



For The Greater Good

Curriculum Guide



Northwest Association for Biomedical Research
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Introduction

The appropriate use of animals in research represents a complex ethical issue. In order to understand such an issue and make informed choices about it, students need to thoughtfully consider different viewpoints as well as to learn and apply decision-making skills. Such habits of mind not only have broad applicability for students in their schoolwork but in their life beyond school. This curriculum guide offers strategies for bringing the discussion of this important topic into the classroom.

This teaching guide was designed to accompany 'For the Greater Good', a five-part series about animals in research published by the *Seattle Post-Intelligencer* in the spring of 2000. Letters to the Editor and Opinions published in response to the article are incorporated into the suggested lessons in order to provide a range of viewpoints for students to consider.

The unit was designed to allow students to examine their beliefs and assumptions about the use of animals in research and to learn more about the process of scientific research itself. In addition, the unit explores the unifying concept of models, both scientific and ethical.

Central Ideas *Scientific Literacy, Rights and Responsibilities of Citizenship*

Scientific Literacy

- Appropriate selection of model systems for scientific investigation
- Individuals and society must make decisions on the application of science and technology

Citizenship

- Informed and reasoned decision-making
- Laws, values and principles in a democratic society

Introduction

Overview of Lessons and Culminating Assessment

Lesson	Topic
1	Examining the Relationships Between Humans and Animals Students consider their position on the relationship between humans and animals, first individually, then as a group. This process allows for the examination of the currently held assumptions of students, as well as for the analysis of changes that occur as a result of the subsequent lessons.
2	Models in Science Diabetes case study scenarios are used to introduce the concept of models and the need for scientific models in research. Discussion highlights the need for understanding biomedical research and the role of bioethics. Students use 'research process' cards to try to ascertain the overall pathway for drug development, and reflect on their understanding of the process.
3	Models in Ethics Students are introduced to ethical principles, as well as a bioethical decision-making model. They work through the model with a familiar example, and then complete the first sections of the model as applied to the question of the use of animals in biomedical research.
4	For the Greater Good Students are assigned one of the five stakeholder perspectives (physician, veterinary oncologist, biomedical researcher, spiritual leader, or laboratory animal veterinarian.) Before reading the articles, they imagine the issues that would be of concern to each perspective. They then read the appropriate article and summarize the main points, taking note of the degree to which they anticipated the important issues. They meet in small groups to share the perspectives of the articles and begin to 'formulate the facts' for their decision-making model.
5	Letters and Opinions Each student follows a particular thread of responses and opinions to the articles. Students share what they have read with each other and complete the 'formulate the facts' section of their decision-making model. They clarify what they have learned so far, and what more they would like to know. Alternate strategies for presenting opposing opinions are also provided as optional lessons.

Culminating assessment

- **Decision-making model based on personal position**

Students finish the decision-making model. They formulate several options and weigh the relative merits of each, using ethical principles as well as an understanding of scientific processes. Students' work is assessed according to thoroughness and thoughtful completion and by the rationale presented for the final decision.

- **Letter to the Editor**

Students complete a letter to the editor using the decision-making model as a starting point. The letter is assessed according to appropriate use of language, as well as to the use of specific scientific examples to make a persuasive statement.

Field test teachers recommended this unit prior to dissection studies or other examples of use of animals in the classroom.

Introduction

Essential Question

Under what circumstances, if any, is the use of animals in research ethically justifiable?

Unit Objectives



After completion of the unit, students will:

- Understand different viewpoints surrounding the use of animals in research.
- Understand the biomedical research process and the role of animal models within it.
- Be able to analyze a complex ethical issue using a decision-making model and knowledge of ethical principles.
- Be able to clearly synthesize their analysis of the issue of animal research into writing.

Understandings

Science Understandings

Students will understand that:

- Scientists use models to represent complex systems in order to investigate and study them.
- Animals are effective model organisms for medical research because they share many common elements and features with humans.

Civics Understandings

Students will understand that:

- Laws, regulations and codes of ethics and principles govern the use of animals for research purposes.
- Responsible citizenship requires scientific literacy to discern information and make well reasoned decisions about appropriate applications of research and technology.
- Critical and ethical reasoning need to be applied to bioethical decisions and can be applied to choices faced in many areas of life.

