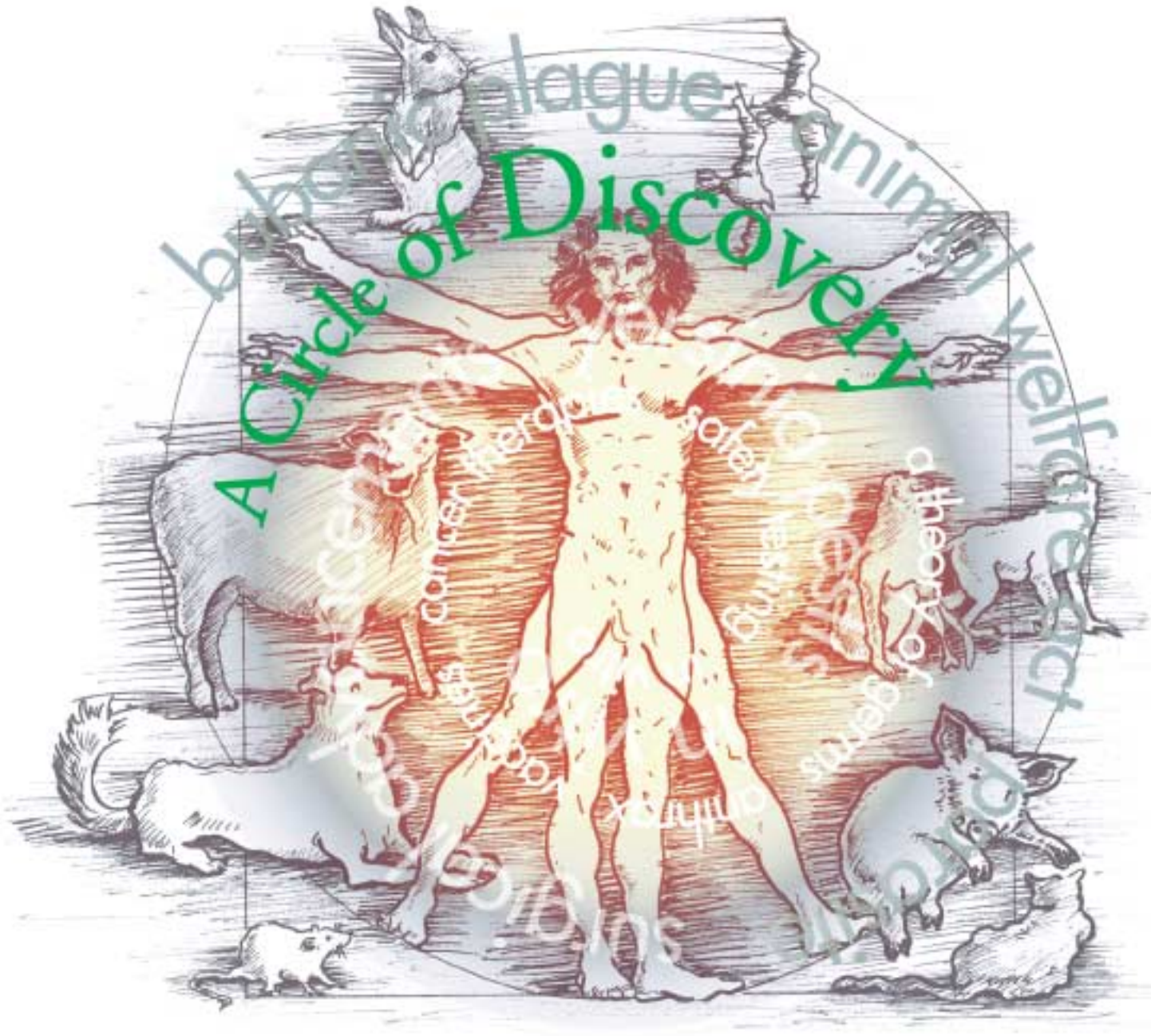
Science, Medicine, and Animals

NATIONAL RESEARCH COUNCIL
OF THE NATIONAL ACADEMIES

TEACHER'S GUIDE



Science, Medicine, and Animals

A Circle of Discovery

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THE NATIONAL ACADEMIES PRESS
Washington, D.C.
www.nap.edu

The National Academies Press
500 Fifth Street, N.W.
Washington, DC 20001

Support for the development of this *Teacher's Guide* was provided by the American Association for Laboratory Animal Science (AALAS) Foundation, the National Institutes of Health Office of Science Education, The Esther A. and Joseph Klingenstein Fund, Inc., the President's Circle Communications Initiative of the National Academies, and funds from the National Research Council.

The *Teacher's Guide* was written by Lisa C. Moran and developed by Nancy Huddleston and Joanne Zurlo.

Cover design by: Landam Design Works, Rockville, Maryland

Additional copies of this *Teacher's Guide* are available from the National Academies Press, 500 Fifth Street, N.W., Washington, D.C., 20001; 800-624-6242 or 202-334-3313 (in the Washington area); http://www.nap.edu.

Printed in the United States of America

TABLE OF CONTENTS

PREFACE

One of the goals of science education in the classroom is to help students recognize how scientific exploration can contribute to the well being of humanity and the natural world. Scientific research can lead to better uses of natural resources, treatments for diseases, and preservation of the world's varied species. As students delve into the processes used by practicing scientists, however, they become aware that research sometimes involves difficult choices. The use of laboratory animals is one area of research that raises ethical and moral questions.

The report *Science, Medicine, and Animals* attempts to explain the role that animals play in biomedical research and the ways in which scientists, governments, and citizens have tried to balance the experimental use of animals with a concern for all living creatures. This *Teacher's Guide* aims to help teachers of middle and high school students use *Science, Medicine, and Animals* in the classroom. It offers suggestions to help students comprehend the report, participate in discussions about the report's content, and perform minds-on activities to explore its concepts. As they examine the issues in *Science, Medicine, and Animals*, students will gain a greater understanding of the goals of biomedical research and the real-world practice of the scientific method in general.

Science, Medicine, and Animals and the *Teacher's Guide* were written by the Institute for Laboratory Animal Research and published by the National Research Council of the National Academies. The publications were reviewed by a committee made up of experts and scholars with diverse perspectives, including members of the U.S. Department of Agriculture, the National Institutes of Health, the Humane Society of the United States, and the American Society for the Prevention of Cruelty to Animals.

Teachers should be aware, however, that *Science, Medicine, and Animals* reflects the views of many people in the scientific community and the public at large, but not all. Groups who advocate for animal rights might disagree with some or all of the content in the report. Teachers should encourage students to explore the positions of these groups as they consider the issues surrounding the experimental use of animals in biomedical research. Some of these groups already may have sent information to students or to the school. Teachers should encourage students to verify the statements in all materials discussed.

INTRODUCTION

This *Teacher's Guide* is designed as a tool to assist teachers of grades 5 through 12 in using the report *Science, Medicine, and Animals* in their classrooms. It groups the chapters in *Science, Medicine, and Animals* into six lessons that may be taught separately or together. There are also notes on how each lesson may be shortened or lengthened and there are activities for advanced- or below-level learners. This guide also shows how using *Science, Medicine, and Animals* can support teaching of the national science standards.

