the localized purulent osteomyelitis which closely resemble the human disease radiologically and histologically was fully recognized. For the first 2 weeks, the mice received both of the agents showed a statistically higher amount of prostaglandin in the tibia compared with the group of the staphylococci alone. In the leukopenic mice due to cyclophosphamide, the osteomyelitis occured in 90% of the mice by an intramedullary inoculation of 104.2 CFU of Staphylococcus aureus without use of the sclerosing agent. The evaluation method of the osteomyelitis was contrived by the score expressing the lesion of the osteomyelitis numerically in terms of its radiological, bacteriological and histological appearance, and the relative severity which was calculated from each score of the three findings made it possible to evaluate the osteomyelitic lesion quantitatively. It was made possible to compare the rate of formation and the severity of the osteomyelitis among experimental groups with a high accuracy, especially through the three criteria for determining the formation of osteomyelitis, based on the soft X-ray findings and the relative severity.

Sample citations continued on next page

Descriptors: mouse (animal); osteomyelitis; Staphylococcus aureus; experimental disease; X-ray inspection; vitamin F; polyene; aliphatic carboxylic acid; unsaturated carboxylic acid

Broader Descriptors: Myomorpha; Rodentia; Mammalia; Vertebrata; animal; inflammation; disease; infectious disease; bone disease; bone and joint disease; bone marrow disease; hematologic disease; Staphylococcus; Micrococcaceae; bacterium; microorganism; model; radiographic inspection; nondestructive inspection; inspection; fatty acid; carboxylic acid;

Sample citations from Set 8

The effect of wound environment on the incidence of acute osteomyelitis.

Evans RP; Nelson CL; Harrison BH

Clin Orthop 1993, (286) p289-97.

A model was developed to identify and compare the local wound factors that induce acute osteomyelitis in a prospective, controlled investigation. When compared with wounds containing either virulent bacteria or dead bone, statistical analysis disclosed a significant increase in the incidence of osteomyelitis when virulent bacteria and dead bone were combined. The incidence of osteomyelitis in wounds containing an inoculated, hematoma-filled dead space was significantly less when compared with wounds containing dead bone and virulent bacteria. The incidence of osteomyelitis is significantly less when a nonvirulent strain of bacteria is substituted for a virulent strain. Although rigid internal fixation increased the incidence of osteomyelitis to 100% and long-term antibiotic therapy decreased the incidence, these changes were not statistically significant. These data allow the authors to predict the relative risk of osteomyelitis when these wound factors are present. The prevention of osteomyelitis depends on the clinical identification and modification of these local wound factors.

Descriptors: *Models, Biological; *Osteomyelitis—Physiopathology—PP; *Wounds and Injuries—Physiopathology—PP ; Acute Disease; Ceftriaxone—Therapeutic Use—TU; Osteomyelitis—Drug Therapy—DT; Osteomyelitis—Microbiology—MI; Prospective Studies; Rabbits ; Risk; Staphylococcus aureus—Pathogenicity—PY; Virulence; Wounds and Injuries—Microbiology—MI

CAS Registry No.: 73384-59-5 (Ceftriaxone)

A new model for posttraumatic osteomyelitis in rabbits.

Eerenberg JP; Patka P; Haarman HJ; Dwars BJ

J Invest Surg 1994, 7 (5) p453-65.

A new animal model for posttraumatic osteomyelitis was designed. This model mimics the pathogenesis of the human disease more accurately than models presently available. Femora of New Zealand white rabbits were exposed at the greater trochanter and a stainless steel rod was inserted into the marrow cavity. A Staphylococcus aureus suspension was placed in and around a bone defect, which was drilled midshaft. The disease was evaluated by clinical observation and roentgenographic, hematologic, bacteriologic, and histologic parameters. Osteomyelitis developed in all 24 infected rabbits. None of the five rabbits receiving only an intramedullary rod developed an osteomyelitis. This model proves that an experimental posttraumatic osteomyelitis associated with a foreign body can be reliably induced, even when no infection-promoting chemical agents, small inoculum of bacteria, or minimal bone trauma is present.

Descriptors: *Disease Models, Animal; *Femur Neck—Injuries—IN; *Foreign Bodies —Complications—CO; *Osteomyelitis; *Prostheses and Implants—Adverse Effects—AE; *Staphylococcal Infections ; Bone Marrow—Injuries—IN; Bone Marrow—Microbiology—MI; Bone Marrow —Pathology—PA; Equipment Contamination; Femur Neck—Surgery—SU; Osteomyelitis—Etiology—ET; Osteomyelitis—Pathology—PA; Osteomyelitis —Radiography—RA; Rabbits; Reoperation; Staphylococcal Infections —Etiology—ET; Staphylococcal Infections—Pathology—PA; Staphylococcal Infections—Radiography—RA

Sample citations from Set 11

An experimental model of post-traumatic osteomyelitis in rabbits.

Worlock P; Slack R; Harvey L; Mawhinney

Br J Exp Pathol (ENGLAND) 1988, 69 (2) p235-44

An experimental model of a contaminated open fracture, using the tibia of male New Zealand white rabbits, is described. Post-traumatic osteomyelitis can be reliably induced in this model, with no systemic ill-effects. The characteristic bacteriological, radiological and histological findings are described. Inoculation of the fracture site with Staphylococcus aureus in a concentration of 10(6) bacteria caused osteomyelitis in two out of five rabbits. When the concentration of inoculum was increased to 10(7) organisms, osteomyelitis was seen in four out of five rabbits. No cases of infection were seen in the control animals. This is a simple and reliable model for studies into the prevention and treatment of post-traumatic osteomyelitis.

Tags: Animal; Male; Support, Non-U.S. Gov't

Descriptors: *Disease Models, Animal; *Fractures, Open—Complications—CO; *Osteomyelitis—Etiology—ET ; Bone and Bones—Pathology—PA; Fracture Fixation, Intramedullary; Neutrophils—Pathology—PA; Osteomyelitis—Pathology—PA; Osteomyelitis —Radiography—RA; Rabbits; Staphylococcal Infections—Complications—CO; Tibial Fractures—Complications—CO; Tibial Fractures—Radiography—RA

Chronic staphylococcal osteomyelitis: a new experimental rat model

Spagnolo, N. Greco, F.; Rossi, A.; Ciolli, L.; Teti, A.; Posteraro, P.

Infection and immunity 1993. 61 (12) p. 5225-5230.

A rat model of chronic staphylococcal osteomyelitis was developed. Fibrin glue (5 microliters) and Staphylococcus aureus [2x10(6) CFU/5 microliters] were inoculated into the proximal metaphysis of the tibia. The rats were killed at intervals of between 1 and 6 months, and the tibias were removed. Induced lesions were evaluated by radiographic, macroscopic, and histological examinations and bacterial counts. Roentgenograms revealed osteomyelitis in more than 90% of the tibias. Gross bone pathology revealed skeletal deformation, new bone formation, abscesses, and draining skin fistulas in more than 80% of cases. Histological examination revealed osteomyelitis in more than 90% of cases, and bacterial counts were positive in 86% of cases. Only fibrin glue (5 microliters) was inoculated into controls. Controls showed no osteomyelitic lesions, and counts were negative in seven of eight control tibias. The main feature of this model is the use of fibrin glue instead of the sclerosing agents and foreign bodies used in other models. The model reproduces lesions similar to those of human posttraumatic osteomyelitis and can be reliably used in pathophysiological and therapeutic studies.

Descriptors: rats - disease models - staphylococcus aureus - osteomyelitis;

Sample citations from Set 17

Application of a rat osteomyelitis model to compare in vivo and in vitro the antibiotic efficacy against bacteria with high capacity to form biofilms.

Gracia E; Lacleriga A; Monzon M; Leiva J; Oteiza C; Amorena B

J Surg Res 1998 , 79 (2) p146-53

A rat experimental osteomyelitis model was used to study the efficiency of antibiotics on biofilm bacteria adhered to implants in relation to the efficiency obtained in vitro. In the osteomyelitis model, 10(4) bacteria of the strain variant used for the in vitro studies (a slime-producing variant of Staphylococcus aureus) were inoculated into the rat tibia at surgery, after implanting a stainless steel canula precolonized for 12 h with this strain. After 5 weeks, a 21-day antibiotic treatment was applied (using cefuroxime, vancomycin, or tobramycin). Subsequently, implant and tibia were studied for presence of bacteria. In this osteomyelitis model, cefuroxime inhibited bone colonization and reduced the number of bacteria in metal and bone at a higher degree ($P < 0.05$) than vancomycin and tobramycin (the latter antibiotic did not have this reduction effect). The in vitro assay was applied using three concentrations of each antibiotic (8, 100, and 500 microg/ml) and 6-, 24-, and 48-h biofilms. Bacterial viability was evaluated by ATP-bioluminescence after 24 h of antibiotic treatment. In this in vitro assay, cefuroxime significantly ($P < 0.05$) reduced in all cases the number of viable bacteria in biofilms, tobramycin did not affect viability, and vancomycin affected viability except at the lowest concentration used (8 microg/ml, i.e., 8x the minimal bactericidal concentration of this antibiotic) when facing the oldest (48 h) biofilm. These results demonstrate the usefulness of the osteomyelitis model applied in providing evidence for a close correlation between the in vitro and in vivo findings on the effect of three antibiotics under study.

Mechanisms of Staphylococcus aureus invasion of cultured osteoblasts

Ellington J.K.; Reilly S.S.; Ramp W.K.; Smeltzer M.S.; Kellam J.F.; Hudson M.C.

Microbial Pathogenesis 1999, 26/6 (317-323)

Staphylococcus aureus is a bacterial pathogen causing approximately 80% of all cases of human osteomyelitis. This bacterium can adhere to and become internalized by osteoblasts and previous studies indicate that osteoblasts are active in the internalization process. In the current study, we examined the roles of microfilaments, microtubules and clathrin-dependent receptor-mediated endocytosis in the internalization of S. aureus by MC3T3-E1 mouse osteoblast cells. Microfilament and microtubule polymerization was inhibited with cytochalasin D and colchicine. Clathrin-coated pit formation was examined by using the transaminase inhibitor, monodanslycadaverine. The results of this study indicate that mouse osteoblasts utilize actin microfilaments, microtubules and clathrin-coated pits in the internalization of S. aureus; however, microfilaments seem to play the most significant role in the invasion process.

Excretion of urinary hydroxyproline in correlation with severity of induced osteomyelitis in rabbits

ABBAS H L.

JACTA PHYSIOL HUNG 78 (3). 1991. 235-239.

Osteomyelitis was induced artificially by injecting Staphylococcus aureus culture in the tibiae of young rabbits. Weekly estimations of hydroxyproline in urine were done for six weeks. It was found that the osteomyelitic rabbits excreted more hydroxyproline (about 96%) two weeks after the infection in comparison to the control animals and it continued to be very high (about 138%) six weeks after the infection. The results indicate that urinary hydroxyproline reflects degradation of collagen fibers in the bone, and may be an indicator of the severity of the disease.

(99m)Tc-E-selectin binding peptide for imaging acute osteomyelitis in a novel rat model.