Introduction

Issues

Issues that could be explored using this unit include:

- Why should citizens be responsible for understanding scientific issues?
- Why are bioethical decisions so “hard”?
- Are there universal principles that guide effective decision-making?
- Does the promise of medical progress inherently lead us simultaneously into peril?
- What factors should be considered when experimenting with living organisms and why?
- Can we learn about humans by studies performed on other animals? Why or why not?
- What makes an “appropriate” model organism for scientific research?
- Should the species relationships between humans and animals influence the selection of animal models? Why or why not?

Key Points

Key Points:

- The practice of science has ethical implications for individuals and society, and should be conducted in an environment of transparency and public discourse.
- Laws and structures provide parameters to guide scientific research.
- Analyzing controversial issues in science requires an understanding of scientific concepts, as well as ethical principles and decision-making models.
- All organisms have common genetic, cellular and physiological structures and functions.
- Specific criteria are used to select appropriate model systems for scientific investigation. (e.g. lifespan, anatomic structures, cost of maintenance, reproductive capacity, genetic stocks, phylogenetic relationships)

Skills

Skills:

- Use inquiry & information skills to evaluate reliability, credibility and validity of information from a variety of sources.
- Understand and use interpersonal and group process skills utilized by citizens in a democratic society.
- Understand and apply critical thinking and problem solving skills to make informed and reasoned decisions.

Introduction

Standards

National Science Education Standards Addressed

Science in Personal and Social Perspectives, Content Standard F:

As a result of activities in grades 9-12, all students should develop understandings of **Science and technology in local, national, and global challenges.**

Science and technology are essential social enterprises, but alone they can only indicate what can happen, not what should happen. The latter involves human decisions about the use of knowledge. Understanding basic concepts and principles of science and technology should precede active debate about the economics, policies, politics, and ethics of various science - and technology-related challenges. However, understanding science alone will not resolve local, national, or global challenges.

Washington State Essential Academic Learning Requirements Addressed

Primary Focus:

Science

- 3.2.2.3 Analyze how the scientific enterprise and technological advances influence and are influenced by human activity, for example societal, environmental, economical, political, or ethical considerations.

Social Studies (Civics)

- 4.1.3b Analyze why democracy requires citizens to deliberate on public problems and participate in collective decision-making.
- 4.2.3a Engage in oral and written civic discourse to analyze pressing controversial issues and evaluate competing solutions.

Secondary Focus:

Science

- 1.1.5.3 Classify organisms into distinct groups according to structural, cellular, biochemical, and genetic characteristics.
- 3.1.4.3 Analyze and evaluate the quality and standards of investigative design, processes, and procedures.

Social Studies (Civics)

- 1.3.3a Examine and evaluate how citizens use and influence governmental institutions and processes to solve problems.
- 2.33c Analyze and explain how citizens can influence governments through voting, lobbying, protesting, and revolution
- 4.1.3a Analyze how individual rights can be balanced with the common good.

Introduction

Instructional Components

Length of Unit

This unit is designed to be one week in length, and each lesson can be completed in a 50-minute period. Lessons are intended to be used in sequence, although certain elements (such as the decision-making model) may easily be used in conjunction with discussion of other bioethical issues. In addition, the unit may readily be modified to incorporate a longer period for research.

Field test teachers make the following recommendations:

- The unit works well in conjunction with dissection.
- The unit can easily run 2 weeks, especially at the middle school level.
- There are lots of different ways to use the lessons - review the material beforehand and select the material you wish to focus on.

Audience

Lessons are targeted for grades 7-12, although may be modified to suit other audiences.

Assessment Opportunities

Through a series of learning activities, students will have an opportunity to demonstrate their understanding of core concepts through a variety of mechanisms, including:

Explanation

Justifying position and explaining thinking process

Interpretation

Making meaning from published newspapers articles
Making meaning by assuming a role and developing that perspective

Application

Applying decision making model and critical reasoning

Perspective

Analyzing supporting and opposing arguments for animal research

Empathy

Expressing the perspective of and assuming stakeholder roles

Self-knowledge

Journalling and reflection in response to key focus questions at the conclusion of each learning activity

Lesson 1



Lesson 1

Examining the Relationships Between Humans and Animals

What are the ranges of the relationships between humans and animals and to what extent are those relationships ethically justifiable?

Purpose:

Students will consider the diversity of relationships between humans and animals, and their knowledge and assumptions about those relationships.