Science, Medicine, and Animals is written for the general public. It will benefit students to have certain background knowledge to understand the text and lesson concepts. Students should be familiar with: systems, order, and organization; the processes of scientific inquiry; evidence and models; evolution; the characteristics of organisms; the difference between natural and human-made objects; concepts of personal and community health; and the differences between risks and benefits.

HOW TO USE THIS GUIDE

The guide contains the following resources:

- a chart that shows the correlation between lessons in the guide and the national science standards for grades 5-12;
- six lessons with flexible plan elements; and
- six reproducible student worksheets.

Teacher Guide Component Description

Lesson Title and Chapters/Pages: The title of the lesson and the corresponding pages from *Science, Medicine, and Animals* that the students will read as part of the lesson.

Number of Periods: The number of standard 45-minute class periods the lesson should take.

Lesson Summary: A brief description of the content of the lesson.

Objective: The instructional goal of the lesson.

Vocabulary: A list of vocabulary words found in the text for that lesson. These vocabulary words are essential to students' comprehension of the text and related classroom activities. Some of the words are defined in *Science, Medicine, and Animals*. Teachers should provide definitions for those that are not defined.

Activate Prior Knowledge: An activity by which teachers assess student background knowledge of the lesson topic and stimulate student interest in the lesson.

Alternate Lesson Plans: Suggestions for modifying the lesson. This section has two parts:

- Condense/Extend the Lesson: Suggestions for shortening the lesson or expanding it into more class periods.
- For Below-/Advanced-Level Learners: Suggestions for adapting the lesson to learners who may need more help achieving the lesson objective or an activity to broaden students' comprehension of the lesson objective.

Student Worksheets

Reproducible student worksheets for each of the six lessons are included in the back od this guide. Answers to the questions in the student worksheets appear bracketed in red in the *Teacher's Guide*. The worksheets include the following sections:

A. Read to Learn More: A series of reading comprehension questions teachers can use to guide students' reading of the text. The questions may be used during or after reading to check for understanding. Sample answers are provided in the guide.

B. Questions for Discussion: Springboards for classroom discussions of the topics in the text. When conducting a classroom discussion, keep the following in mind:

- Conduct class discussions as dialogues, in which all positions are heard and respected; the goal is to find common ground. Discussions should NOT be debates, in which the goal is to win the argument.
- Set discussion ground rules: (a) a person must be allowed to speak without interruption; (b) participants may critique ideas, not individuals; (c) everyone must respect each other's views and avoid inflammatory language such as "You're wrong."
- Suggest that students back their positions, whenever possible, with supporting information from *Science, Medicine, and Animals* or other sources, including textbooks and personal experiences.

C. Minds-on Activity: A suggested activity designed to enrich students' understanding of the lesson objective.

Correlation of *Science, Medicine, and Animals* to the National Science Standards: Grades 5–12	Lesson 1	Lesson 2	Lesson 3	Lesson 4	Lesson 5	Lesson 6
Unifying Concepts and Processes						
Systems, order, and organization	•	•	•	•		
Evidence, models, and explanation	•	•	•	•		•
Constancy, change, and measurement		•	•	•		•
Evolution and equilibrium		•	•			
Form and function	•	•	•	•		
Correlation of *Science, Medicine, and Animals* to the National Science Standards: Grades 5–8						
Science as Inquiry						
Abilities necessary to do scientific inquiry	•	•	•	•	•	•
Understandings about scientific inquiry	•	•	•	•	•	•
Life Science						
Structure and function in living systems	•	•	•	•		•
Reproduction and heredity		•	•	•		
Regulation and behavior		•				
Diversity and adaptations of organisms	•	•	•			
Science and Technology						
Abilities of technological design	•				•	•
Understandings about science and technology	•	•	•	•	•	•
Science in Personal and Social Perspectives						
Risks and benefits	•	•	•	•	•	•
Science and technology in society	•	•	•	•	•	•
History and Nature of Science						
Science as human endeavor	•	•	•	•	•	•
Nature of science	•	•	•	•	•	•
History of science	•	•	•	•	•	•
Correlation of *Science, Medicine, and Animals* to the National Science Standards: Grades 9–12						
Science as Inquiry						
Abilities necessary to do scientific inquiry	•	•	•	•	•	•
Understandings about scientific inquiry	•	•	•	•	•	•
Physical Science						
Structure and properties of matter	•	•	•			
Chemical reactions		•	•	•		
Life Science						
The cell	•	•	•	•		•
Molecular basis of heredity	•	•	•	•		
Biological evolution	•	•	•	•		
Interdependence of organisms	•	•	•	•		•
Matter, energy, and organization in living systems	•	•	•			•
Behavior of organisms	•	•	•	•		
Science and Technology						
Abilities of technological design	•			•	•	
Understandings about science and technology	•	•	•	•	•	•
Science in Personal and Social Perspectives						
Personal health and community health	•	•	•	•		•
Science and technology in local, national, and global challenges	•	•	•	•	•	•
History and Nature of Science						
Science as human endeavor	•	•	•	•	•	•
Nature of scientific knowledge	•	•	•	•	•	•
Historical perspectives	•	•	•	•	•	•

LESSON 1: WHY USE ANIMALS?

Chapters and Pages: Preface, Introduction, Why Use Animals? (pages 1-6)

Number of Periods: 1-3

Lesson Summary: Lesson 1 presents an overview of the many issues relevant to the use of animals in biomedical research. Students will discover the links between animals and human beings that make many animals suitable subjects for the study of human disease. The lesson touches on some of the difficult questions surrounding the use of animals, such as the morality of inflicting pain, as well as the drawbacks to alternative research models, such as computers and even humans, that make the use of animals essential to biomedical research.

Objective: Students will consider the scientific reasons animal models are used in biomedical research and evaluate the ethical questions surrounding the experimental use of animals.

Vocabulary: AIDS, animal model, bacteria, biomedical, bubonic plague, ethical, infectious, parasite, pathology, physiology

Activate Prior Knowledge: Have students demonstrate, by show of hands, how many have friends or relatives with medical conditions such as arthritis, diabetes, cancer, epilepsy, or others. Provide students with an example of how drugs or medical devices may improve a person's quality of life. Have volunteers offer similar examples from their own experiences. Discuss with students the significant amount of research required to bring these medications and devices to the public.

Lesson 1 Student Worksheet

A. Read to Learn More. Use these questions to facilitate student comprehension of the text.

1. (Pages 1-2): *What are some of the different public viewpoints on how animals should be used in biomedical research?* [Possible responses: to find new treatments and cures only if it does not cause pain to the animals; animals shouldn't be used at all, but rather human and nonanimal or computer models should be used.]

2. (Page 4 and 6): *Why do some animals make good research subjects for studying human disease?* [Possible response: humans and animals suffer from many of the same disorders, diseases, parasites, viruses, and bacteria; if an animal shares characteristics with humans and if it is vulnerable to the same disease or medical condition.]