Gratz,-S; Behe,-M; Boerman,-O-C; Kunze,-E; Schulz,-H; Eiffert,-H; O'Reilly,-T; Behr,-T-M; Angerstein,-C; Nebendahl,-K; Kauer,-F; Becker,-W. Nucl-Med-Commun. 2001 Sep; 22(9): 1003-13

Nuclear-medicine-communications

INTRODUCTION: In the present study, (99m)Tc-radiolabelled E-selectin binding peptide ((99m)Tc-IMP-178) was investigated for its potential to image acute pyogenic osteomyelitis in a new animal model. Intraindividual comparisons were performed using an irrelevant peptide ((99m)Tc-IMP-100) to demonstrate specificity. METHODS: An acute pyogenic osteomyelitis was induced by injecting 0.05 ml of 5% sodium morrhuate and 5x10(8) CFU of Staphylococcus aureus into the medullary cavity of the right tibia in 16 rats. Sixteen additional rats served as untreated controls. Whole-body imaging of pyogenic (n=4) and untreated (n=4) animals was performed continuously during the first 8 h (12 MBq i.v. of (99m)Tc-IMP-178 and (99m)Tc-IMP-100 for control), and one further single image was acquired after 16 h p.i. Tissue biodistribution studies were performed in 12 rats with an acute pyogenic osteomyelitis and in 12 untreated rats 1, 4 and 24 h after injection. Data of the histological/radiological and haematological investigations were obtained in all animals.RESULTS: Histopathologically, 15 of 16 treated rats (93%) developed an acute pyogenic osteomyelitis showing a major infiltration of the bone marrow by polymorphonuclear leukocytes as well as the formation of sequestra. Haematologically, the number of leukocytes increased by 100%, the lymphocytes by 11% and the granulocytes decreased by 39%. After i.v. injection, (99m)Tc-IMP-178 rapidly cleared from the body resulting in good scintigraphic target-to-background (T/B) ratios. The highest uptake of the tracer in the pyogenic bone was observed at 60 min p.i. (0.43+/-0.02% ID.g-1 for (99m)Tc-IMP-178 and 0.30+/-0.02% ID.g-1 for (99m)Tc-IMP-100), resulting in a higher osteomyelitis-to-healthy collateral ratio with T/B of 2.40+/-0.65 ((99m)Tc-IMP-178) compared with 1.85+/-0.48 ((99m)Tc-IMP-100). No adverse reactions were seen after injection of (99m)Tc-IMP-178. CONCLUSIONS: (99m)Tc-IMP-178 allows imaging of an acute osteomyelitic lesions, presumably by interaction of (99m)Tc-IMP-178 with activated upregulated vascular endothelium.

MJME: *Carrier-Proteins-metabolism; *E-Selectin-metabolism; *Osteomyelitis-radionuclide-imaging; *Technetium-diagnostic-use

MIME: Acute-Disease; Amino-Acid-Sequence; Disease-Models,-Animal; Molecular-Sequence-Data; Osteomyelitis-blood; Osteomyelitis-pathology; Rats-; Rats,-Wistar; Tissue-Distribution

Sample Citations from Set 18

Excretion of urinary hydroxyproline in correlation with severity of induced osteomyelitis in rabbits

ABBAS H L.
JACTA PHYSIOL HUNG 78 (3). 1991. 235-239.
Osteomyelitis was induced artificially by injecting Staphylococcus aureus culture in the tibiae of young rabbits. Weekly estimations of hydroxyproline in urine were done for six weeks. It was found that the osteomyelitic rabbits excreted more hydroxyproline (about 96%) two weeks after the infection in comparison to the control animals and it continued to be very high (about 138%) six weeks after the infection. The results indicate that urinary hydroxyproline reflects degradation of collagen fibers in the bone, and may be an indicator of the severity of the disease.

(99m)Tc-E-selectin binding peptide for imaging acute osteomyelitis in a novel rat model.
Gratz,-S; Behe,-M; Boerman,-O-C; Kunze,-E; Schulz,-H; Eiffert,-H; O'Reilly,-T; Behr,-T-M; Angerstein,-C; Nebendahl,-K; Kauer,-F; Becker,-W. Nucl-Med-Commun. 2001 Sep; 22(9): 1003-13
Nuclear-medicine-communications
INTRODUCTION: In the present study, (99m)Tc-radiolabelled E-selectin binding peptide ((99m)Tc-IMP-178) was investigated for its potential to image acute pyogenic osteomyelitis in a new animal model. Intraindividual comparisons were performed using an irrelevant peptide ((99m)Tc-IMP-100) to demonstrate specificity. METHODS: An acute pyogenic osteomyelitis was induced by injecting 0.05 ml of 5% sodium morrhuate and 5x10(8) CFU of Staphylococcus aureus into the medullary cavity of the right tibia in 16 rats. Sixteen additional rats served as untreated controls. Whole-body imaging of pyogenic (n=4) and untreated (n=4) animals was performed continuously during the first 8 h (12 MBq i.v. of (99m)Tc-IMP-178 and (99m)Tc-IMP-100 for control), and one further single image was acquired after 16 h p.i. Tissue biodistribution studies were performed in 12 rats with an acute pyogenic osteomyelitis and in 12 untreated rats 1, 4 and 24 h after injection. Data of the histological/radiological and haematological investigations were obtained in all animals. RESULTS: Histopathologically, 15 of 16 treated rats (93%) developed an acute pyogenic osteomyelitis showing a major infiltration of the bone marrow by polymorphonuclear leukocytes as well as the formation of sequestra. Haematologically, the number of leukocytes increased by 100%, the lymphocytes by 11% and the granulocytes decreased by 39%. After i.v. injection, (99m)Tc-IMP-178 rapidly cleared from the body resulting in good scintigraphic target-to-background (T/B) ratios. The highest uptake of the tracer in the pyogenic bone was observed at 60 min p.i. (0.43+/-0.02% ID.g-1 for (99m)Tc-IMP-178 and 0.30+/-0.02% ID.g-1 for (99m)Tc-IMP-100), resulting in a higher osteomyelitis-to-healthy collateral ratio with T/B of 2.40+/-0.65 ((99m)Tc-IMP-178) compared with 1.85+/-0.48 ((99m)Tc-IMP-100). No adverse reactions were seen after injection of (99m)Tc-IMP-178. CONCLUSIONS: (99m)Tc-IMP-178 allows imaging of an acute osteomyelitic lesions, presumably by interaction of (99m)Tc-IMP-178 with activated upregulated vascular endothelium.
MJME: *Carrier-Proteins-metabolism; *E-Selectin-metabolism; *Osteomyelitis-radionuclide-imaging; *Technetium-diagnostic-use

Sample Citations from Set 22

Anesthesia-associated depression of peripheral node lymphocyte traffic and antibody production in sheep accompanied by elevations in arachidonic acid metabolites in efferent lymph
Spruck C.H.; Moore T.C. Transplantation Proceedings 1988 , 20/6 (1169-1174).

The present study extends earlier observations of prostaglandin Einf 2 (PGEinf 2) involvement in depression in lymphocyte traffic and accompanying alterations in immune response factors, including involvement of other arachidonic acid metabolites and changes in lymphocyte types and subtypes. Prior studies of arachidonic acid metabolites have involved the use of both barbiturate-halothane and ketamine-xylazine general anesthesias.
Drug Descriptors:* prostaglandin e2; *ketamine—pharmacology—pd; *xylazine—pharmacology—pd
Medical Descriptors: * anesthesia; *antibody production; *arachidonic acid metabolism; *lymph node sheep; nonhuman; intramuscular drug administration; priority journal; complication
CAS Registry Number: 363-24-6 (prostaglandin e2); 1867-66-9, 6740-88-1, 81771-21-3 (ketamine); 23076-35-9, 7361-61-7 (xylazine)

A role for arachidonic acid in general anesthetic action
Denson D D(a); Eaton D C. Society for Neuroscience Abstracts 21 (1-3): p 1833 1995
Registry Numbers: 506-32-1: ARACHIDONIC ACID; 6740-88-1: KETAMINE;
7440-09-7: POTASSIUM; 9001-84-7: PHOSPHOLIPASE A-2
Descriptors: ARACHIDONIC ACID; KETAMINE; POTASSIUM; PHOSPHOLIPASE A-2
Miscellaneous Terms: KETAMINE; MEETING ABSTRACT; MEETING POSTER; PHOSPHOLIPASE A-2; POTASSIUM CHANNEL ■

Grants for Refinements of Animal Studies Available

The ECLAM/ESLAV Foundation is a charitable organisation that funds studies for the discovery, validation and implementation of refinement of the care and use of animals in research. In particular the Foundation funds small studies, up to 20,000 Euros in the following areas:

- Refinement in experimental techniques, anaesthesia and analgesia to reduce pain and distress
- Objective measures of animal welfare
- Studies to ensure scientific basis for housing and husbandry standards
- Validation of environmental enrichment to improve behavioural well being

It is now accepting applications for funding in 2006-2007. For details of the straightforward application process see the attached leaflet.
The Foundation's website can be found at http://www.eclam.eslavfoundation.org
A grant application form is available at http://www.eclam.eslavfoundation.org/applications.htm

United Egg Producers Animal Care Certified Program Adopts Even Higher Standards of Care Research Proves Non-Feed Withdrawal Molts Are Effective

Continuing their commitment to the highest levels of scientific-based care, the United Egg Producers' (UEP) Board of Directors has approved a recommendation from an independent Scientific Advisory Committee allowing only non-feed withdrawal molts.

"Recognizing that this is a major undertaking for the betterment of hens and our industry, our producers have until January 2006 to integrate this newly designed system for molting," said Gene Gregory, vice president of United Egg Producers. "As animal welfare issues continue to be an important and growing concern for consumers, retailers can be assured that eggs carrying the Animal Care Certified seal are from farms following even higher standards for proper hen care."

The new molting guidelines are a giant leap forward for the egg industry and producers will need time to educate themselves on the new methods. After January 1, 2006, only molt programs that provide the hens with nutritionally adequate and palatable feed suitable for a non-producing hen will be allowed to use the Animal Care Certified seal on their packaging. Additionally, all farms must still maintain 100 percent compliance with the Animal Care Certified's strict housing, space, air, feed and water guidelines as well as submitting to annual independent audits from organizations such as the United States Department of Agriculture.

Until recently the only known method to extend the life of a hen and rejuvenate its reproductive cycle was through the use of a feed withdrawal molt. Through UEP-funded research, new methods have been found to induce a successful molt that does not include feed withdrawal. An independent Scientific Advisory Committee of scientists and researchers have reviewed and endorsed these research findings.

Induced molting of egg-laying hens has been used since the very early 1900's. The industry will quickly change this long history by implementing the new guidelines.

The Animal Care Certified program is one of the first and largest nationwide animal welfare programs adopted by the food industry. It provides a set of strict, science-based animal welfare guidelines developed by independent experts that egg producers must adhere to in order to be allowed to use the Animal Care Certified logo. Ninety percent of all shell eggs sold in the U.S. are produced under these guidelines. For more information on the Animal Care Certified egg program, visit www.animalcarecertified.com.