Understandings:

- Multiple relationships exist between humans and animals.
- Different perspectives and values generate different decisions.
- Complex decisions require a system to arrive at well-reasoned choices.

Assessment:

- Individual worksheet to consider self-knowledge.
- Four Corners activity to see group perspectives and hear justifications.

Materials and Preparation:

- Copy one Relationship chart (HANDOUT 1) for each student.
- Make overhead masters for journal questions (OVERHEAD 1.1), relationship chart (OVERHEAD 1.2) and for class results if desired (OVERHEAD 1.3).
- Put up one of each of the 'Four Corners' Posters in corners of room. Putting them in plastic sleeves allows for easy re-use.

Lesson Plan

1. Introduce the ENTIRE UNIT to students as an examination of the ethical issues surrounding the use of animals in research.

The following elements of this lesson will help students put the issue in context:

- Exploring relationships that humans have with animals.
- Understanding the biomedical research process.
- Understanding the ethical principles and a decision-making process
- Examining different viewpoints provided by a newspaper series and the responses to those articles.

2. Introduce the final outcome/expectations for students:

- Better understanding of the process of biomedical research and of different stakeholder viewpoints.
- Ability to utilize a decision-making model to consider various options and to arrive at a well-reasoned decision. Stress how applicable this is to their lives in general.
- Ability to apply the reasoning developed in the decision-making model to clarify their own viewpoint and write a letter to the editor.

Lesson 1

3. Introduce LESSON 1 as a chance for them to examine some of their current knowledge and attitudes about the relationships between humans and animals.
4. Distribute relationship sheets to each student (HANDOUT 1). Have students brainstorm, *in pairs or small groups*, some of the relationships humans have with animals. students fill in the FIRST TWO columns in pairs.
5. As a class, discuss what they have written using OVERHEAD 1.2
6. Have students reflect *individually* and silently whether they consider the use of animals ethically justifiable for each relationship, with 1 being Strongly NOT Justified, and 4 being Strongly Justified. Ask them to provide written justification for their ranking.

7. Four Corners Activity

Point out the POSTERS around the room labeled:

Strongly Agree (4), Agree (3), Disagree (2), Strongly Disagree (1).

Select 1-3 Relationships to Explore (for example, Hunting, Food, and Research). If time is limited, reduce the number of relationships explored, **but be sure to include Research for unit continuity.**

Have students stand in the area that appropriately corresponds to their values. Indicate that students can move to a different corner if their position changes over the course of the activity.

8. Class Discussion

Field test teachers recommend that each of the groups should appoint 1-2 people to represent their position. Allow a few minutes for the groups to decide on a summary statement, and then let each group speak in turn. Since students become very excited when speaking about their positions, effective classroom management is important.

Alternatively, ask 1-2 students from each group to explain their position, or challenge them with a question from the list below.

Allow students to see and hear the range of perspectives. Probe for explanations from students on why they chose their area. What is most likely to emerge is that student differences will correspond to some extent to the ranges within each relationship (for example, that hunting can be for sustenance or sport). Strive to demonstrate range of positions within a certain perspective. Both teacher and students can probe others on their stance, seeking the “justification of reasoning”-- asking students to avoid simple yes or no responses.

Allow time for students to return to their desks and add to their individual worksheets if needed.

Lesson 1

Handout 1 Example	
Relationship	Range of Examples
Hunting and Fishing	Recreational, sustaining
Food/Consumption	Dairy products, eggs, fish, free range poultry, veal vs. beef
Companionship	Pets, elderly, depression
Work	Sled Dogs, plow horses
Human assistance	Seeing eye dogs, police dogs
Clothing	Leather, fur coats, shoes
Research	Cosmetics, consumer products, medical: cures for balding vs. cancer
Entertainment	Circus, horse racing