3. (Page 5): *What types of research mentioned in the text require the use of whole organism (animal) models?* [Possible response: How the digestive and cardiovascular systems interact or how the environment affects an organism] What other types of research might also make use of animal models? [Possible responses: what side effects a drug might have; how the body might react to an organ transplant]

B. Questions for Discussion: Use the questions on the student worksheet to engage students in a dialogue.

C. Minds-on Activity — Identifying Models: Have students read the abstracts of published studies provided on the Student Worksheet. Ask them to determine which of the research models listed on page 5 of the text is being used in each of the studies. Italicized words can be useful in determining the model used. Have students look up additional abstracts on the PubMed database at http://www.ncbi.nlm.nih.gov/entrez/query.fcgi and determine the models being used in those studies. Suggested search terms: allergens, caffeine and cardiac, obesity, autoimmune. [Answers: 1) organism or animal model (humans); 2) cell model; 3) organ model ; 4) tissue model ; 5) cell model; 6) organism or animal model (rats and mice)]

Alternate Lesson Plans

- **Condense the Lesson (1 period):** Have students read the text and answer the comprehension questions for homework and review answers before the class discussion. Have students complete the Minds-on Activity as an individual homework assignment.
- **Extend the Lesson (1 period):** Conduct a class survey on students' attitudes toward animal research and compare it with published data from a 1999 National Science Foundation survey. Ask by a show of hands whether students strongly disagree, disagree, agree, or strongly agree with the following statement and record the answers.

  Scientists should be allowed to do research that causes pain and injury to animals such as mice if it produces new information about human health problems. [NSF survey results; about 66 percent agreed or strongly agreed; 33 percent expressed disagreement. When asked if they would agree to the same research using animals such as dogs and monkeys, 26 percent said they were generally opposed to research involving animals, 28 percent had mixed feelings, and 46 percent expressed general support for such animal-based research.]

LESSON 2: GERMS AND VACCINES

Chapters and Pages: A Theory of Germs, Overcoming Disease, Vaccines, Penguins! (pages 7-12)

Number of Periods: 1-2

Lesson Summary: In Lesson 2, students examine how animal models have helped scientists understand germs and fight deadly diseases. The lesson also discusses the role animals have played in treating animal diseases.

Objective: Students will recognize and evaluate how scientists have used animals to study diseases and develop vaccines.

Vocabulary: anthrax, antibodies, culture, germ, inoculated, malaria, metamorphoses, postulate, transmitted, vaccine

Activate Prior Knowledge: Brainstorm with students a list of diseases that affect humans, and write the list on the board. The list may include diseases such as AIDS, diabetes, cancer, Alzheimer's, measles, or chicken pox. Information may be found at http://www.nih.gov and typing in the disease in the search box. Then write down whether there is a vaccine or cure for the disease. Ask students how they think scientists study such diseases and search for ways to prevent or cure them. Point out that students are about to read how scientists use animals to study such diseases.

Lesson 2 Student Worksheet

Read to Learn More: Use these questions to facilitate student comprehension of the text.

1. (Page 7): *How did Robert Koch use animals to discover how a germ causes a specific disease?* [Possible response: He injected mice with the blood of cows that had died of anthrax. The mice developed anthrax, too, so Koch realized that the bacteria in the cows' blood caused anthrax.]

2. (Page 8): *What two deadly diseases can be prevented with vaccines?* [smallpox and polio]

3. (Pages 10-12): *How have scientists used animals to search for a vaccine against malaria in both humans and animals?* [Possible responses: Scientists have studied chickens, rodents, and penguins with malaria to understand how the disease changes and how a host makes antibodies against it. Mice and primates have been used to create and test malaria vaccines.]

4. (Page 11): *What justification does Dr. Kumar give for using animals to study malaria?* [A child dies of malaria every 20 seconds.]

B. Questions for Discussion: Use the questions on the student worksheet to engage students in a dialogue.

C. Minds-on Activity — Finding Treatments: Have students explore how researchers are using animals models to find cures for untreatable diseases. Divide students into groups and assign each group a disease for which there is no known vaccine or cure, such as some types of leukemia or cystic fibrosis. For homework, have each group use the Internet to prepare a report on its disease. Reports should include how the disease affects humans, how many people are affected, and how researchers are using animals to find treatments. Have groups share their reports and discuss as a class whether the animal research is justified. Helpful information on diseases can be found at http://www.nih.gov and http://medlineplus.gov.

Alternate Lesson Plans

- **Condense the Lesson (half period):** Have students read the text and answer the comprehension questions for homework. Review answers before the class discussion.
- **Extend the Lesson (1 period):** Have groups perform the Minds-on Activity during class time.
- **For the Below-Level Learner:** Provide students with the profiles of the diseases from the Minds-on Activity. Have students write paragraphs in which they support or oppose the use of animals in the research on each disease.

LESSON 3: DISEASE AND SURGERY

Chapters and Pages: Understanding Epilepsy, Surgical Advancements, Cancer Therapies (pages 13-19)

Number of Periods: 1

Lesson Summary: Lesson 3 details how scientists use animal models to study serious, widespread diseases such as epilepsy and cancer and develop life-saving surgical procedures. The lesson also discusses the types of animals researchers use, including genetically modified animals and how scientists use them.

Objective: Students will examine how animal cell cultures and animal models contribute to research on some chronic diseases, as well as some surgical procedures.

Vocabulary: anticonvulsant, cancer, chemotherapy, epilepsy, genome, Gleevec, hypertension, *in vitro*, National Institutes of Health (NIH), neuron

Activate Prior Knowledge: Ask students if they have ever heard of a disease called epilepsy. Put the word *epilepsy* at the center of a concept web on the board and write what students know about the disease in the outer circles of the web. Then add what scientists know about epilepsy, such as its characteristics and treatments. (See http://www.ninds.nih.gov/disorders/epilepsy/epilepsy.htm for information.) Perform the same webbing activity for cancer. Explain that students will read about the use of animals to further study these diseases.

Lesson 3 Student Worksheet

A. Read to Learn More: Use these questions to facilitate student comprehension of the text.

1. (Page 14): *What three biomedical research models have been used to find drugs to treat epilepsy?* [cell, tissue, and organism models]

2. (Pages 14): *What are some arguments both for and against using rat brain slices?* [Possible responses: For: dozens of slices from one brain reduce animals used; Against: only useful in early research, and slices can't predict response to a drug of an intact brain.]

3. (Pages 15-16): *Which animals are used most often in research?* What makes these animals helpful in studying human disease? [Possible responses: rats and mice; they breed easily and may be genetically modified to mimic humans.]

4. (Pages 16): *Which genetically modified animals (also called transgenics) are used most often in research and how have they been modified?* [Mice that have been modified to mimic human diseases.]

5. (Page 18): *Why would a chemotherapy drug like Gleevec need to be tested on whole animal and human models?* [Possible responses: to test for side effects or to find out whether the drug is effective when it is given to a whole organism.]

B. Questions for Discussion: Use the questions on the student worksheet to engage students in a dialogue.

C. Minds-on Activity — Genetically Modified Animals: Have students read the articles provided below or find other examples of the use of genetically modified animals in research the Internet or on databases such as PubMed. In groups or individually, have students choose one example of the use of genetically modified animals. Have them write a brief report on how the animals were modified and what scientists hope to learn from them. Students can share the reports in class.