The Animal Care Certified guidelines for responsible, modern-day egg production were established by an independent scientific committee for the United Egg Producers and are supported by the U.S. Department of Agriculture. These guidelines ensure that hens have scientifically recommended space, continuous access to fresh air and water, nutritious food, are kept clean, are protected from other hens, are transported in a safe and protected manner, and their overall welfare is promoted to the best of the producer's ability. Adherence to these guidelines is audited by independent inspectors – most of who are U.S. Department of Agriculture personnel. For more information, please visit www.animalcarecertified.com. ■

USDA's Agricultural Research Service has 264 documents on induced molting available by searching its website at http://www.ars.usda.gov/main/main.htm

AVAILABLE FROM THE ANIMAL WELFARE INSTITUTE

"Variables, Refinement and Environmental Enrichment for Rodents and Rabbits kept in Research Institutions—Making Life Easier for Animals in Laboratories"

You may request a free copy from Dr. Viktor Reinhardt at: viktorawi@yahoo.com

The book is also online at: http://www.awionline.org/pubs/rabrodent/rodrab.html

Also available is a presentation given at the 2006 conference of the Canadian Association for Laboratory Animal Science on "The Overlooked 3rd R: Refinement" at http://www.awionline.org/lab_animals/index.htm

Legislation cont'd from p.1

or the taking of evidence: (1) any horse at any horse show, horse exhibition, or horse sale or auction which is sore or which the Secretary has probable cause to believe is sore; and (2) any horse or other equine which the Secretary has probable cause to believe is being shipped, transported, moved, delivered, received, possessed, purchased, sold, or donated in violation of such prohibition.

- **H.R.1256 To amend the Animal Health Protection Act to exempt certain animal identification information from disclosure under the Freedom of Information Act.**

Introduced on March 10, 2005, by Colin Peterson (D-Minnesota) and referred to the Committee on Agriculture, and in addition to the Committee on Government Reform. On April 4, executive comment was requested from the Department of Agriculture.

Amends the Animal Health Protection Act to exempt certain animal identification information from disclosure under the Freedom of Information Act. Exceptions are made for Limited Release of Information if—(1) the information involves livestock threatened by disease or pest; (2) the release of the information is related to actions the Secretary may take under this subtitle; and (3) the person obtaining the information needs the information for reasons consistent with the public health and public safety purposes of the livestock identification system, as determined by the Secretary. The Secretary of Agriculture shall release information obtained through a livestock identification system regarding particular livestock–(1) to the person who owns or controls the livestock, if the person requests such information; (2) to the Attorney General for the purpose of law enforcement; (3) to the Secretary of Homeland Security for the purpose of national security; (4) to a court of competent jurisdiction; and (5) to the government of a foreign country, if release of the information is necessary to trace livestock threatened by disease or pest, as determined by the Secretary.

Sets forth discretionary and mandatory limited disclosure provisions.

- **H.R.1329 To amend the Lacey Act Amendments of 1981 to treat nonhuman primates as prohibited wildlife species under that Act.**

Introduced on March 16, 2005, by Eddie Bernice Johnson (D-Texas). On March 23, it was referred to the House Resources Subcommittee on Fisheries and Oceans and executive comment was requested from [the Department of the] Interior. This act may be cited as the "Captive Primate Safety Act." Related Bill: S.1509

Amends the Lacey Act Amendments of 1981 to add non-human primates to the definition of "prohibited wildlife species."

- **H.R.1558 To amend title 18, United States Code, to prohibit certain computer-assisted remote hunting, and for other purposes.**

Introduced on April 12, 2005, by Tom Davis (R-Virginia) and referred to the House Committee on the Judiciary. On May 10, it was referred to the Subcommittee on Crime, Terrorism, and Homeland Security. This act may be cited as the "Computer-Assisted Remote Hunting Act."

Amends the Federal criminal code to prohibit and to establish penalties for knowingly making available a computer-assisted remote hunt (i.e., using a computer or other device, equipment, or software to allow a person remotely to control the aiming and discharge of a weapon to kill or injure an animal while not in the targeted animal's physical presence).

- **H.R.1707 To assist in the conservation of rare felids and rare canids by supporting and providing financial resources for the conservation programs of nations within the range of rare felid and rare canid populations and projects of persons with demonstrated expertise in the conservation of rare felid and rare canid populations.**

Introduced on May 17, 2005, by Clay Shaw (R-Florida) and referred to the House Resources Subcommittee on Fisheries and Oceans. This act may be cited as the "Great Cats and Rare Canids Act of 2005."

Directs the Secretary of the Interior to provide assistance for projects for the conservation of rare felids and rare canids. Authorizes the Secretary to convene an advisory group of individuals representing public and private organizations actively involved in the conservation of felids and canids.

Restricts the use of grants for captive breeding or display purposes.

Establishes in the Multinational Species Conservation Fund as a separate account the Great Cats and Rare Canids Conservation Fund.

Defines "rare canid" to: (1) mean any canid species, subspecies, or population that is not native to the United States and Canada, and is included in the threatened or endangered lists of the World Conservation Union, the Convention on International Trade in Endangered Species of Wild Fauna and Flora, or the Endangered Species Act of 1973; and (2) include such a subspecies or population of dhole, gray wolf, Ethiopian wolf, African wild dog, or maned wolf.

Defines "rare felid" to: (1) mean any felid species, subspecies, or population that is not native to the United States and Canada, and is included in the threatened or endangered lists of the World Conservation Union, the Convention on International Trade in Endangered Species of Wild Fauna and Flora, or the Endangered Species Act of 1973; and (2) include such a subspecies or population of lion, leopard, jaguar, snow leopard, clouded leopard, cheetah, or Iberian lynx. Does not include any tiger.

- **H.R.2130 To amend the Marine Mammal Protection Act of 1972 to authorize research programs to better understand and protect marine mammals, and for other purposes.**

Introduced on May 5, 2005, by Wayne Gilchrest (R-Maryland) and referred to the House Committee on Resources. On May 18, it was ordered to be reported by unanimous consent. On July 21, it was placed on the Union Calendar, Calendar No.

112. This act may be cited as the "Marine Mammal Protection Act Amendments of 2005." Related Bill: H.R.4075

Amends the Marine Mammal Protection Act of 1972 (the Act) to grant limited authority for a marine mammal product to be exported from the United States, including in cases where an Indian, Aleut, or Eskimo residing in Alaska exports the animal as part of a cultural exchange.

Makes it unlawful for anyone under U.S. jurisdiction to release any captive marine mammal unless authorized under the Act.

Increases civil fines and criminal penalties, including vessel penalties for violations of the Act.

Directs the Secretary of Commerce (currently, the Secretary of the department in which the National Oceanic and Atmospheric Administration is operating) to carry out a research and development program to devise fishing methods and gear that reduce the incidental taking of marine mammals. Authorizes the Secretary to establish a gear research mini-grant program for the development of such fishing gear.

Applies provisions concerning the incidental taking of marine mammals to all fishing operations (currently, only commercial fishing). Requires take reduction plans to track the number of animals from strategic stocks being incidentally lethally taken or seriously injured each year through recreational fishing (in addition to commercial fishing), and to publish proposals for reducing such incidents within a strategic stock under certain conditions.

Requires research on the nonlethal removal and control of nuisance pinnipeds (seals and sea lions), including the development of new technologies to deter such animals. Authorizes the Secretary to provide a grant to an eligible applicant to carry out a qualified nonlethal control project.

Directs the Secretary to collect and update existing practices and procedures for rescuing and rehabilitating entangled (currently, only stranded) marine mammals (having gear, rope, line, or net wrapped around it). Authorizes the Secretary to enter into entanglement response agreements.

Renews the scrimshaw exemption (allowing the processing and sale of pre-Endangered Species Act ivory) for the 11-year period beginning October 31, 1999.

- **H.R.2206 To amend the Public Health Service Act to establish a competitive grant program to build capacity in veterinary medical education and expand the workforce of veterinarians engaged in public health practice and biomedical research.**

Introduced May 9, 2005, by Charles Pickering (R-Mississippi) and referred to the House Energy and Commerce Subcommittee on Health. This Act may be cited as the "Veterinary Workforce Expansion Act of 2005." Related Bill: S.914

Congress makes the following findings:

(1) Veterinary medicine is an integral and indispensable component of the Nation's public health system. Veterinarians protect human health by preventing and controlling infectious diseases, ensuring the safety and security of the nation's food supply, promoting healthy environments, and providing health care for animals. (2) Veterinarians are essential for early detection and response to unusual disease events that could be linked to newly emerging infectious diseases, such as monkeypox, SARS, and West Nile Virus, or other biothreat agents of concern. (3) There is a need to build national capacity in research and training in the prevention, surveillance, diagnosis, and control of newly emerging and re-emerging infectious diseases. (4) Veterinarians are uniquely qualified to address these high priority public health issues because of their extensive professional training in basic biomedical sciences, population medicine, and broad, multi-species, comparative medical approach to disease prevention and control. (5) There is a shortage of veterinarians working in public health practice. As used in the preceding sentence, the term `public health practice' includes bioterrorism and emergency preparedness, environmental health, food safety and food security, regulatory medicine, diagnostic laboratory medicine, and biomedical research. (6) The Bureau of Labor Statistics expects there to be 28,000 job openings in the veterinary medical profession by 2012 due to growth and net replacements, a turnover of nearly 38 percent. (7) The Nation's veterinary medical colleges do not have the capacity to satisfy the current and future demand for veterinarians and veterinary expertise that is vital to maintain public health preparedness.

SEC. 3. COMPETITIVE GRANTS PROGRAM.

Part E of title VII of the Public Health Service Act (42 U.S.C. 294n et seq.) is amended by adding at the end the following: Subpart 3—Veterinary Medicine

SEC. 771. COMPETITIVE GRANT PROGRAM.

(a) In General- The Secretary shall award competitive grants to eligible entities for the purpose of improving public health preparedness through increasing the number of veterinarians in the workforce.

Also defines eligible entities.

- **H.R.2428 To provide for the protection of the last remaining herd of wild and genetically pure American Buffalo.**

Introduced on May 18, 2005 by Maurice D. Hinchey (D-New York) and referred to the House Committee on Resources. This act may be cited as the "Yellowstone Buffalo Preservation Act."

Prohibits any federal or state government agent from: (1) killing, hazing, or capturing any buffalo on federal land or land held under federal conservation easements; or (2) using any form of bait to lure buffalo from any federal land onto private land until specified duties are accomplished by the Secretary of the Interior and certain other federal agencies. Provides exceptions for: (1) legally-authorized, state-managed buffalo hunts; (2) hazing if a person is physically endangered or property is damaged; (3) National Park Service employees moving buffalo to address physical public safety threats; and (4) certain non-lethal federal research. Establishes criminal penalties and fines for violations of this Act.

Sets forth duties of the Secretary relating to grazing and other matters affecting the Yellowstone buffalo herd that must be accomplished within three years after the enactment of this Act.

- **H.R.2744 Making appropriations for Agriculture, Rural Development, Food and Drug Administration, and Related Agencies for the fiscal year ending September 30, 2006, and for other purposes.**

Introduced June 3, 2005, by Henry Bonilla (R-Texas). Became Public Law No: 109-97.

From the Conference Report:
Section 794- The conference agreement includes language regarding inspection activities under the Federal Meat Inspection Act or the Federal Agriculture Improvement and Reform Act of 1966.