Sample questions to challenge thinking during four corners activity	
Hunting:	Is there a (moral, ethical) difference between hunting for sustenance versus recreation? Is there a difference between hunting for sustenance and buying meat from a supermarket?
Food:	Is there a difference between eating beef versus veal? How many students are vegetarians? Of those, how many are vegetarians for health reasons? For other reasons? How many students would eat meat if they had to kill the animals themselves?
Companionship:	Is having pets ethically justified? What if they are dangerous or endangered? Is it OK to have a dog or a cat and not 'fix' it?
Clothing:	Would you wear a fur coat made from a common animal (rabbit) or one that is farmed (mink)? Would you wear a leather coat? Is there a difference?
Research:	Are certain types of research using animals more justified than others? Is there a difference between doing research to test cosmetics and to try to find medical cures? Between research for cures for balding and cancer? Is the use of particular animals more justified than others? Should cosmetics and drugs be tested on humans without testing on animals beforehand? What does it mean when a label says that a cosmetic is 'cruelty-free'?
Entertainment:	Should animals be used for our own entertainment? Would you attend a circus featuring animal acts? Would you attend a horse race or dog race? How are animals portrayed in the media (in cartoons, movies, children's books)?

Lesson 1

9. Closure

End of activity reflection or journal question: (See Overhead 1.1 for Journal Questions for Unit)

- What questions do you have about the use of animals in medical research? List at least five questions.

Indicate that the following lesson will examine the process of biomedical research in more detail.

Optional Homework

Have students read the Case Studies: Mari's Story and Kaya's Story in preparation for Lesson 2, if students will not be reading these in class.

Have students consider a medical treatment of interest to them and speculate on the process whereby that treatment was discovered and brought into practical use. If students are able to, they should investigate the actual historical circumstances around the development of the treatment.

Extension

Graph results of student 'rankings' related to the use of animals in research to show distribution of perspectives using OVERHEAD 1.3. Alternatively, gather data and have students complete the graph themselves. Repeat individual worksheet and graphing activity at end of the entire unit to compare results.

Journaling Questions

Lesson 1

What questions do you have about the use of animals in research? (Ask at least five questions).

Lesson 2

Summarize the main ideas that you have learned about the research process and the importance of scientific models.

Lesson 3

How do you go about making difficult decisions?

How can an ethical decision-making model help you in the future?

Compare and contrast scientific and ethical models. What similarities do they share? What is unique and different about each?

Lesson 4

How can an understanding of both science and ethics help us to analyze bioethical issues?

Why is understanding different perspectives important for society?

Lesson 5

Has your perspective on the use of animals in research changed over the course of the unit? If so, how? What questions do you still have?

Overhead 1.2

Relationship	Range of Examples
1.	
2.	
3.	
4.	
5.	
6.	
7.	
8.	
9.	
10.	

Overhead 1.3

Overall Class Positions

Relationship:

Number Responding

Pre	Post	Pre	Post	Pre	Post	Pre	Post
1		2		3		4	
Strong NO						Strong YES	

Use of animals ethically justifiable?

Handout 1

Name:			
Period:		Date:	
<i>Relationships between Humans and Other Animals</i>			
Relationship	Range of Examples	Is the use of animals ethically justifiable? 1 (strong no) – 4 (strong yes)	Justification
1.			
2.			
3.			
4.			
5.			

Relationship	Range of Examples	Is the use of animals ethically justifiable? – 1 (strong no) – 4 (strong yes)	Justification
6.			
7.			
8.			
9.			
10.			
11.			

Strongly Disagree

1

Disagree 2

Agree

3

Strongly

Agree

4

Lesson 2



Lesson 2

Models in Science

*How is the biomedical research process dependent on scientific models?
What role do animal models play in the process?*

Purpose:

Students will understand the use of models in biomedical research through analysis of a 'case study' and consideration of how scientific models fit into the research process.

Understandings:

- Models provide a "simplified" representation used to study complex systems.
- Some models are more appropriate in certain circumstances than others.
- Biomedical research raises questions that require both science and ethics to address.
- Citizens need effective tools for scientific analysis.

Assessment:

- Students will create flow charts summarizing the process of drug development, and compare their initial conception about the role of scientific models within that research process with their understanding at the end of the lesson.

Materials and Preparation:

- Copy HANDOUT 2.1, Diabetes Case Studies, for each student.
- Copy HANDOUT 2.2, Diabetes Information, for each student (optional)
- Copy HANDOUT 2.3 and 2.4, Research Model, Comparison Chart (optional)
- Copy HANDOUT 2.5, Research Process Cards onto card stock, 1 set for every 2-4 students, cut the cards out, and insert them into envelopes.
- Create OVERHEAD 2, Overall Drug Development Summary
- Copy HANDOUT 2.6, Overall Drug Development Process (optional)

Lesson Plan

I. Introduce Lesson 2 as a chance for students to focus on the process of research and how scientists try to find cures and treatments for disorders. Indicate that several different scientific research models, including animal ones, will be explored.