General information on genetic modification:
http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hmg.chapter.2702,

Article links:
http://www.cumc.columbia.edu/news/review/archives/medrev_v2n1_0002.html

http://dels.nas.edu/ilar_n/ilarjournal/43_2/Welfare.shtml

Alternate Lesson Plans

- **Condense the Lesson (half period):** Have students read the text and answer the comprehension questions for homework. Review the answers before the class discussion.
- **Extend the Lesson (1 period):** Have students complete the Minds-on Activity during class. Ask volunteers to share their graphs and responses and discuss the answers as a group.

LESSON 4: BASIC RESEARCH AND SAFETY TESTING

Chapters and Pages: The Concept of Basic Research, Safety Testing, Cruelty Free (pages 20-28)

Number of Periods: 2

Lesson Summary: In Lesson 4 students will consider whether animals should be used in research that has no expected benefit to humans. Students also will examine the essential role of animals in product safety testing, in light of historical instances where consumer products caused suffering and even death to humans.

Objective: Students will recognize the goals of basic research and identify the stages in drug and consumer product safety testing. Students will use their knowledge of product safety testing to make their own decisions about a drug's safety.

Vocabulary: antibacterial, clinical testing, evaluate, fen-phen, Food and Drug Administration (FDA), magnetic resonance imaging (MRI), nuclear magnetic resonance (NMR), pathologist, preclinical research, toxicology

Activate Prior Knowledge: Brainstorm with students all the products, other than food, that they put in or on their bodies. Suggest categories such as personal care (soap, toothpaste, shampoo, and sunscreen, for example), cosmetics, dietary supplements, and medications (both over-the-counter drugs and prescriptions). List items on the board. Point out that all of the items were once or

still are safety tested on animals. Explain that the selection students are about to read will provide more information about the procedures scientists use to safety test many products on animals.

Lesson 4 Student Worksheet

A. Read to Learn More: Use these questions to facilitate student comprehension of the text.

1. (Page 20): *What is basic research?* [Possible response: experiments that are performed to further scientific knowledge without an obvious or immediate benefit to humans.]

2. (Page 21): *How have scientists reduced the numbers of animals used in consumer product safety testing?* [Possible response: They have developed alternative tests, such as the skin damage test on in vitro cell cultures, which have reduced the use of animals by 90 percent.]

3. (Pages 22-23): *What incidents led to the passage of the Food, Drug, and Cosmetic Act of 1938?* [Possible responses: injuries and deaths from Lash Lure and Elixir Sulfanilamide.]

4. (Pages 24-26): *What are the states of the drug safety testing process?* [Preclinical research, preclinical safety assessment testing, and clinical trials (Phase I, II, III, and IV).] Which stages of drug safety testing require the use of animals? Which stages require the use of people? [Preclinical research and preclinical safety assessment testing require the use of animals. Clinical trials require the use of humans.]

5. (Page 27): *What is one reason that a drug may be found dangerous even after preclinical and clinical testing showed that the drug was safe for public use?* [Possible response: The drug may cause a disease like cancer, which could take 20 years to develop.]

B. Questions for Discussion: Use the questions on the student worksheet to engage students in a dialogue.

C. Minds-on Activity — Safety Testing: The U.S. Food and Drug Administration (FDA) is responsible for approval of food additives, drugs, vaccines, and medical devices (such as artificial hips). All of these require specific animal testing. Cosmetics must also be approved by the FDA, but testing for their safety in humans is left to the cosmetics companies and in some cases this may be done without animal testing (see p. 28). For the list below: Have the students determine the class of the product and how it is used. Then have them divide into small groups to discuss whether they think the use of the product ethically warrants animal testing. Have them explain their decisions.

1. Retrovir (antiviral drug used to treat HIV)

2. *C. botulinum* toxin type A (also called Botox Cosmetic) (drug used as antiwrinkle treatment)

3. C. botulinum toxin type B (also called Myobloc) (drug used to treat debilitating muscle spasms)

4. FluMist (inhaled flu vaccine)

5. Thicker-Lash Mascara (cosmetic)

6. Heartgard (drug to prevent heart worm in dogs)

7. Artificial Heart Valve (medical device used as a replacement for failed or faulty heart valves)

8. Aspartame (food additive—artificial sweetener)

Alternate Lesson Plans

- **Condense the Lesson (1 period):** Have students read and answer the comprehension questions for the Safety Testing chapter only. Eliminate the first and last questions from the class discussion. Assign the Minds-on Activity to groups as a long-term homework assignment. Instruct each group to evaluate all phases of data for the drug and present their results in a written report.
- **Extend the Lesson (1 period):** Have students complete the Minds-on Activity during class. Ask volunteers to share their groups' responses and open the discussion to the class.
- **For the Advanced-Level Learner:** The controversial drug thalidomide was introduced in the 1960s and used in England and Canada to treat morning sickness in pregnant women. The drug caused serious limb malformations and birth defects in the babies born of mothers who had taken the drug. Have the students research the thalidomide debacle and determine whether the drug had been tested appropriately. [Many people maintain that this is an example of animal testing that was not predictive of human adverse effects, but the fact is that the drug had not been tested in pregnant animals before being used in humans. Thalidomide was later shown to be teratogenic (i.e., to cause birth defects) in animal models.]
- **For the Below-Level Learner:** Have students create a flow chart of the stages in the safety testing process. Charts should include the main stages of testing as well as the smaller steps that comprise each stage.

LESSON 5: REGULATION OF ANIMAL RESEARCH

Chapters and Pages: Regulation of Animal Research (pages 29-36)

Number of Periods: 2

Lesson Summary: Lesson 5 describes how the use of animals in biomedical research is regulated by various governmental and private organizations. Students will have the opportunity to explore and evaluate the efficiencies and inefficiencies of animal research regulation.

Objective: Students will identify the different regulations regarding the use of animals in research and distinguish the various organizations that are responsible for the enforcement of those regulations. Students will make decisions about hypothetical protocols for animal research.

Vocabulary: accredit, alternative, compliance, funding, humane, inspect, oversight, regulate, 3 Rs, welfare

Activate Prior Knowledge: Discuss with students some of the rules that are in place within their school. Have students list some of the school's rules and explain why they think schools need to have rules. Also have students describe how the rules are enforced and what school personnel are responsible for enforcing the rules. Discuss what role, if any, students have in enforcing school rules. Then shift the discussion to the oversight of laboratory animals. Ask students to brainstorm the types of rules they believe should be in place to govern the use of animals in research and write their ideas on the board. Have students suggest which government organizations or private groups should be responsible for enforcing the rules. Point out to students that they will read about the rules governing animal use in research and the agencies responsible for enforcing these rules.

Lesson 5 Student Worksheet

A. Read to Learn More: Use these questions to facilitate student comprehension of the text.

1. (Page 29): *What actions caused Congress to pass the Animal Welfare Act in 1966?* [Possible responses: the work of the Animal Welfare Institute and public outrage after an article in Life magazine reported the sale of stolen pets to research facilities.]

2. (Page 30): *Why are rats, mice, and birds not covered by the Animal Welfare Act? What policy does cover these animals?* [Possible response: The USDA does not have the resources to inspect all of the facilities that use these animals; the Public Health Service Policy covers these animals when they are used in facilities that receive federal funding.]