It is the understanding of the conferees that the Department is obliged under existing statutes to provide for the inspection of meat intended for human consumption (domestic and exported). The conferees recognize that the funding limitation in Section 794 prohibits the use of appropriated funds only for payment of salaries or expenses of personnel to inspect horses.
[Editor's note: This amendment (H.Amdt. 236) introduced by John Sweeney (R-New York) prohibits USDA inspection of horses destined for slaughter in American slaughterhouses. It does not prevent the export of horses to Canada or Mexico for slaughter. See H.R. 503 for legislation which addresses horse slaughter in an amendment to the Horse Protection Act.]

- **H.R.3858 To amend the Robert T. Stafford Disaster Relief and Emergency Assistance Act to ensure that State and local emergency preparedness operational plans address the needs of individuals with household pets and service animals following a major disaster or emergency.**

Introduced on September 22, 2005, by Tom Lantos (D-California) and referred to the Committee on Transportation and Infrastructure and the Subcommittee on Economic Development, Public Buildings and Emergency Management. This act may be cited as the "Pets Evacuation and Transportation Standards Act of 2005."

Section 613 of the Robert T. Stafford Disaster Relief and Emergency Assistance Act (42 U.S.C. 5196b) is amended– (2) by inserting after subsection (f) the following:
'(g) Standards for State and Local Emergency Preparedness Operational Plans- In approving standards for State and local emergency preparedness operational plans pursuant to subsection (b)(3), the Director shall ensure that such plans take into account the needs of individuals with household pets and service animals following a major disaster or emergency.'

- **H.R.4075 To amend the Marine Mammal Protection Act of 1972 to provide for better understanding and protection of marine mammals, and for other purposes.**

Introduced on October 18, 2005, by Richard W. Pombo (R-California) and referred to the House Committee on Resources. This act may be cited as the "Marine Mammal Protection Act Amendments of 2005." Related bill: H.R.2130

Amends the Marine Mammal Protection Act of 1972 (the Act) to grant limited authority for a marine mammal product to be exported from the United States, including in cases where an Indian, Aleut, or Eskimo residing in Alaska exports the animal as part of a cultural exchange.

Makes it unlawful for anyone under U.S. jurisdiction to release any captive marine mammal unless authorized under the Act.

Increases civil fines and criminal penalties, including vessel penalties for violations of the Act.

Directs the Secretary of Commerce (currently, the Secretary of the department in which the National Oceanic and Atmospheric Administration is operating) to carry out a fishing gear development program to devise fishing gear and methods that reduce the incidental taking of marine mammals. Authorizes the Secretary to establish a gear improvement mini-grant program for the development of such fishing gear.

Applies provisions concerning the incidental taking of marine mammals to all fishing operations (currently, only commercial fishing). Requires take reduction plans to track the number of animals from strategic stocks being incidentally lethally taken or seriously injured each year through recreational fishing (in addition to commercial fishing), and to publish proposals for reducing such incidents within a strategic stock under certain conditions.

Requires the Secretary to conduct a program on the nonlethal removal and control of nuisance pinnipeds (seals and sea lions), including the development of new technologies to deter such animals. Authorizes the Secretary to provide a grant to an eligible applicant to carry out a qualified nonlethal control project.

Directs the Secretary to collect and update existing practices and procedures for rescuing and rehabilitating entangled (currently, only stranded) marine mammals (having gear, rope, line, or net wrapped around it). Authorizes the Secretary to enter into entanglement response agreements.
Renews the scrimshaw exemption (allowing the processing and sale of pre-Endangered Species Act ivory) for the 11-year period beginning October 31, 1999.

- **H.R.4764 To amend section 1368 of title 18, United States Code, to include rescue dogs in its protection.**

Introduced on February 15, 2006, by Rob Simmons (R-Connecticut) and referred to the Committee on the Judiciary. This act may be cited as the "Canine Volunteer Protection Act of 2006."

From introductory remarks by Mr. Simmons:
The Canine Volunteer Protection Act would give members of volunteer canine search and rescue teams the same protections current law gives other law enforcement animals. This includes both a monetary fine and/or imprisonment of those persons who willfully and maliciously harm any search and rescue dog.

- **S.73 A bill to promote food safety and to protect the animal feed supply from bovine spongiform encephalopathy.**

Introduced on January 24, 2005, by Maria Cantwell (D-Washington) and referred to the Senate Committee on Agriculture, Nutrition, and Forestry. This act may be cited as the "Animal Feed Protection Act of 2005."

Makes it unlawful for any person to introduce into interstate or foreign commerce a covered article that contains: (1) specified risk material from a ruminant, or any material from a ruminant that was in any foreign country when there was a risk of transmission of bovine spongiform encephalopathy (BSE), and may contain specified risk material from a ruminant; or (2) any material from a ruminant exhibiting signs of a neurological disease.

States that the head of a Federal agency may: (1) seize and destroy an article that is introduced into interstate or foreign commerce in violation of this Act; or (2) require any person who is in violation of this Act to cease the violation, to recall any sold article and refund the purchase price, to destroy or forfeit the article to the United States for destruction, or to cease production operations until the head of the appropriate Federal agency determines that there is no longer a violation of this Act. Directs the Secretary of Health and Human Services to provide for related civil and monetary penalties.

Defines "covered article" as: (1) animal feed, nutritional supplement, or medicine; and (2) any other article that is ordinarily ingested, implanted, or otherwise taken into an animal. Sets forth exceptions.

Defines "specified risk material" as: (1) the skull, brain, trigeminal ganglia, eyes, tonsils, spinal cord, vertebral column, or dorsal root ganglia of cattle and bison 30 months of age and older, or sheep, goats, deer, and elk 12 months of age and older; (2) the intestinal tract of any ruminant; and (3) any other material of a ruminant that may carry a prion disease.

- **S.304 A bill to amend title 18, United States Code, to prohibit certain interstate conduct relating to exotic animals.**

Introduced on February 7, 2005, by Frank Lautenberg (D-New Jersey) and referred to the Senate Committee on the Judiciary. This Act may be cited as the "Sportsmanship in Hunting Act of 2005." Related Bill: H.R.1688

Amends the Federal criminal code to prohibit knowingly transferring, transporting, or possessing a confined exotic animal for purposes of allowing the killing or injuring of that animal for entertainment or the collection of a trophy. Provides that such prohibition shall not apply to the killing or injuring of an exotic animal in a State or Federal natural area reserve undertaking habitat restoration.

Permits any person authorized by the Secretary of the Interior, acting through the Director of the United States Fish and Wildlife Service, to: (1) arrest without warrant any person who violates this Act in the presence or view of the arresting person; (2) execute any warrant or other process issued by an officer or court of competent jurisdiction to enforce this Act; and (3) with a search warrant, search for and seize any animal taken in violation of this Act.

Declares that any animal seized shall be held by the Secretary of the Interior or a U.S. marshal and, upon a defendant's conviction, be forfeited to the United States and disposed of by the Secretary.

Permits the Director to use by agreement the personnel and services of any other Federal or State agency to enforce this Act.

- **S.382 A bill to amend title 18, United States Code, to strengthen prohibitions against animal fighting, and for other purposes.**

Introduced on February 15, 2005, by John Ensign (R-Nevada) and passed by the Senate on April 29 without amendment. On May 10, it was referred to the House Judiciary Subcommittee on Crime, Terrorism, and Homeland Security, and in addition, on May 19, to the House Agriculture Subcommittee on Livestock and Horticulture. This act may be cited as the "Animal Fighting Prohibition Enforcement Act of 2005." Related bill: H.R. 817.

Amends the Federal criminal code to prohibit: (1) sponsoring or exhibiting a bird in a fighting venture in a State where it would not otherwise be in violation of the law, only if the person knew that any bird in the venture was knowingly bought, sold, delivered, transported, or received in interstate or foreign commerce for such purpose; or (2) knowingly sponsoring or exhibiting in an animal fighting venture any other animal that was moved in interstate or foreign commerce.

Prohibits knowingly: (1) selling, buying, transporting, delivering, or receiving, for purposes of transportation in interstate or foreign commerce, any dog or other animal to participate in an animal fighting venture; (2) using interstate mail service for commercial speech promoting an animal fighting venture except as performed outside the limits of the States (with an exception for bird fights in States whose laws allow them); or (3) selling, buying, transporting, or delivering in interstate or foreign commerce a knife, gaff, or other sharp instrument to be attached to the leg of a bird for use in an animal fighting venture.

Sets penalties of a fine under the code, two years' imprisonment, or both for violations of this Act. (Repeals conflicting provisions of the Animal Welfare Act.)

- **S.451 A bill to amend the Animal Welfare Act to ensure that all dogs and cats used by research facilities are obtained legally.**

Introduced on February 17, 2005, by Daniel Akaka (D-Hawaii) and referred to the Senate Committee on Agriculture, Nutrition, and Forestry. This act may be cited as the "Pet Safety and Protection Act of 2005."

Amends the Animal Welfare Act to list permissible sources of dogs and cats used by research facilities to include dogs and cats obtained: (1) from a licensed dealer; (2) from a publicly owned and operated pound or shelter that meets specified requirements; (3) by donation from a person who bred and raised the dog or cat and owned it for not less than one year; or (4) from a research facility licensed by the Secretary of Agriculture. Increases monetary penalties for related violations.

Prohibits Federal facilities from purchasing or otherwise acquiring dogs or cats for exhibition purposes except from: (1) the operator of an auction that comports with legal requirements; or (2) a person holding a valid dealer or exhibitor license.

Prohibits dealers from selling or otherwise providing a research facility with random source dogs or cats unless specified certification requirements are met.

- **S.659 A bill to amend title 18, United States Code, to prohibit human chimeras.**

Introduced on March 17, 2005, by Sam Brownback (R-Kansas) and referred to the Committee on the Judiciary. This act may be cited as the "Human Chimera Prohibition Act of 2005." Related Bill: S.1373

Amends the Federal criminal code to prohibit and to set penalties for: (1) creating or attempting to create a human chimera (a being with human and non-human tissue as specified in this Act); (2) transferring or attempting to transfer a human embryo into a non-human womb, or a non-human embryo into a human womb; or (3) transporting or receiving a human chimera.

- **S.975 A bill to provide incentives to increase research by private sector entities to develop medical countermeasures to prevent, detect, identify, contain, and treat illnesses, including those associated with biological, chemical, nuclear, or radiological weapons attack or an infectious disease outbreak, and for other purposes.**

Introduced on April 28, 2005, by Joseph Lieberman (D-Connecticut) and on May 9, placed on Senate Legislative Calendar under General Orders. Calendar No. 97. On July 21, the Committee on Health, Education, Labor, and Pensions Subcommittee on Bioterrorism and Public Health Preparedness held hearings.With printed Hearing: S.Hrg. 109-210. This act may be cited as the "Project BioShield II Act of 2005."

"SEC. 1904. APPROVALS OF CERTAIN DRUGS BASED ON ANIMAL TRIALS.