*In particular, the lesson highlights the use of **MODELS** in research.*

- All models provide 'simplified' representations to study complex systems.
- Research models provide representations of *biological* systems that allow scientists to draw preliminary conclusions about research questions.

Lesson 2

2. Ask if any students have a relative or friend with a medical condition such as diabetes (clearly, sensitivity will need to be used in probing for this information.) Ask whether the individual takes medication to control their condition, and (if known) what that medication is. Elicit ideas about how drugs are developed, and indicate to students that they will be examining that process during this lesson.

3. Have students individually spend a few moments to draw a 'Drug Development Process Flow Chart' of how they think a drug is developed before it is marketed to the public. Explain that they will compare this initial 'flow chart' to a second one they will generate at the end of the lesson. Tell them not to be discouraged if they are having difficulty, but to try to make an attempt.

Things to consider including in their Drug Development Process Flow Chart:

- Where do scientists find new drugs?
- How do they determine that the new drugs work well and are safe in humans?
- How do scientists decide which system model to use?

Try to elicit some of the model categories from student flow charts (*in vitro* testing, computer modeling, animal models, or clinical trials) and write them on the board or overhead. Indicate that you will be interested in trying to learn about each of the models scientists use in research, how the various models are related, and how scientists decide which model to use.

4. Diabetes Case Study; Introducing the Need for Research

- Explain the use of a 'case study' to follow a drug from discovery to use in humans, and show the use of models in context.

- Have students read the Case Studies: Mari's Story and Kaya's Story. (HANDOUT 2.1)

These could be split up between pairs, and then shared.

Alternatively, these stories could be assigned as homework the previous night.

Field test teachers also suggested having students complete concept maps on the readings.

Suggested questions:

1. How was insulin discovered? What kind of biological models were used in the discovery of insulin?
2. What kind of insulin is used today? What kind of biological models *might* have been used in the manufacture of recombinant insulin?
3. What biological models *do you think* were used in the testing of insulin before widespread use in humans?

Although the answers to the first questions from 1 and 2 above will come directly from the case studies, allow students to speculate on the role of models in the development of insulin.

OPTIONAL: Review in more detail the role of animal models in the development of insulin, using the additional background material provided (HANDOUT 2.2 'Diabetes Information').

Lesson 2

5. Models in Diabetes Research

Review with students where scientific models have been used in development of treatments for diabetes. Explain that scientists must carefully consider which model is most appropriate to select, based on the question they are trying to answer. Potential answers might include:

Animal Models

Discovery of insulin and subsequent testing, development of new therapies for diabetes

Clinical Models

Widespread use in humans

In vitro Models

Development of recombinant insulin

6. Comparison of research models (optional, depending on level of class and time available).

For some classes, a more detailed comparison of research models may be appropriate. A chart (HANDOUT 2.3) summarizing the main models is enclosed, and/or students may fill in a blank chart (HANDOUT 2.4) as the various models are discussed in class. Additional background information about each model is included in the appendix.

7. Provide one set of HANDOUT 2.5, Research Process Cards, to small groups of 2-4 and allow them time to try and put the cards in order. Review with them the appropriate order when finished, again pointing out the role of different models in the process.

8. Show OVERHEAD 2 as a Summary of the Research Process. You may want to point out that approximately 5000 drugs are tested for every one marketed. OPTIONAL HANDOUT 2.6, Research Process, shows this in more detail.

Suggested questions:

- How many years does it take to get the average drug to market?
- Where are the scientific models in this process?
- Why do some models, such as animal ones, precede human trials?
- What role does the FDA play in the process?
- What kind of oversight goes into tests involving animals?
- What are the 3R's?
 1. Reduction-using the minimum number of animals necessary.
 2. Refinement-enhancing animal welfare and ensuring the best conditions possible.
 3. Replacement-using other models when appropriate.
- Would students personally want to take an experimental drug that had only been modeled on a computer and not tested in a living organism? If so, under what circumstances?
- Where in this process do bioethical questions come into play?

Lesson 2

9. Have students draw a *new, revised* Drug Development Process Flow Chart based on their learning. Stress to them that they *do not need to write down the details*, simply the *names* of the models and the order in which they are used in developing a new drug. Also indicate that the process is somewhat flexible (and that not all research necessarily uses all models), but that this order represents one common pathway.