3. (Pages 31-32): *How are Institutional Animal Care and Use Committees (IACUCs) different from government agencies that regulate the oversight of laboratory animals?* [Possible response: They are established by research institutions to review all proposed animal experiments. They include private citizens. They inspect research facilities more often—twice a year.]

4. (Pages 33-34): *How is the Guide for the Care and Use of Laboratory Animals used by research facilities?* [Possible response: Research facilities have to prove their compliance with the Guide to receive funding from the Public Health Service and accreditation by the AAALAC.]

B. Questions for Discussion: Use the questions on the student worksheet to engage students in a dialogue.

C. Minds-on Activity — Regulate Animal Use: Have students play the roles of research scientists and members of an IACUC at a research facility in order to understand the process of creating and evaluating a protocol for animal research.

Divide students into groups, with one group acting as the IACUC and the other groups acting as teams of scientists conducting research. Instruct each research team to create an idea for an experiment on animals in the classroom, such as dissecting frogs or studying the effect of a certain diet on an animal species. Have each "research team" create a protocol for conducting its experiment on animals. Worksheets are at the end of this document.

Direct the classroom IACUC to evaluate each group's protocol and approve or deny the experiment. Have the IACUC members explain their decisions to the class.

Alternate Lesson Plans

- **Condense the Lesson (1 period):** Have students read the text and answer the comprehension questions at home the night before the class discussion. Review the questions in class and conduct the discussion without posing the last two questions. Have groups design animal research protocols as long-term homework projects.
- **Extend the Lesson (1 period):** If possible, have a scientist from a nearby research institution visit the class with his or her own example of an animal research protocol. Invite the scientist to describe the process involved in developing protocols and submitting to

inspections by the USDA, PHS, or AAALAC. Have students themselves evaluate the scientist's protocol and explain their decisions to approve or deny the protocol.

- **For the Below-Level Learner:** Have students create Venn diagrams to compare and contrast two of the following regulations or oversight bodies: the Animal Welfare Act and PHS Policy; the USDA and the PHS; PHS and AAALAC International; European Union animal research regulations and the U.S. Animal Welfare Act; the United Kingdom's Animals (Scientific Procedures) Act and the U.S. Animal Welfare Act.

LESSON 6: THE 3 Rs

Chapters and Pages: Continuing Efforts to More Efficiently Use Laboratory Animals, The 3 Rs in Action, Conclusion (pages 37-40)

Number of Periods: 2

Lesson Summary: Lesson 6 explains the ways in which researchers try to reduce, refine, or replace the numbers of animals used in biomedical research (the concept known as the 3 Rs). Students also will consider the benefits and risks involved in using the 3 Rs and apply the concept to actual biomedical research proposals.

Objective: Students will identify and explain the 3 Rs of animal research and evaluate the designs of experiments for adherence to the 3 Rs.

Vocabulary: collaboration, compassion, efficiently, minimize, Nobel Prize, reduce, refine, replace

Activate Prior Knowledge: Invite students to imagine that they are going to conduct a survey on whether to add an unpopular vegetable, such as Brussels sprouts, to the school lunch menu. As a class, have students consider answers to the following questions: *What is the fewest number of students needed to try the vegetable in order to get a large enough sampling of the student body to make the decision?* [reducing] *How much of the vegetable should students be required to eat—a mouthful or an entire portion?* [refining] *Should the school do something to help students who do not like the vegetable, such as offer a dessert afterwards?* [refining] *Should the school not add the vegetable at all, or ask the faculty to test it instead of the students?* [replacing] *After a brief discussion of these questions, point out that students have just conducted a process similar to the 3 Rs of animal research.*

Lesson 6 Student Worksheet

A. Read to Learn More: Use these questions to facilitate student comprehension of the text.

1. (Page 37): *In your own words, what is the goal of reducing the number of animals used in experiments?* [Possible response: to use the fewest number of animals possible and still get enough information to have a successful experiment.]

2. (Page 38): *Name the 3 Rs.* [Reducing, refining, replacing.] *Why do you think it took 30 years before the 3 Rs received much attention?* [Possible response: Scientists did not have the interest or ability to put the 3 Rs into practice.]

3. (Page 39): *How did Dr. Hampshire apply the 3 Rs to the heart attack research on dogs?* [She had the scientists use the same set of dogs to reduce the number of animals and institute 24-hour critical care to refine the treatment of the dogs.]

4. (Page 40): *How does use of the 3 Rs lead to more accurate research?* [Possible response: Better care of animals means researchers can be more certain that pain or distress is not affecting the outcome of their studies.]

B. Questions for Discussion: Use the questions on the student worksheet to engage students in a dialogue.

C. Minds-on Activity — How Many Animals Should I Use?: Have the students read the scenario about an experiment with rats on the Lesson 6 handout. Using the information provided, ask students to determine the optimal number of rats to be used in the experiment. Is it possible to replace animals in this experiment? Why or why not? Explanations are provided in red below to help teachers guide students through the exercise.

Scenario: A scientist working in a pharmaceutical company has developed a new compound that she thinks might reduce blood pressure and decides to test it in rats. Her company maintains a colony of Sprague-Dawley rats and she knows from previous studies that adult males weighing 450-500 g have a mean blood pressure of 105 mmHg (1). They vary, and this variation is quantified by the "standard deviation" (2), which is 9mmHg. She plans to have a "control" group, which will receive an injection of saline, and a "treated" group, which will have an injection of the new drug dissolved in saline. After an appropriate treatment period, she will measure the blood pressure in each rat and compare the mean blood pressure in the two groups using a statistical test called

"Student's t-test" of group means (3). If the new compound reduces blood pressure by 12 mmHg or more she thinks that it might be worth further development as a human medicine.

Her problem is to decide how many rats she needs to do the experiment. She knows that the mathematical equations are very complex, but has found a web site http://www.biomath.info that will allow her to put in the details of her experiment and will do the calculations for her. The only additional information she needs is to decide what "significance level" (4) to use, how "powerful" (5) her experiment needs to be and the "sidedness" (6) of the test. She decides to use a significance level of 0.05 and a power of 90 percent. She can now enter into the Web site the data on standard deviation (9 mmHg), the mean blood pressure in the controls (105 mmHg) and in the treated group (assuming a difference of 12 mmHg), the sidedness (two-sided), the significance level (0.05), and the power (90 percent or 0.90), and the Web site will tell her how many rats will be needed in each group assuming she is to compare means using a Student's t-test on group means (7).

[Explanation: (1) Blood pressure is measured in mm of a mercury (Hg) column, which exerts sufficient pressure to just stop blood flowing in an artery.

(2) the standard deviation is a measure of variation.

(3) Student's t-test of group means is widely used to compare the means of two groups to determine whether differences between them are likely to have arisen simply by chance. It was developed in 1908 by W. S. Gosset, a statistician working for Guinness the brewers in Dublin, Ireland, under the pseudonym "Student."

(4) The significance level is the chance that two means differ to the extent actually observed in an experiment, simply by chance. If this is chance is very low, say less than 5 percent, then the difference is usually attributed to the effect of the treatment.