(a) FEDERAL FOOD, DRUG, AND COSMETIC ACT- Section 505(d) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(d)) is amended by adding at the end the following: 'In the case of drugs and diagnostic devices for use against infectious disease or lethal or permanently disabling toxic biological, chemical, radiological, nuclear, or other substances, when adequate and well-controlled studies of effectiveness in humans cannot ethically be conducted because the studies would involve administering a potentially lethal or permanently disabling toxic substance or organism to healthy human volunteers, and when adequate field trials assessing use of the drug or diagnostic device (in situations such as after accidental or hostile exposure to the substance) have not been feasible or where adequate volumes of human samples for diagnosis from previous exposures is not available, the Secretary may grant approval based on evidence of effectiveness derived from appropriate studies in animals. The Secretary may promulgate regulations establishing standards, criteria, and procedures for use of the authority contained in the preceding sentence.'

(b) PUBLIC HEALTH SERVICE ACT- Section 351 of the Public Health Service Act (42 U.S.C. 262) is amended by adding at the end the following:

'(k) APPROVAL OF CERTAIN PRODUCTS AND DIAGNOSTIC DEVICES BASED ON ANIMAL TRIALS- In the case of biological products and diagnostic devices for use against infectious disease, or lethal or permanently disabling toxic biological, chemical, radiological, nuclear, or other substances, when definitive human effectiveness studies in humans cannot ethically be conducted because the studies would involve administering a potentially lethal or permanently disabling toxic substance or organism to healthy human volunteers, and when adequate field trials assessing use of the drug (in situations such as after accidental or hostile exposure to the substance) have not been feasible, the Secretary may grant approval based on evidence of effectiveness derived from appropriate studies in animals. The Secretary may promulgate regulations establishing standards, criteria, and procedures for use of the authority provided under this subsection.'

SEC. 511. CLINICAL TRIAL GUIDELINES FOR ANTI-INFECTIVES.

(a) IN GENERAL- Not later than 1 year after the date of enactment of the Project BioShield II Act of 2005, the Secretary, acting through the Commissioner of Food and Drugs, shall issue guidelines for the conduct of clinical trials with respect to anti-microbials, including anti-microbials to treat resistant pathogens, bacterial meningitis, acute bacterial sinusitis, acute bacterial otitis media, and acute exacerbation of chronic bronchitis. Such guidelines shall indicate the appropriate animal models of infection, in vitro techniques, and valid microbiologic surrogate markers.

(b) REVIEW- Not later than 5 years after the date of enactment of the Project BioShield II Act of 2005, the Secretary, acting through the Commissioner of Food and Drugs, shall review and update the guidelines described under subsection (a) to reflect developments in scientific and medical information and technology.

TITLE XX—ANIMAL MODELS

SEC. 2001. ANIMAL MODELS FOR CERTAIN DISEASES.

(a) FINDING- Congress finds that the development of well-characterized animal models for identified threat agents is crucial for testing the efficacy of medical countermeasures, and that data is crucial for licensure of products to protect the Nation, particularly those animals genetically designed and bred to mimic the disease or toxic response of humans to a particular biological insult.

(b) ESTABLISHMENT OF WORKING GROUP; GRANTS TO STUDY ANIMAL RESPONSES- Subpart 6 of part C of title IV of the Public Health Service Act (42 U.S.C. 285f et seq.) is amended by adding at the end the following:

SEC. 447C. ESTABLISHMENT OF WORKING GROUP.

(a) IN GENERAL- The Director of the Institute, in consultation with the Assistant Secretary for Medical Readiness and Response of the Department of Homeland Security and the Director of the Centers for Disease Control and Prevention, shall establish a working group to carry out the duties described in subsection (b) (referred to in this section as the "Working Group").

(b) DUTIES- The Working Group shall determine the most pressing scientific gaps in understanding that must be addressed to create accurate animal models used to determine disease processes for agents that threaten humans.

©) MEMBERSHIP- The Working Group shall include not less than one Director of a center in the National Private Research Program.

SEC. 447D. GRANTS TO STUDY ANIMAL RESPONSES.

(a) IN GENERAL- The Secretary, in consultation with the Commissioner of Food and Drugs and the Secretary of Homeland Security, shall—(1) establish and award grants under this section to eligible entities to study the physiological responses of certain animal species to bioterrorism agents and other infectious agents; and (2) coordinate efforts to identify and develop well-characterized animal models, including correlates of protection, when feasible, for categories of infectious diseases, and classes of toxins considered the most likely threats to human populations, as identified as bioterror agents by the Office of Emergency Preparedness and Response of the Centers for Disease Control and Prevention.

(b) ELIGIBILITY; APPLICATION- To be eligible to receive a grant under this section, an entity shall—(1) provide assurances to the Secretary that the entity has a biosafety level 3 or 4 facility that is approved by the Centers for Disease Control and Prevention or has a contractual relationship with such a facility; and (2) with respect to an animal biosafety lab, provide assurances that such lab is in compliance with the Guide for the Care and Use of Laboratory Animals and the Animal Welfare Act (7 U.S.C. 2131 note); and (3) submit to the Secretary an application at such time, in such manner, and containing such information as the Secretary may require.

c) BENEFITS UNDER PROJECT BIOSHIELD-

(1) IN GENERAL- If the Secretary determines that an entity receiving a grant under this section has successfully and thoroughly created an animal model for the purpose of testing and regulating novel countermeasures, such animal model shall be considered a research tool for purposes of receiving the benefits under the amendments made by the Project BioShield II Act of 2005.

(2) CLARIFICATION- An animal model may be developed, and subsequently recommended by the Food and Drug Administration, separately from a countermeasure application so that such animal model is regarded as a research tool for the countermeasure and such Administration may require such recommended animal model in clinical trials to fulfill regulatory requirements.

(d) DEFINITIONS-

(1) BIOSAFETY LEVEL 3 FACILITY- The term "biosafety level 3 facility" means a facility described in section 627.15 of title 32, Code of Federal Regulations (or any successor regulation).

(2) BIOSAFETY LEVEL 4 FACILITY- The term "biosafety level 4 facility" means a facility described in section 627.16 of title 32, Code of Federal Regulations (or any successor regulation).

(3) RESEARCH TOOL- The term "research tool" includes the full range of tools that scientists may use in the laboratory, including animal disease models, cell lines, cell line cultures for the production of biologics, monoclonal and polyclonal antibodies, reagents, drug delivery technologies, vaccine adjuvants, laboratory animals, large animals including nonhuman primates and large animals used for drug production, growth factors, combinatorial chemistry and DNA libraries, antigen libraries, clones and cloning tools (such as PCR or Real Time PCR), methods, laboratory equipment and machines, databases, and other technologies that enable the rapid and effective development of countermeasures, including diagnostics, vaccines, and drugs.

(e) AUTHORIZATION OF APPROPRIATIONS- There are authorized to be appropriated such sums as may be necessary for the development of animals models described under subsection (a)(2).

SEC. 2002. ANIMAL MODELS FIVE-YEAR INITIATIVE.

(a) FINDINGS- Congress finds the following:

(1) The United States Government has made an unprecedented commitment to expanding and advancing the biomedical research program at the National Institutes of Health, and the success of the Government's efforts is contingent upon the availability of quality resources that will enable and enhance all research endeavors ranging from the most basic and fundamental to the most highly innovative.

(2) Biomedical research has relied on such quality resource, the National Primate Research Centers Program, for more than 40 years, for research models and expertise with non-human primates.

(3) The National Primate Research Centers Program is comprised of a network of 8 National Primate Research Centers (referred to in this section "NPRCs") that provide centralized housing and care for non-human primates, as well as the facilities and support necessary for research conducted with such primates. Scientists from almost every State use the resources of the NPRCs for a vast array of studies.

(4) As a result of expanded investment in biomedical research from 2000 to 2005, the demand for the resources of the NPRCs has increased significantly, but several important impediments have become barriers to successful non-human primate research, including the limited number of such primates available, the lack of infrastructure to breed and house animals for research, and the need for trained staff for handling and sophisticated care.

(5) In order to remedy such problems, the National Institutes of Health needs to support a Federal advancement initiative for the NPRCs that addresses the necessary upgrades and program capacity expansions.

(b) FIVE-YEAR INITIATIVE FOR PRIMATE CENTERS-

Subpart 1 of Part E of title IV of the Public Health Service Act (42 U.S.C. 287 et seq.) is amended by—(1)

redesignating the section 481C as added by Public Law 106-505 as section 481D; and (2) by adding at the end the following:

SEC. 481E. FIVE-YEAR INITIATIVE FOR PRIMATE CENTERS.

(a) IN GENERAL- The Secretary shall provide additional sums to the base grants provided to the National Primate Research Centers by the National Center for Research Resources in order to– (1) increase domestic breeding capabilities; (2) develop bridging programs to effectively utilize additional primate species; (3) increase the quality and capacity of primate housing and breeding facilities and the availability of related state-of-the-art diagnostic and clinical support equipment for primates; and (4) increase the number of personnel trained in primate care and management at the National Primate Research Centers.

(b) AUTHORIZATION OF APPROPRIATIONS- There are authorized to be appropriated such sums as may be necessary to carry out this section.

- **S.1139 A bill to amend the Animal Welfare Act to strengthen the ability of the Secretary of Agriculture to regulate the pet industry.**

Introduced on May 26, 2005, by Rick Santorum (R-Pennsylvania) and referred to the Senate Committee on Agriculture, Nutrition, and Forestry. On November 8, the Committee on Agriculture, Nutrition, and Forestry held hearings. This act may be cited as the "Pet Animal Welfare Statute of 2005." Related bill: H.R. 2669

Amends the Animal Welfare Act by redefining the term "dealer", redefining the term "retail pet store" to exclude A) a person breeding animals to sell to the public as pets; (B) a person selling hunting, security, or breeding dogs; or ©) a person selling wild animals. It also provides USDA access to source records for dogs and cats. Other provisions allow the Secretary [of Agriculture] to extend a temporary license suspension for up to 60 days if the violation will place the health of any animal in serious danger or to seek an injunction or restraining order.

- **S.1273 A bill to provide for the sale and adoption of excess wild free-roaming horses and burros.**

Introduced on June 20, 2005, by Harry Reid (D-Nevada) and referred to the Committee on Energy and Natural Resources. This act may be cited as the "Wild Free-Roaming Horses and Burros Sale and Adoption Act of 2005." Related bill: H.R.2993

Provides, with respect to the protection, management, and control of wild free-roaming horses and burros on public lands, for: (1) removing the limitation on the number of animals that may be adopted; and (2) the sale of excess wild free-roaming horses and burros for which an adoption demand by qualified individuals does not exist. Sets a $25 minimum adoption fee required for the adoption of an excess animal.

- **S.1509 A bill to amend the Lacey Act Amendments of 1981 to add non-human primates to the definition of prohibited wildlife species.**

Introduced on July 27, 2005, by James M. Jeffords (I-Vermont) and referred to the Committee on Environment and Public Works. This act may be cited as the "Captive Primate Safety Act of 2005." Related bill: H.R.1329

Amends the Lacey Act Amendments of 1981 to add non-human primates to the definition of "prohibited wildlife species" to which such Act's requirements (e.g., prohibition against sale or purchase in interstate or foreign commerce) apply.