10. Closure

- End of activity reflection or journal questions
- How different were your initial and final research process flow charts? What do you feel you have learned about the research process and the importance of biomedical models?
- Summarize the main ideas that you have learned about the research process and the importance of scientific models.

Extensions

1. The detailed comparison of **Scientific Models Used in Biomedical Research** is provided in the Appendix. It could be used in several ways:

- Provide students with the reading and a blank comparison chart (HANDOUT 2.4) and have students complete the chart as homework (recommended for advanced students).
 - Have students fill in the blank chart as the teacher reviews the various models.
2. Have students research the development of a particular drug or treatment that is of personal interest to them, identifying specifically which kinds of test models were used in the process.
3. Have students conduct additional research on how various models are used in developing new treatments for diabetes.
4. Have students explore the rules and regulations governing the use of animals in research, including the importance of IACUCs (Institutional Animal Care and Use Committees.)

RULES and REGULATIONS: More information about the biomedical research process and the rules and regulations governing the use of animals in research is available at the NWABR website under ‘Biomedical Research’: <http://www.nwabr.org/research/understanding.html>

Case Studies

Mari's Story

At the age of 34, I was in the prime of health. I ran 6 miles a day, hiked in the Cascades whenever I could find the time, and worked long hours at a community health center. One spring day, this all changed when, after a few days of profound fatigue, frequent getting up at night to urinate, and unquenchable thirst, I was diagnosed with Type I Diabetes. This is an autoimmune disease that systematically destroys the insulin-producing islet cells in the pancreas. In the simplest terms, insulin is responsible for providing energy to our cells; without insulin, our cells starve to death.

Being diagnosed with diabetes meant that my life would be permanently altered. I knew that I would no longer be able to take a simple walk to the store without first making sure that my blood sugar was stable. I knew that a pregnancy would now be considered “high risk” and would require more medical intervention. I knew that unless I made a concentrated, life-long effort to control this disease, that I would be faced with the possibilities of blindness, kidney failure, amputation and a very reduced life span. Now, before I could even begin the simple tasks we all take for granted, I would need to have a variety of safeguards in place to prevent low blood sugar, which can result in coma or even death. The knowledge of my sudden, new reality caused me to fall into a heap on the couch and cry.

The positive side of my story is that I am among the 1.4 million Americans living today with Type I diabetes. This disease was once fatal, but can now be controlled through an injectable miracle drug - insulin. In the 1920's, the research team of Drs. Banting and Best discovered that dogs with diabetes survived and even gained weight when injected with insulin from pig or cow pancreas. Pig and cow insulin were then purified and manufactured for use in patients with diabetes. Numerous children with Type I diabetes have been brought back from the brink of death because of the discovery of insulin. Dr. Banting and his research team won the Nobel Prize in 1923 for this life-saving research.

Recent advances in molecular biology now allow human insulin to be produced for diabetics. Continued research and the use of animal models has led to the development of an insulin pump, which allows me to closely regulate my blood sugar. Thanks to this incredible invention, I was able to have two beautiful, healthy sons and can look forward to watching them grow to adulthood.

Case Studies

Kaya's Story

Kaya is a gray domestic short-haired tabby, and has been part of our family for almost 17 years. She's more like a dog than a cat; she comes when you call her and she 'fetches' rubber bands. She makes cackling noises at crows and loves to be picked up and held like an infant. Because she is such a good hunter, we've had to put a bell on her collar to warn birds of her approach.

My daughter and son have always enjoyed a special bond with Kaya. I think in part because Kaya was a mother herself, she seemed to have a high tolerance for young children. She would often cuddle with my daughter or let my son put his head on her like a pillow.

Several years ago, we noticed that Kaya was starting to get lethargic and listless. She would lie in the corner of our living room without moving much. In addition, she seemed to drink water and urinate constantly. When we brought her to the veterinarian for tests, we learned that Kaya was diabetic. I was surprised, as I had never before heard of diabetes in animals. I was also relieved, because it meant that she would not die immediately. We were fortunate; because of scientific research that had been done to develop treatment for human diabetes, Kaya is still with us today.