(5) The power of an experiment is the probability that it will be capable of detecting a specified difference between the means of two groups. Scientists often specify that their experiments should have a power of 80-90 percent.

(6) In this case it is possible that the new drug could actually increase, rather than decrease, blood pressure so a two-sided test should be used. However, there are situations when the treated group could only differ from the control group in one direction, in which case a two-sided test will be needed.

ANSWER: 13 rats per group. Nothing other than a whole organism model can be used for this experiment because studying the effect of a drug on blood pressure requires the interaction of intact systems within the organism.]

Alternate Lesson Plans

For the Advanced-Level Learner: An investigator is designing an experiment to determine whether a new compound isolated from a rare tropical plant has antibacterial activities. He plans to infect mice with several different types of bacteria: *streptococcus*, *staphylococcus*, and *Pasteurella*, and then administer the compound to find out which bacteria the compound will affect, if any. Have students use the concept of the 3 Rs to develop a research protocol for the experiment. Instruct students to explain how they might be able to replace the mice or reduce the number of mice and to determine the appropriate number to use. Have them describe what methods, if any, they can use to minimize the pain and suffering of the animals (refinement).

[The compound can first be tested on the three types of bacteria in culture to find out if it has antibacterial properties against one or all of them (replacement). Students may suggest that only the bacteria killed in culture should be used to test the compound in mice (reduction). (Keep in mind that it is possible that, although the compound doesn't kill bacteria in culture, it may be metabolized by the mice to a form that will kill the bacteria in the mice.) Students may use the exercise from the Minds-on Activity to determine the appropriate number of animals to use. They can propose to use analgesic drugs to reduce pain in the animals, and if the drug does not appear to be working, i.e., the infection is causing the animals to lose weight or look scruffy, then the animals should be humanely killed to reduce suffering.]

LESSON 1: WHY USE ANIMALS?

A. Read to Learn More

Read the "Preface," "Introduction," and "Why Use Animals?" (pages 1-6) to answer the following questions.

1. What are some of the different public viewpoints on how animals should be used in biomedical research?

_____

_____

_____

2. Why do some animals make good research subjects for studying human disease? _____

_____

_____

3. What types of research mentioned in the text require the use of whole organism (animal) models? What other types of research might also make use of animal models? _____

_____

_____

B. Questions for Discussion

1. *Do you think it's important to search for cures or treatments for diseases and other medical conditions? Why or why not?*
2. *Are there medical conditions or illnesses that are more important to study than others? If so, which ones are more important and why?*
3. *Should treatments for pain be a priority for researchers? Explain your position.*
4. *When is it acceptable to use animals in research? Give examples to support your opinion.*
5. *If animals could not be used in research, what would be the alternatives?*
6. *What do you think might be the risks of relying on other research models, such as computer, cellular, or tissue models?*

C. Minds-on Activity — Real Research

Part 1. Read the abstracts of published studies provided on the back of this worksheet. Determine which of the research models listed on page 5 of the text is being used in each of the studies. Italicized words provide useful new vocabulary to help determine the type of model being used.

Part 2. Look up three new abstracts at PubMed* (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi) and determine the models being used in those studies. **Suggested search terms:** allergens, caffeine and cardiac, obesity, autoimmune.

*PubMed is a service of the National Library of Medicine and includes more than 15 million citations from MEDLINE and additional life science journals for biomedical articles back to the 1950s. PubMed includes links to full text articles and other related resources.

Excerpts from Abstracts of Published Research – Definitions of italicized words may be found in online medical dictionaries, such as:
http://cancerweb.ncl.ac.uk/omd/index.html

Abstract 1. Caffeine intake is associated with an increase in heart rate (HR) variability. This study sought to examine the effects of caffeine on HR variability measures before and during progressive exercise in 11 healthy volunteers in a *double-blind* and counterbalanced *placebo*-controlled paradigm. As expected, there were significant increases in HR and decreases in HR variability after exercise during both placebo and caffeine conditions.

Abstract 2. Allergic reactions to foods are specific problems for infants and young children. Ovomucoid (OM) is one of the major *allergens* found in egg-white. We previously established several *T-cell clones* (TCCs) specific to OM in nonpolarizing conditions from four patients (TM and YN are immediate-type, IH and YT are nonimmediate-type) with egg-white allergy. The objective of this study was to characterize these seven clones (TM 1.3, TM1.4,YN 1.1, YN1.5, IH3.1, IH3.3 and YT6.1) for *cytokine* production patterns and cell-surface-marker phenotypes.

Abstract 3. Heart failure leading to *ventricular arrhythmogenesis* is a major cause of clinical mortality and has been associated with a leak of *sarcoplasmic reticular* (SR) calcium (Ca^{2+}) into the cytosol due to increased open probabilities in cardiac *ryanodine* receptor (RyR2)-Ca^{2+} release channels. Caffeine similarly increases such open probabilities and so we explored its arrhythmogenic effects in intact *murine* hearts. A clinically established programmed electrical stimulation (PES) protocol adapted for studies of isolated intact mouse hearts demonstrated that caffeine increased the frequency of ventricular *tachycardia* from 0 to 100 percent, yet left *electrogram* duration and latency unchanged during PES, thereby excluding slowed conduction as a cause of arrhythmogenesis.

Abstract 4. Brain injury secondary to hypoxic-ischemic disease is the predominant form of damage encountered in the *perinatal* period. The impact of neonatal *hypoxia-ischemia* (HI) in 7-day-old pups on the high-affinity [^{3}H] glutamate uptake into *hippocampal* slices at different times after insult was examined. Immediately following and 1 day after the insult, there was no effect. But at 3 to 5 days after the HI insult, glutamate uptake into the hippocampus was markedly reduced; however, after 30 or 60 days the glutamate uptake into hippocampal slices returned to control levels.

Abstract 5. Factors contributing to "local control" of Ca^{2+} release in cardiac *myocytes* are incompletely understood. We induced local release of Ca^{2+} by regional exposure of mouse atrial and ventricular myocytes to 10 mM caffeine for 500 ms using a rapid solution switcher. The density of mitochondria was greater in ventricular than in atrial myocytes, although the abundance of ryanodine receptors and myofilaments was similar. Partial inhibition of Ca^{2+} uptake via a mitochondrial Ca^{2+} *uniporter* caused an increase in the [Ca^{2+}](i) transient in paced ventricular myocytes and consistently resulted in propagation of Ca^{2+} release.

Abstract 6. Epidemiological studies show an inverse relationship between plasma DHEAS (*dehydroepiandrosterone sulfate*) levels in men and age-related illnesses, including cardiovascular and metabolic diseases, immune disorders, malignancies, and neurological dysfunction. This has generated great interest on the putative role of DHEA in age-associated illnesses. Administration of DHEA to rats and mice reduces visceral fat accumulation and improves insulin resistance in experimental models of diet-induced obesity and/or Type 2 diabetes. In addition, recent studies *in vitro* have shown that DHEA has the capacity to improve endothelial function by increasing *nitric oxide* (NO) synthesis.