- **S.1779 A bill to amend the Humane Methods of Livestock Slaughter Act of 1958 to ensure the humane slaughter of nonambulatory livestock, and for other purposes.**

Introduced on September 28, 2005, by Daniel K. Akaka (D-Hawaii) and referred to the Committee on Agriculture, Nutrition, and Forestry. This act may be cited as "Downed Animal Protection Act." Related bill: H.R.3931

States that it is U.S. policy that all nonambulatory livestock in interstate and foreign commerce be immediately and humanely euthanized when such livestock become nonambulatory.

Amends the Humane Methods of Slaughter Act of 1958 to direct the Secretary of Agriculture to promulgate regulations providing for the humane treatment, handling, and disposition of nonambulatory livestock by a covered entity, including a requirement that nonambulatory livestock be humanely euthanized.

Requires an entity to: (1) humanely euthanize nonambulatory livestock (while not limiting the Secretary's ability to test nonambulatory livestock for disease, such as bovine spongiform encephalopathy); and (2) not move nonambulatory livestock while such livestock is conscious, and ensure that such livestock remains unconscious until death.

Prohibits an inspector at an establishment covered by the Federal Meat Inspection Act to pass nonambulatory livestock, carcass, or carcass parts through inspection. Requires an inspector or other employee at such establishment to label such material as "inspected and condemned."

Defines "covered entity," "nonambulatory livestock," and "humanely euthanize."

- **S.1926 To provide the Department of Justice the necessary authority to apprehend, prosecute, and convict individuals committing animal enterprise terror.**

Introduced on October 27, 2005, by James M. Inhofe (R-Oklahoma) and referred to the Committee on the Judiciary. This Act may be cited as the "Animal Enterprise Terrorism Act." Related bill: H.R.4239

Rewrites federal criminal code provisions regarding animal enterprise terrorism to prohibit anyone from traveling in, or using the mail or any facility of, interstate or

foreign commerce for the purpose of damaging or disrupting an animal enterprise and, in connection with such purpose: (1) intentionally damaging, disrupting, or causing the loss of property used by or owned in connection with such enterprise; (2) intentionally placing a person in reasonable fear of death or serious bodily injury to that person or a family member through threats, vandalism, property damage, trespass, harassment, or intimidation; or (3) conspiring or attempting to do so. Prescribes escalating penalties.

Authorizes restitution for: (1) the reasonable cost of repeating any experimentation that was interrupted or invalidated as a result of such offense; (2) the loss of food production or farm income reasonably attributable to such offense; and (3) any other economic damage, including any losses or costs caused by economic disruption, resulting from such offense.

S.2043 A bill to amend the Robert T. Stafford Disaster Relief and Emergency Assistance Act to provide grants for mass evacuation exercises for urban and suburban areas and the execution of emergency response plans, and for other purposes.

Introduced on November 17, 2005, by Richard Durbin (D-Illinois) and referred to the Committee on Homeland Security and Governmental Affairs. This act may be cited as the "Mass Evacuation Exercise Assistance Act of 2005."

(3) PLAN CONTENTS- State, county, and municipal mass evacuation plans shall, to the maximum extent practicable–(K) establish procedures for protecting property, preventing looting, and accounting for pets...

For more information about legislationa go to the Library of Congress Thomas web site at: http://www.thomas.gov/

Welfare® Quality
Science and society improving animal welfare

Animal welfare is of considerable importance to European consumers. Nowadays food quality is not only determined by the overall nature and safety of the end product but also by the perceived welfare status of the animals from which the food is produced. The fact that improving the animal's welfare can positively affect product quality, pathology and disease resistance also has a direct bearing on food quality and safety.

The Welfare Quality project is about integration of animal welfare in the food quality chain: from public concern to improved welfare and transparent quality. The project aims to accommodate societal concerns and market demands, to develop reliable on-farm monitoring systems, product information systems, and practical species-specific strategies to improve animal welfare. Throughout this Integrated Project effort is focused on three main species and their products: cattle (beef and dairy), pigs, and poultry (broiler chickens and laying hens).

The research program is designed to develop European standards for on-farm welfare assessment and product information systems as well as practical strategies for improving animal welfare. The standards for on-farm welfare assessment and information systems will be based upon consumer demands, the marketing requirements of retailers and stringent scientific validation. The key is to link informed animal product consumption to animal husbandry practices on the farm. The project therefore adopts a "fork to farm" rather than the traditional "farm to fork" approach. Welfare Quality will make significant contributions to the societal sustainability of European agriculture.

Welfare Quality is a project funded by the European Commission (EU funded project FOOD-CT-2004-506508). It is an integrated project in the sixth framework programme, priority 5: Food Quality and safety. Thirty-nine institutes and universities (representing 13 European countries) with specialist expertise participate in this integrated research project. The project started in May 2004 and will take 5 years to complete.

For more information, contact Adrian Evans, Welfare Quality Project at email: EvansA18@Cardiff.ac.uk

Welfare Qualityis an European Union funded project about integration of animal welfare in the food quality chain.
http://www.welfarequality.net

Announcements...

UPCOMING MEETINGS

★ National Animal Welfare Education Program

OLAW Sponsored IACUC 101s and animal welfare conferences.

The IACUC 101 series consist of didactic and interactive training programs designed to provide IACUC (Institutional Animal Care and Use Committee) members, administrators, veterinarians, animal care staff, researchers, regulatory personnel and compliance officers with information on the role and responsibilities of IACUCs, including an understanding of federal policies and regulations governing laboratory animal welfare. A complete description and schedule of upcoming workshops can be found at http://grants.nih.gov/grants/olaw/iacuc101s.htm

The OLAW-sponsored IACUC 101 series are planned, coordinated and administered by Mary Lou James, Regulatory Consultant, 314-997-6896, email: mljames@mo.net.

Schedule of Upcoming 2006 events (subject to change)

November 8-9 Honolulu, Hawaii

★ 14th International Workshop on In Vitro Toxicology

INVITOX 2006, the 14th International Workshop on In Vitro Toxicology will be held in Ostend, Belgium from October 2-5, 2006. While more advanced products, new compounds and chemicals are introduced in our everyday life, there is a continuously increasing societal demand for more safety, hazard and risk evaluation to protect men and the environment. Such evaluation should be cost-effective and bear in mind ethical constraints on the use of animals. In vitro technology combined with new scientific concepts for toxicity testing will contribute to this demand. The scientific programme will include state-of-the-art lectures, workshops, original communications and poster sessions. INVITOX 2006 will cover strategies to develop sensitive and specific molecular markers (genes and proteins), the use of advanced cell technology, how to address sensitive subgroups e.g. children, ecotoxicology and testing for endpoints related to major human health effects, e.g. teratogenesis, endocrine disruption and immune effects. Registration will be open after the 2nd Announcement in April 2006 and close on September 15, 2006. For more information, visit the conference website at http://www.invitox2006.org

★ Workshop On Surgical Techniques In The Laboratory Mouse

This five-day, intensive hands-on workshop will be held from November 5-10, 2006 at the Jackson Laboratory, Bar Harbor, Maine. It is for those wishing to obtain practical training in surgical techniques for the laboratory mouse. Topics to be covered include basic handling, anesthesia, routes of administration, telemetry, and procedures for the identification and tracking of individual mice. A wide range of standard and non-standard surgical techniques are also taught and students are encouraged to submit requests for specific procedures. Enrollment is limited to 16. Applications will be reviewed through September 5th, or until the workshop is full. For more information, contact Judi Medlin at e-mail: judi.medlin@jax.org, phone: (207) 288-6326, fax: (207) 288-6080, http://www.jax.org/courses/events/coursedetails.do?id=342

★ IACUC: The Charge & The Challenge 12

The New Jersey Association for Biomedical Research (NJABR) presents their annual one-day training seminar focusing on practical and philosophical issues affecting the IACUC process. This years workshop will be held on Friday, November 17, 2006, at the Ramada Inn and National Conference Center in East Windsor, New Jersey.

Registration: $195 for NJABR members; $250 for non-members

For registration information, contact NJABR at 908-964-9449, e-mail: info@njabr.org or visit their website at www.njabr.org.

★ Mouse Colony Management: Principles and Practices

This workshop will be held from December 3-8, 2006, at the Jackson Laboratory, Highseas Conference Center, Bar Harbor, Maine. It is designed to provide training in the theory and practice of maintaining mouse colonies for production and research. The newly expanded four-day program is designed for colony managers, animal care technicians and students requiring an understanding of issues relating to the management of animal research and production colonies. (technicians, colony managers, students, Ph.D. scientists).

Topics include basic principals of mammalian genetics, overview of JAX mice, breeding strategies, genetics quality control, importation and animal health, resources for genetically engineered mice, facility design, and considerations in tracking and storage of colony data. For more information, contact Nancy Place at phone: (207) 288-6257, fax: (207) 288-6080, e-mail: nancy.place@jax.org or http://www.jax.org/courses/events/coursedetails.do?id=343&detail=regproc

PUBLICATIONS, DVDs, SOFTWARE

- **Assessing the Welfare of Genetically Altered Mice**

This report, produced by the UK Animal Procedures Committee Working Group sets out recommendations for a standard welfare assessment scheme for genetically altered (GA) mice and the establishment of a "passport" system for GA mice transferred between establishments nationally and internationally. The report can be found at http://www.nc3rs.org.uk/page.asp?id=231

- **America's Wildest Places—Volume 1, A Video Tour of Eight National Wildlife Refuges.**

This DVD is available from the U.S. Fish and Wildlife Service. In the new "Wildest Places" collection, you'll fly

among the stately white whooping cranes of Aransas and Matagorda Island national wildlife refuges in Texas. You'll track the stealthy endangered red wolf in the gloomy backwaters of North Carolina's Pocosin Lakes national wildlife refuge. You'll tumble alongside rollicking Alaska brown bears at Kenai National Wildlife Refuge. Your video tour continues at five other of America's finest windows on wildlife - Caribbean Islands refuge, Eufaula in the marsh country of Alabama and Georgia, Horicon's duck and goose haven in Wisconsin; the bottomland woods of Muscatatuck refuge in Indiana; and the John Heinz/Tinicum urban oasis with the Philadelphia skyline as wildlife's backdrop. Volumes 1 sells for $6.00 each, plus $2.50 shipping and handling, regardless of quantity ordered.To order go to http://training.fws.gov/refugedvd/ or call (304) 876-7692.

- **Animal Bioware Series II Software Suite and Simple Census**
  http://www.dpiboston.com/dpiboston/default.aspx

Produced by Digital Paradigm in Boston. This software package contains modules on Animal Health, Animal Order, Breeding, Census, Facilities, Husbandry, IACUC, Inventory, Purchasing & Billing, and Technical Services. Simple Census system automates your census, cage card printing, and animal health reporting.

- **Animal Welfare: Limping Towards Eden**

The followup book to *Animal Welfare: A Cool Eye Towards Eden* by John Webster, Emeritus Professor of Animal Husbandry at the University of Bristol. This is the third title in the Universities Federation for Animal Welfare *Animal Welfare Series*. Special consideration is given to:

★ Defining animal welfare ("fit and happy") and establishing a systematic approach for its evaluation (the "five freedoms");
★ Providing a sound ethical framework that affords proper respect to animals within the broader context of our duties as citizens to the welfare of society;
★ Developing comprehensive, robust protocols for assessing animal welfare and the provisions that constitute good husbandry; and
★ Introducing an education policy that will increase human awareness of animal welfare problems and promote action to reduce suffering.