It turns out that Kaya needed the same type of treatment that people with Type 1 diabetes need – daily injections of insulin. I learned how to pick up the skin on her neck, and to inject her every morning and evening with insulin. The insulin that she uses was developed using recombinant DNA techniques and is the exact same kind that humans use. Scientists combine human DNA (coding for the human insulin protein) with bacterial DNA, insert the combined DNA back into bacteria, and allow the bacteria to make human insulin in large batches. This type of insulin results in fewer allergic reactions in humans than the pig or cow insulin formerly used.

Following treatment with insulin, Kaya's recovery was dramatic. Even though she is an older cat, she has the playfulness of a much younger animal. We are thankful that biomedical research is able to contribute to the health of humans as well as the animals such as Kaya that are our beloved companions.

Handout 2.2 Diabetes Information

What is diabetes?

Diabetes mellitus is a disease in which the body does not make or use insulin correctly in response to an increase in blood sugar after a meal. The major problem associated with diabetes is an excessive amount of glucose or sugar in the blood (hyperglycemia), which can result in the following symptoms of diabetes: increased urination, thirst and hunger along with feelings of tiredness. People with diabetes may also experience abnormal weight loss and blurry vision.

Type 1 diabetes: Type 1 diabetes is usually diagnosed in children and was generally referred to as insulin-dependent diabetes. In type 1 diabetes, the body does not produce insulin at all. This is believed to be caused by an autoimmune reaction in which the body's own defense systems attack and destroy the cells responsible for making insulin.

Type 2 diabetes: Type 2 diabetes is generally referred to as insulin-independent diabetes and is usually diagnosed in older adults. However, more and more young people are developing type 2 diabetes as well. In type 2 diabetes, the body either does not produce enough insulin in response to a meal or cells in the body no longer respond to the insulin.

Facts and Figures

- Almost 17 million Americans have diabetes, but about 6 million don't even know they have it.
- The majority of people with diabetes have type 2 diabetes.
- Diabetes is the 6th leading cause of death in the U.S.

What is insulin?

- Insulin is a hormone produced by the pancreas, an organ near the stomach, and released into the bloodstream. Insulin controls the amount of glucose in the bloodstream by either promoting its entry into muscle cells for use as energy or into fat cells for storage.

- Inside the pancreas, insulin is produced by beta cells which are part of the islets of Langerhans, groups of cells which were discovered by **Dr. Langerhans**.

- Insulin is now commercially made using genetically engineered cells.

What are the factors that contribute to the development of diabetes?

- **Genetics:** Patients with type 1 diabetes are believed to have genetic defects that make them more susceptible to the autoimmune attack that results in the destruction of the beta cells that produce insulin.

- **Diet:** Along with genetics, obesity and high fat diet are believed to contribute to the effects of high glucose levels in the blood resulting in the development of type 2 diabetes.

What kind of research is being done?

- Research to understand why islets are destroyed in the development of type 1 diabetes.
- Research to understand why islets do not work well in type 2 diabetes.

- Research to design ways to replace defective islets and testing of methods to either transplant a whole pancreas or islets from healthy donors to diabetic recipients.

Handout 2.2

What kind of treatments exist for diabetes?

Insulin Injections, Diet: Type 1 diabetes: People with type 1 diabetes need to have multiple injections of insulin every day while carefully monitoring their diet and the level of glucose in their blood.

Drugs, Diet and Exercise: Type 2 diabetes: People with type 2 diabetes can control the amount of glucose in their blood with drugs that promote the production of insulin as well as a strict regimen of diet and exercise.

Transplantation: Successful transplantation of a healthy pancreas into a diabetic patient has enabled many of these patients to lead relatively normal lives for up to 18 years after receiving the new pancreas. A series of trials have now been started in Washington State to transplant islets of Langerhans into diabetic patients.

Animal models in diabetes research

1. Animal models have been key in the discovery and extraction of insulin.

In 1890, German scientists who were researching the process of digestion discovered that removing the pancreas from a dog would cause it to develop diabetes. For the next 30 years, researchers used animals to try to isolate a substance from the pancreas that might cure diabetes.

Drs. Frederick Banting and Charles Best discovered insulin in 1921 at the University of Toronto, Canada. Animals were essential at every stage of this research. Banting and Best obtained extracts from the pancreases of cows and pigs that had been killed for food. They then tested their extract on rats, rabbits and diabetic dogs. One year later in 1922, the first human patient was successfully treated with an insulin injection. Previously, children with diabetes seldom lived for a year after diagnosis, as they literally starved to death no matter how much they ate.