LESSON 2: GERMS AND VACCINES

A. Read to Learn More

Read "A Theory of Germs," "Overcoming Disease," "Vaccines," and "Penguins!" (pages 7-12) to answer the following questions.

1. How did Robert Koch use animals to discover how a germ causes a specific disease? _____

_____

_____

2. What two deadly diseases can be prevented with vaccines? _____

3. How have scientists used animals to search for a vaccine against malaria in both humans and animals?

_____

_____

4. What justification does Dr. Kumar give for using animals to study malaria? _____

_____

B. Questions for Discussion

1. *Why do you think scientists need to use laboratory animals, instead of other models, to test whether a germ causes a disease?*
2. *The text tells how many people have died of diseases like smallpox, polio, and malaria. Do you think these numbers support the use of animals to develop vaccines? Why or why not?*
3. *Some diseases such as arthritis and glaucoma do not cause death, but rather pain or other problems. Should animals be used to find treatments for diseases that do not cause death to humans? What types of diseases justify animal research?*
4. *If a disease affects only animals and not humans, should animals be used in research to find a vaccine or cure? What if it is a disease that affects pets, like rabies? What if the disease is for example, mad cow disease, which affects animals we eat? Explain your answers.*

C. Minds-on Activity — Finding Treatments

The story of Dr. Kumar (page 10-11) provides an example of animal research on diseases for which there is no known vaccine or cure. Below is a partial list of diseases for which there is still no vaccine or cure. Choose one of them and use the Internet to prepare a report on it. Reports should include how the disease affects humans, how many people are affected, and how researchers are using animals to find treatments. Include 1-2 paragraphs on whether you think the animal research is justified. Information about diseases can be found at the http://www.nih.gov or http://medlineplus.gov.

Some Diseases for Which There Are No Cures or Vaccines: Common cold, some cancers, Alzheimer's disease, Lou Gehrig disease, epilepsy, malaria, AIDS, scleroderma, arthritis, heart disease, multiple sclerosis, muscular dystrophy, cystic fibrosis, and Tay-Sachs disease.

Science, Medicine, and Animals: Student Worksheet

LESSON 3: DISEASE AND SURGERY

A. Read to Learn More

Read "Understanding Epilepsy," "Surgical Advancements," and "Cancer Therapies" (pages 13-19) to answer the following questions.

1. What three biomedical research models have been used to find drugs to treat epilepsy? _____

_____

2. Which animals are used most often in research? What makes these animals helpful in studying human disease?

_____

_____

_____

3. What are some of the arguments both for and against using rat brain slices in epilepsy drug studies?

_____

_____

4. Which genetically modified animals (also called transgenics) are most commonly used in research and how have they been modified? _____

_____

5. Why would a chemotherapy drug like Gleevec need to be tested on whole animal and human models?

_____

_____

B. Questions for Discussion

1. *Do you think research into epilepsy drugs is justified? Would you feel differently if the research were conducted on dogs or baboons, which also suffer from epilepsy? Explain.*
2. *Do you think it is acceptable for scientists to genetically modify mice to study human diseases and disorders? Does your response depend on the illness? Explain your answers.*
3. *Do you think it is acceptable for scientists to genetically modify dogs, cats, or chimpanzees to study human diseases? Why or why not?*

C. Minds-on Activity — Genetically Modified Animals

Read the articles provided below on the use of genetically modified animals in research. Using one of these examples, or finding another example on the Internet or on databases such as PubMed, write a brief report on how the animals were modified and what scientists hope to learn from them.

General information on genetic modification:
http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hmg.chapter.2702)

Articles:
http://www.cumc.columbia.edu/news/review/archives/medrev_v2n1_0002.html
http://dels.nas.edu/ilar_n/ilarjournal/43_2/Welfare.shtml

LESSON 4: BASIC RESEARCH AND SAFETY TESTING

A. Read to Learn More

Read "The Concept of Basic Research," "Safety Testing," and "Cruelty Free" (pages 20-28) to answer the following questions.

1. What is basic research? _____

_____

2. How have scientists reduced the numbers of animals used in consumer product safety testing? _____

_____

_____

3. What incidents led to the passage of the Food, Drug, and Cosmetic Act of 1938? _____

_____

4. What are the stages of the drug safety testing process? Which stages require the use of animals? Which stages require the use of people? _____

_____

_____

5. What is one reason that a drug may be found dangerous even after preclinical and clinical testing showed that the drug was safe for public use? _____

_____

B. Questions for Discussion

1. *Do you think animals should be used in basic research where there is no predictable benefit to humans? Why or why not?*
2. *Do you think scientists should have to explain what they expect to learn from research if they are going to use animals in their experiments? Explain your answer.*
3. *Is the use of animals justified in the safety testing of all consumer products, including cosmetics, personal care products, and over-the-counter medicine like aspirin? Or are there some products that you think should be tested only on humans? Explain.*
4. *Do you think the FDA is justified in hurrying drugs like Gleevec (page 18) to market? What circumstances would justify shortening a product safety testing process to get it to the public faster? What problems could arise from shortening or eliminating testing of a drug or product?*
5. *Imagine that there is a law preventing the use of animals in safety testing of consumer products or drugs. If you were a scientist, how would you prove your drug or product is safe for people?*

Lesson 4 (continued)

C. Minds-on Activity — Product Safety Testing

The U.S. Food and Drug Administration (FDA) is responsible for approval of food additives, drugs, vaccines, and medical devices (such as artificial hips). All of these require specific animal testing. Cosmetics must also be approved by the FDA, but testing for their safety in humans is left to the cosmetics companies and in some cases this may be done without animal testing (see page 28). For the following list of products, determine the class of the product and how it is used. Discuss in small groups whether you think the use of the product ethically warrants animal testing. Explain your decisions.

1. Retrovir
2. *C. botulinum* toxin type A
3. *C. botulinum* toxin type B
4. FluMist
5. Thicker-Lash Mascara
6. Heartgard
7. Artificial Heart Valve
8. Aspartame

LESSON 5: REGULATION OF ANIMAL RESEARCH

A. Read to Learn More

Read "Regulation of Animal Research" (pages 29-36) to answer the following questions.

1. What actions caused Congress to pass the Animal Welfare Act (AWA) in 1966? _____

_____

2. Why are rats, mice, and birds not covered by the Animal Welfare Act? What policy does cover these animals?

_____

_____

3. How are Institutional Animal Care and Use Committees (IACUCs) different from government agencies that regulate the oversight of laboratory animals? _____

_____

_____

4. How is the Guide for the Care and Use of Laboratory Animals used by research facilities? _____

_____

_____

B. Questions for Discussion

1. *Do you think the Animal Welfare Act should be changed to include rats, mice, and birds? What about creatures such as reptiles, worms, or bacteria? Why or why not?*
2. *If the AWA were changed to include rats, mice, and birds, how should the government handle the large increase in inspections? Who should pay for the increased costs of the additional inspections, the taxpayers or the research facilities? Explain your answers.*
3. *What are the benefits of having Institutional Care and Use Committees at research facilities? What are the drawbacks of these groups? Explain your answers.*
4. *What are the benefits of the AAALAC International? What weaknesses do you see in the services that the organization provides?*
5. *Do you think there are any rules in the European Union or the United Kingdom that should be applied to the regulation of laboratory animals in the United States?*

C. Minds-on Activity — Defending Research Plans

Split up into groups—half acting as an IACUC and the other half acting as teams of scientists conducting research. Each research team should create an idea for an experiment on animals in the classroom, such as dissecting frogs or studying the effect of a certain diet on an animal species, then create a protocol for conducting its experiment on animals using the "Animal Study Proposal" worksheet provided on the following pages. The IACUC groups should then evaluate each research group's protocol and approve or deny the experiment. IACUC members must explain their decisions to the class.