Ordering information is available at http://www.ufaw.org.uk/webster%20book.htm#start

- **Controlled Atmosphere Stunning for Broilers**

This report from the Corporate Responsibility Committee of the Board of Directors of McDonald's Corporation discusses the feasibility of implementing controlled atmosphere stunning for broilers being killed for McDonald's restaurants. Released on June 29, 2005, it is available at http://www.mcdonalds.com/corp/invest/gov/mcd_cr062905.html

McDonald's corporate webpage for animal welfare is at http://www.mcdonalds.com/corp/values/socialrespons/market/animalwelfare.html

- **The Development of Science-based Guidelines for Laboratory Animal Care: Proceedings of the November 2003 International Workshop**
  http://books.nap.edu/catalog/11138.html

This 264 page report looks at animal housing needs, environmental enrichment, control of the animal house environment, assessment of current regulations around the world and the utility of regulatory harmonization. The purpose of this workshop was to bring together experts from around the world to assess the available scientific knowledge that can affect the current and pending guidelines for laboratory animal care.

- **IATA Live Animal Regulations (LAR)**

The International Air Transport Association Live Animals Regulations (LAR) is an excellent resource on how to ship animals safely. It specifies the minimum requirements for the international transport of animals and wildlife, and indicates what precautions airlines, shippers, cargo agents and animal care professionals should take on the ground and in the air. The LAR is enforced by the European Union and the U.S. Fish and Wildlife Services for import and export of live animals and meets or exceeds the requirements of the U.S. Animal Welfare Act. It is available for purchase at http://www.iata.org/ps/publications/9105

- **New from Blackwell Publishing**

★ *Poultry Welfare Issues–Beak Trimming*, edited by P.C. Glatz, examines the role of beak trimming in the poultry industry and the welfare problems associated with it. Other topics covered include beak anatomy; acute and chronic pain and the physiological changes in the bird associated with beak trimming; and an evaluation of production, egg quality, and health of birds relative to the severity and method of beak trimming. It is available at http://store.blackwell-professional.com/1904761208.html

★ *Handbook of Primate Husbandry and Welfare* covers all aspects of primate care and management both in the laboratory environment and in zoos. From the welfare and ethics of primate captivity through to housing and husbandry systems, environmental enrichment, nutritional requirements, breeding issues, primate diseases, and additional information on transportation and quarantine proceedings, this book provides a completely comprehensive guide to good husbandry and management of primates. It is available at http://store.blackwell-professional.com/1405111585.html

★ *Aquaculture Biosecurity: Prevention, Control, and Eradication of Aquatic Animal Disease*–Aquaculture biosecurity programs addressing aquatic animal pathogens and diseases have become an important focus for the aquaculture industry. Key representatives of international, regional and national organizations have presented their views of this important issue as part of a workshop at the World Aquaculture Society Triennial Conference 2004. The chapters of this book cover the wealth of experience from the varied perspectives of these experts on using biosecurity measures to take the offensive against the spread of diseases and parasites. It is available at http://store.blackwell-professional.com/0813805392.html .

On the Web

- **Animal Disease Information**
  http://www.cfsph.iastate.edu/DiseaseInfo

An information-rich site from the Center for Food Security and Public Health at Iowa State University. In cooperation with the World Organization for Animal Health (OIE), these 3-5 page factsheets provide detailed information on more than 100 animal diseases including zoonotic agents.

- **Application of the 3Rs in Medicines Research**
  http://science.gsk.com/about/animal-application.htm

A nice site from UK-based GlaxoSmithKline about the use and development of alternatives by GSK scientists.

- **Basic Guidelines for Operating an Equine Rescue or Retirement Facility**
  http://www.awionline.org/farm/horses/guidelines.htm

These guidelines were developed by a working group of veterinarians, equestrians, and public policy experts in association with the Animal Welfare Institute and the Doris Day Animal League. They include information on feeding, enclosures, veterinary care, new arrivals and other fundamentals.

- **Biological Risk Management for Livestock Facilities and Veterinary Facilities**
  http://www.cfsph.iastate.edu/BRM/default.htm

Improved infection/disease control is becoming the standard of care, not only for foreign animal disease threats but endemic diseases as well. To address these concerns, Iowa State University has designed resources that enable a veterinarian to evaluate their clinic or their client's animal facility, identify opportunities for improvement, and provide management recommendations to decrease disease risk.

- **Compendium of Measures To Prevent Disease Associated With Animals in Public Settings**
  http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5404a1.htm

From the summary, "This report provides standardized recommendations for those concerned with disease-control and with minimizing risks associated with animals in public settings."

- **Farm Fires—Protecting farm animal welfare**
  http://www.defra.gov.uk/animalh/welfare/pdf/farmfires.pdf

This booklet, produced by the U.K. Department for Environment, Food, and Rural Affairs examines the fire dangers which are commonly found on farms and identifies simple ways in which risks can be reduced.

- **Focus on Alternatives**
  http://www.focusonalternatives.org.uk/available%20information.htm

The Early Planning Poster provides a strategy to follow in the the early stages of planning experiments involving animals. It guides scientists in meeting their legal obligations in consideration of alternatives. A second poster illustrates how a hypothetical project might follow the strategy. Although these posters were developed for U.K. researchers, the strategies are equally valid for researchers complying with U.S. animal welfare regulations.

- **Guidelines on Recognition & Assessment of Animal Pain**
  http://www.vet.ed.ac.uk/animalpain/

The Animal Welfare Research Group at the Royal (Dick) School of Veterinary Studies, University of Edinburgh has launched a new multimedia website to help people working with animals recognize and assess pain in order to treat them appropriately. The site contains written guidelines, photographic and video evidence, and a bibliography. Topics covered include the types and causes of pain, methods used to assess pain and how the methods may be validated, different types of treatments, and a test.

- **Heat Stress in Poultry–Solving the Problem**
  http://www.defra.gov.uk/animalh/welfare/pdf/hstress05.pdf

This book from the U.K. Department for Environment, Food, and Rural Affairs describes the main causes of heat stress in poultry. It outlines some of the common sense management measures that will help to prevent it.

- **Mayday Conference: A Cross-Species Approach to Pain and Analgesia**
  http://www.ivis.org/proceedings/Mayday/toc.asp

Proceedings of a conference held in 2002. Topics include: animals and humane endpoints, analgesic screening, Glasgow Pain and Welfare Research Group, recognition, assessment, and treatment of pain. Species include laboratory animals, birds, horses, humans, wildlife, and amphibians. Requires free registration.

- **The Norwegian Reference Centre for Laboratory Animal Science & Alternatives**
  http://oslovet.veths.no/

This website, produced by Drs. Adrianand Katrina Smith, provides access to a wealth of information on laboratory animal science, the use of alternatives in biomedical research, and extensive resources on fish models. A tour of the laboratory animal unit at the Norwegian School of Veterinary Science is available. It also is the home of NORINA—A Norwegian Inventory of Audiovisuals. This is a wonderful compilation, in English, of approximately 3,700 audiovisual aids and other alternatives that can be used in teaching and training from Junior School to University level. ■

ARS Animal Welfare Research...

Alternatives to feed withdrawal induced molting in laying hens (Dr. Heng-wei Cheng)

Traditional induced molting by feed withdrawal is a common practice used in the egg industry to extend the productive life of hens. However, traditional induced molting disrupts normal feeding patterns, causes considerable stress, increases susceptibility to disease and mortality, and decreases well-being. The aim of the program is to develop an alternative to feed withdrawal molting which improves animal welfare and maintains or improves the efficacy and profitability of present practices. We will specifically examine two hypotheses: 1) that neuroendocrine regression of the reproductive system is an efficient and more welfare-friendly alternative to feed withdrawal molting, and 2) that different molting practices (traditional versus alternatives) differently influence hens' health, immunity, and behavior, as well as their ability to cope with stress. [B]enefits to the egg industry include a reduction or elimination of molting-related stress, improved health and well-being and a decline in *Salmonella enteritis* infections and transmission.

Alternatives to hot-blade beak trimming in laying hens: Infrared beak treatment vs. hot-blade beak cutting (Dr. Heng-wei Cheng)

Beak trimming (BT), removal of 1/3 to 1/2 of the beak, is a common practice in the poultry industry to prevent feather pecking and cannibalism. Feather pecking and cannibalism occur in all current housing environments and can lead to suffering and death in laying hens without BT. However, BT may decrease well-being by disrupting normal behavior and by causing tissue damage resulting in pain (acute, chronic or both). The objectives of the proposal are to evaluate and recommend less painful methods of beak trimming by determining the effects of various beak trimming methods (infrared beak treatment vs. hot blade beak cutting) and the effects of bird age on behavioral indicators of pain, pain-related morphopathological beak changes, and their correlations in White Leghorn chickens. The short-term goal is to determine if infrared beak trimming is more acceptable from an animal welfare perspective. The long-term goal is to provide scientific data for developing an animal-friendly alternative for the egg production industry to eliminate beak trimming or to conduct beak trimming with minimized pain and stress.

Alternative housing systems in laying hens: Enriched cage vs. battery cage (Dr. Heng-wei Cheng and Rafael Freire)

Battery (conventional) cage systems have been challenged as an unacceptable method of housing laying hens, on the grounds of not providing the birds with the ability to express most normal behaviors. In the past 20 years, there have been attempts to modify design of laying cages to ameliorate welfare problems. Most of the modern welfare-friendly cages (enriched cage system) now incorporate enough perch space for all birds to be able to perch simultaneously, a nest box to allow the birds to express nesting behavior, a littered area for dustbathing and foraging behavior and a claw shortening device for complete nesting behavior. However, birds' well-being is dependent on genetic-environmental interaction in response to physical stressors. The proposed objective aims to determine the suitability of enriched cage systems for the U.S. layer industry. In particular, the project will investigate various stocking density and group sizes with the aim of identifying an optimum, which should help the U.S. egg producers to develop new guideline for managerial practices to maintain economic profiles for producers and low egg prices for customers.

Bill trimming in ducks: Stress, pain, and neuroma formation

The aims of the project are to determine the effects of various bill-trimming methods (tip-searing, cutting, and cutting followed by hot-blade cautery) on behavioral indicators of pain and morphopathological bill changes in Muscovy and Pekin ducks. The ultimate goal is to determine whether a particular method (or methods) of trimming is more acceptable from an animal welfare perspective. At various time points during the experiment, bills will be examined for neuromas and other morphological changes to the nerve fibers induced by bill trimming. If indicators of pain are found, a second experiment will be carried out in which trimmed and non-trimmed ducks are offered feed mixed with an analgesic, such as carprofen, to determine whether the ducks will self-select feed that reduces pain. Data from this study will provide scientific information to develop new guidelines for the duck industry to improve duck well-being.

Supported by a MPC grant to Dr. Ed Pajor (Purdue University), Dr. Joy Mench (University of California Davis), and Dr. Heng-wei Cheng (USDA-ARS)

Salmonella in Free-Range Chicken

There have been lingering questions about the effects of organic practices on the health of poultry and other livestock produced without conventional medications. So researchers decided to compare levels of Salmonella bacteria in organic free-range and conventionally produced birds. Organic producers often raise their chickens under free-range conditions—that is, allowed to roam outside cages or other confined areas. Free-range birds represent less than 1 percent of the billions of birds produced each year in the United States, but they generally command higher prices in the marketplace.

Salmonella contamination of food causes about 40,000 cases of foodborne illness each year, according to the Centers for Disease Control and Prevention. But since mild cases may not be diagnosed or reported, the actual number of infections may be up to 30 times greater. Of 110 processed free-range chickens from three organic producers that were tested, researchers found that about 25 percent tested positive for Salmonella, which is slightly higher than the rate typically found in commercial chickens.

USDA-ARS Richard B. Russell Research Center, Athens, Georgia

Continued on next page

ARS Animal Welfare Research...

Settling Doubts About Livestock Stress

When scientists talk about animal stress, they're weighing the possibility of real pain and fear—even death—which not only violates animal care ethics, but also costs producers millions of dollars each year. Happy, healthy animals appear most likely to thrive, with the least intervention and fewest food safety problems. So the point of studying animal stress is to find out how livestock view the farm world.

A team of scientists is doing exactly that as part of an Agricultural Research Service national program to see whether current production practices are severely stressing animals—and, if so, to find objective measures to indicate those levels. Such measures could then be used to evaluate new practices that might alleviate pain and suffering. The measures might be behavioral, such as fighting, or physiological, including everything from elevated temperature, heartbeats, and hormone levels to low weight and nerve damage.

The team includes research leader Donald C. Lay, animal scientists Jeremy Marchant-Forde and Ruth Marchant-Forde, animal immunologist Susan Eicher, and neuroscientist Heng-wei Cheng, all with ARS's Livestock Behavior Research Unit, and ethologist Ed Pajor, with Purdue University at West Lafayette, Indiana.

- Begin at the Beginning

Lay is a pioneer in the study of how pregnant livestock can transfer stress to their offspring. He is working with a group in Holland that's one of three others in the world researching prenatal stress in livestock. Lay and colleagues have found that if a pregnant pig or cow, for example, is stressed, profound changes occur in the offspring's physiology and behavior that can affect farmers' income. These include higher levels of the hormone cortisol, which indicate stress, and slow wound healing.

When Lay transferred from Iowa State University, where he was a professor and researcher, he brought this research to ARS. USDA recognized the significance of his findings on neonatal stress by awarding him a competitive USDA National Research Initiative (NRI) grant of $200,000 to continue his work.

Lay's expertise in stress physiology has allowed for an exciting breakthrough by working with Tom Stabel at the ARS National Animal Disease Center to identify characteristics of Salmonella that allow them to more effectively infect their host. Doctoral candidate Mike Toscano found the first instances of bacteria "monitoring" their swine hosts.

"Salmonella respond to higher concentrations of norepinephrine, another hormone that indicates stress," says Lay. The phenomenon had been found in rodents, but not in swine. With the help of an additional 3-year, $300,000 NRI grant, Lay and Scott Willard, a professor at Mississippi State University, will use a new technology called biophotonics to study how Salmonella infect their host.

In this project, the bacteria are engineered to emit light. With a sensitive, photon-sensing camera, Lay and Willard will be able to watch Salmonella as they progress through a living swine. This technology will answer many questions, such as where Salmonella hide in their host and how they manage to travel so quickly once they infect a pig. "This work suggests the possibility of using a blood test for stress-related hormones to spot at-risk animals and isolate them during transport," Lay says. "It also suggests that if farmers used practices to reduce stresses associated with mixing animals from different herds and transporting them in trucks, they could lower norepinephrine levels and reduce Salmonella's ability to infect swine."

As part of her studies on the effects of farm practices on the immune systems of livestock, Eicher has devised a milk formula supplement that helps dairy calves fight Salmonella and other infections, especially during stressful times.

She and colleagues—including Jeremy Marchant-Forde—take calves on 6- to 8-hour trips weekly, as new calves are born. They've found that calves are particularly vulnerable to transport stress when 4 days old. They do better before and after that age, just as farmers reported to a once-skeptical Eicher.

She wonders if it might have to do with the fact that on day 4, the calves make a transition from drinking colostrum (mother's first milk)—which boosts their immune systems—to drinking milk. To measure stress-induced weakened immunity, Eicher tests the reaction of cells taken from calves and exposed to infection. Calves shipped at 4 days of age show a much lower immune response and ability to fight pathogens.

Eicher uses her formula supplement—containing electrolytes, beta-glucan (a yeast supplement), and ascorbic acid—to boost calves' and piglets' immune systems. She checks for effects, including looking at immune system cells under a microscope to see where beta-glucan is accumulating.

"Transporting farm animals is one of the most stressful practices for dairy calves," Eicher says. Her formula restores the calves' immunological systems, gives them back their appetites, and allows them to resume normal growth.

It even reduced stress in Holstein dairy calves taken from their mothers within 4 to 12 hours after birth. They were more active and had higher daily weight gains and levels of immunoglobulin (IgG)—an ingredient in colostrum that's an indicator of a good immune system—and lower levels of a liver protein that indicates stress.

Working with colleagues at the University of Florida-Gainesville, Eicher found that mixing formula-treated beef calves with those from other herds wasn't nearly as stressful as weaning and transporting. As indicators, they used behaviors and blood levels of cortisol, liver proteins and other proteins, and immune system indicators like IgG.

Eicher is also finding that acquainting young, pregnant cows with milking parlors and milking before their first births reduces stress when they're milked after their calves are weaned. She completed two studies with cows in Purdue's herd of 200 confined dairy cattle. She also worked with colleagues at Mississippi State University who did a similar experiment with a grazing herd.

According to Eicher, "There was lowered stress—as measured by increased milk production, less nervous weight shifting in milking stalls, and a quicker return to normal levels of heptaglobin, a protein that cleans up hemoglobin after tissue damage or other stresses—in the cows in all three experiments. But the benefits were clearer in the confined herd."

- The Last Thing Over the Fence

Eicher has been working with Cheng for the past 8 years to see whether removing dairy cows' tails by constrictive banding causes them chronic pain. She is the first U.S. researcher to study the practice, called "tail docking." It's commonly done by dairy farmers for sanitary reasons and is growing in popularity, moving from adults to calves at ever-younger ages.

Eicher and Cheng have found both behavioral and physiological signs indicating that animals may suffer chronic pain from tail docking. Not only do calves pay attention to the stump, they also show physiological and neurological signs usually associated with "phantom limb" pain in people. The data showed that young calves actually respond to the pain more than adult cows do, a finding that doesn't support the normal practice of conducting painful procedures on young animals rather than older ones. Researchers observed an increase in blood temperature in the area around the tail and formation of neuromas—bundles of nerves occurring at their damaged ends—which can transmit pain spontaneously. The fact that Eicher's behavioral observations match up with Cheng's discovery of neuromas makes a stronger case for the likelihood of chronic pain.

Cheng uses a careful procedure to search for neuromas and other possible nerve damage that could cause chronic pain or hypersensitivity to temperature or touch. This includes an elaborate procedure for staining nerve tissue for electron microscopy study.

- The First Thing Into the Feed Bin

Cheng also looks at neuromas to evaluate a similar practice in poultry production: beak-trimming. Farmers trim from a third to a half of the beaks off chickens, turkeys, and ducks to cut losses from poultry pecking each other.

"Poultry beaks are much more complex structures than cattle tails," Cheng says. "They're really intricate, so it's not hard to cause problems when cutting them. Sometimes the beaks are deformed as they heal, which interferes with eating or other instinctive behaviors, like preening."

Cheng is tackling that problem from two angles: finding the most humane way to trim beaks and eliminating the need to trim them. He's first looking at infrared and laser techniques as alternatives to the knives currently used. He recently completed a study with Pajor on trimming the beaks of Muscovy and Pekin ducks. That data is currently being analyzed.

But Cheng thinks the need for trimming can be eliminated by breeding gentler poultry, so he's found a breeding line of such chickens. He and his colleague, Bill Muir, a professor at Purdue University, believe that breeders of many types of livestock have inadvertently bred more aggressive animals—with less maternal instinct and ability to cope with stress—as they've selected for traits such as productivity.

- A House Is Not a Home

Eicher and Pajor found that piglets born to sows housed individually in conventional stalls bore evidence of the stress the housing caused their mothers. Piglets from stall-housed mothers had lower growth rates and increased measures of stress—including more squealing—during an isolation test after weaning than piglets from group-housed sows. Jeremy Marchant-Forde also works with Eicher and Pajor on alternative housing for sows.

Confining pregnant sows in stalls is a major well-being issue. It curtails movement and social interaction and fails to provide dirt or hay to satisfy their instincts to use their snouts to root for food.

So Pajor is asking sows what they prefer. He's set up a way to let them choose either extra food or space and company. Each sow is in a typical gestation stall, but she is able to push a bar to open a door that lets her visit the sow on either side of her stall. Or she can push another bar and get a little extra food. The scientists rate a sow's motivation or priority level by the number of times she's willing to press a bar to get her reward.

To his surprise, so far the sows are choosing extra food. His first project was done with 16 sows, studying 4 at a time from Purdue's herd of 250 sows.

"Scientists have often compared sows in different housing situations," says Pajor. "What's new here is letting them choose the 'extras' to see what their priorities are.

The current setup is a typical, barren environment, with slatted cement floors. The next round of experiments will see whether the sow chooses different options in an enriched environment—where there's more to do, a soft floor, and straw to satisfy instincts like nesting or rooting.

- Getting Along With Others

Lay is also working with Pajor on experiments to show the effects of an enriched environment on baby pigs, including the socializing effects of letting young from different litters play and interact at about 10 days of age.

"We want to see whether there is an age window for socialization," Pajor says. "Could early socialization help piglets cope better when mixed with different pigs later in life? Could it help them spot dominant pigs and get in fewer fights, for example? That would be good for both the pigs and the farmers.

"When a lot of these indicators—behavioral and physiological—come together and point to the same thing, you begin to feel that you've proven the animal is experiencing stress," Pajor says. That has already happened in several cases as ARS farm animal stress research begins its second decade, fulfilling its mandate to seek out objective measures of stress and ways to alleviate it.—By Don Comis, Agricultural Research Service Information Staff, phone (301) 504-1625, fax (301) 504-1486. ■

"Meeting the Information Requirements of the Animal Welfare Act"

The Animal Welfare Information Center (AWIC) of the U.S. Department of Agriculture, National Agricultural Library (NAL) has developed a 2--day workshop for individuals who are responsible for providing information to meet the requirements of the Animal Welfare Act. The workshop will be held at NAL in Beltsville, Maryland. There is no fee for the workshop.

The objectives of the workshop are to provide:

- an overview of the Animal Welfare Act and the information requirements of the act.
- a review of the alternatives concept.
- a comprehensive introduction to NAL, AWIC, and other organizations.
- instruction on the use of information databases/networks.
- online database searching experience.

Workshop dates for 2007 will be announced on the AWIC website at http://awic.nal.usda.gov/workshops

For more information, contact AWIC at phone: (301) 504-6212, fax: (301) 504-7125, or e-mail: awic@nal.usda.gov.

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