Worksheet for Lesson 5 (2 pages)

ANIMAL STUDY PROPOSAL
FOR INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) REVIEW

Name of Investigator:

Project Title:

Names of all persons who are authorized to use animals in this study:

ANIMAL REQUIREMENTS:

Species: Age: Sex: Source:

Number of animals needed:

Room where the animals will be kept:

Person(s) responsible for care of the animals:

STUDY OBJECTIVES:

Explain the purpose of the study and how the study may benefit human or animal health or advance scientific knowledge:

RATIONALE FOR USING ANIMALS:

Why do you need to use animals? Why did you choose the species selected? Justify the number of animals to be used.

DESCRIPTION OF EXPERIMENT AND ANIMAL PROCEDURES:

Briefly explain the experiments you are planning and all procedures using animals.

Specifically address the following:

How will you identify the animals?

What will the effects be on the animals? (e.g., will the animals experience pain or distress)

When will you terminate the experiment? How will you know it is time to do so?

What will you do with the animals at the end of the experiment?

PAIN OR DISTRESS CLASSIFICATION AND CONSIDERATION OF ALTERNATIVES:

1. Pain or Distress Classification

Species (Common Name)	USDA Classification* B, C, D, or E	Number of Animals Used

2. Consideration of Alternatives

If any procedures fall into USDA's Classification D or E, causing more than momentary or slight pain or distress to the animals, describe your consideration of alternatives and your determination that alternatives are not available. Delineate the methods and sources used in the search. Database references must include databases searched, the date of the search, period covered, and the keywords used. Alternatives include methods that (1) refine existing tests by minimizing animal distress, (2) reduce the number of animals necessary for an experiment, or (3) replace whole-animal use with *in vitro* or other tests.

ANESTHESIA, ANALGESIA, TRANQUILIZATION, OTHER AGENTS

For animals under Classification D, specify the anesthetics, analgesics, sedatives or tranquilizers that are to be used. Include the name of the agent(s), the dosage, route and schedule of administration.

PRINCIPAL INVESTIGATOR CERTIFICATIONS

1. I certify that I have been trained to work with the animals listed.
2. I certify that I have determined that the research proposed here does not unnecessarily duplicate previously reported research.
3. I certify that the individuals listed above are trained to work with the animals.
4. For all USDA Classification D and E proposals, I certify that I have searched the pertinent scientific literature and the sources and/or databases and have found no valid alternative to any procedures described herein which may cause more than momentary pain or distress, whether it is relieved or not.
5. I certify that I will obtain approval from the IACUC before initiating any significant changes in this study.
6. I certify that I will notify the IACUC regarding any unexpected study results that impact the animals. Any unanticipated pain or distress, morbidity, or mortality will be reported to the attending veterinarian and the IACUC.
7. I certify that I am familiar with and will comply with all pertinent institutional, state, and federal rules and policies.

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* USDA Classifications

Classification B: Animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery, but not yet used for such purposes. Example: Animals held under proper captive conditions or wild animals that are being observed.

Classification C: Animals upon which teaching, research, experiments, or tests will be conducted involving no pain, distress, or use of pain-relieving drugs.

Classification D: Animals upon which experiments, teaching, research, surgery, or tests will be conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs will be used.

Classification E: Animals upon which teaching, experiments, research, surgery, or tests will be conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs will adversely affect the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. If there are any animals in Classification E, a justification for not using any pain-relieving drugs must be provided.

LESSON 6: THE 3 Rs

A. Read to Learn More

Read "Continuing Efforts to More Efficiently Use Laboratory Animals," "The 3 Rs in Action," and "Conclusion" (pages 37-40) to answer the following questions.

1. In your own words, what is the goal of reducing the number of animals used in experiments? _____

_____

_____

2. Name the 3 Rs. Why do you think it took 30 years before the 3 Rs received much attention? _____

_____

_____

3. How did Dr. Hampshire apply the 3 Rs to the heart attack research on dogs? _____

_____

4. How does use of the 3 Rs lead to more accurate research? _____

_____

B. Questions for Discussion

1. *Why should the 3 Rs be a goal for researchers using laboratory animals? Explain.*
2. *Should the 3 Rs apply to research on creatures other than warm-blooded animals, such as lizards, worms, or even yeast? Why or why not?*
3. *Are there risks in trying to achieve the 3 Rs in an experiment? What might those risks be?*
4. *When, if ever, should risks lead a scientist to decide that it is not possible to achieve 3 Rs?*
5. *What are some possible limitations to the 3 Rs?*

C. Minds-on Activity — How Many Animals Should I Use?

Read through the following scenario about an experiment using rats. Determine the optimal number of rats that should be used in the experiment. Is it possible to use anything other than a whole organism (animal) model for this experiment? Why or why not?

A scientist working in a pharmaceutical company has developed a new compound that she thinks might reduce blood pressure and decides to test it in rats. Her company maintains a colony of Sprague-Dawley rats, and she knows from previous studies that adult males weighing 450-500 g have a mean blood pressure of 105 mmHg. They vary, and this variation is quantified by the "standard deviation," which is 9 mmHg. She plans to have a "control" group that will receive an injection of saline and a "treated" group that will have an injection of the new drug, dissolved in saline. After an appropriate treatment period she will measure the blood pressure in each rat and compare the mean blood pressure in the two groups using a statistical test called "Student's t-test" of group means. If the new compound reduces blood pressure by 12 mmHg or more, she thinks that it might be worth further development as a human medicine.

Her problem is to decide how many rats she needs to do the experiment. She knows that the mathematical equations are very complex, but has found a web site http://www.biomath.info that will allow her to put in the details of her experiment and will do the calculations for her. The only additional information she needs is to decide what "significance level" to use, how "powerful" her experiment needs to be, and the "sidedness" of the test. She decides to use a significance level of 0.05 and a power of 90 percent. She can now enter into the web site the data on standard deviation (9 mmHg), the mean blood pressure in the controls (105 mmHg) and in the treated group assuming a difference of 12 mmHg, the sidedness (two-sided), the significance level (0.05), and the power (90 percent or 0.90), and the Web site will tell her how many rats will be needed in each group assuming she is to compare means using a Student's t-test on group means.

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About the Institute for Laboratory Animal Research

Since 1952, the Institute for Laboratory Animal Research (ILAR) has developed guidelines and disseminated information on the scientific, technological, and ethical use of animals and related biological resources in research, testing, and education. ILAR promotes high quality, humane care of animals and the appropriate use of animals and alternatives. ILAR functions within the mission of the National Academies as an adviser to the federal government, the biomedical research community and the public. For more information, visit *www.national-academies.org/ilar*.