Until 1970, animals were also used to measure the strength of particular batches of insulin. Now, chemical technology has made machines available to conduct such 'assays' or tests. In addition, cows and pigs were the main source of insulin produced until recently. Biotechnology has made possible the insertion of human genes into bacteria for the production of human insulin commercially, thus eliminating many of the allergic reactions humans had to cow and pig insulin.

2. Animal models (usually mice and rats) are used to study how islets can be destroyed or why they lose their ability to produce insulin.

These animals can spontaneously develop diabetes with age or will develop diabetes when placed on a high fat diet or exposed to toxins. Using these animal models, researchers are trying to determine how factors like genetics, diet and environmental factors may cause the destruction of islets and how this destructive process can be prevented.

3. Animal models have been used to develop new drugs that assist the body to produce more insulin or become more responsive to insulin.

For more information: American Diabetes Association, www.diabetes.org
Juvenile Diabetes Foundation, www.jdf.org

Scientific Models Used in Biomedical Research 2.3

Name	Uses	Benefits	Limitations	Dependence on Animal Models
In Vitro Diagnostics (Using cells in test tubes to investigate the effects of drugs or compounds on a specific aspect of normal functions.)	Evaluate whether a compound is toxic or irritating.	<ul style="list-style-type: none"> • Results obtained very quickly. • Easy to use. • Small in scale so researchers may repeat tests often. • Models allow researchers to investigate very specific functions of cells or tissues. • Rigorously controlled environment and test conditions. 	So specific for a particular biological function that they do not mimic what happens in life.	Very High (Cells and tissues obtained from animals.)
Non-Human Tissue Culture Methods (Using cells or tissues from non-human organisms to test new drugs or therapies.)	Evaluate the toxicity and/or efficacy of a particular drug, device, or procedure on a specific type of cell or tissue.	<ul style="list-style-type: none"> • Easy to use. • Strict control over the environment. • One tissue sample can provide millions of cells, so many tests can be conducted using a relatively small amount of tissue. 	<ul style="list-style-type: none"> • Too specific. • Cultured in an artificial environment. • May not behave exactly as human cells. 	Very High (Cells and tissues obtained from animals.)
Human Tissue Culture Methods (Using cells or tissues from humans to test new drugs or therapies.)	Important role in cancer research.	<ul style="list-style-type: none"> • Strict environmental control allows repetition with little variation. • Eliminates the concern over how the drug will react with humans. 	<ul style="list-style-type: none"> • Cultured in an artificial environment. • Human cells/tissues can carry and transmit human diseases. • Difficult to obtain in sufficient quantities. 	Low (Cells and tissues obtained from humans, not animals.)
Computer-Based Modeling (Using computers to simulate how drugs may be absorbed by or react in living organisms.)	<ul style="list-style-type: none"> • Select optimum dosages for clinical studies. • Predict the optimum route of drug administration. • Predict how effective or toxic different versions of the drug are. 	<ul style="list-style-type: none"> • Provide predictions for the drugs behavior in humans. • Reduces the number of animals needed for studies. • Helps to refine studies on animals. 	<ul style="list-style-type: none"> • Only provides predictions. • Model must first be established in animals. • Each model only works for one particular class of drugs. 	Very High (Programming is based on results from animal tests.)
Animal Studies (Using animals to evaluate procedures for efficacy and/or safety.)	Determine effectiveness of a new drug.	<ul style="list-style-type: none"> • New treatments and therapies actually mimic specific disease conditions found in humans. • Cost is less than clinical studies. • Highly specific breeding programs • Easier to conduct than clinical studies. 	<ul style="list-style-type: none"> • In Vitro studies are cheaper, and take less time. • Animals are not identical to human beings. 	Not Applicable (Animal studies always utilize animals.)
Clinical Studies (Using humans as test subjects.)	Investigate the safety and/or efficacy of drug administration.	Drugs are actually tested on humans.	<ul style="list-style-type: none"> • Enrollment in studies is quite low. • Costly and Time-consuming. 	High (Products are not used on humans prior to use on animals.)
Epidemiological Studies (Studying characteristics of certain human populations)	Determine the origin of an infectious agent or the cause of a disease.	Study subjects are human beings.	Study subjects cannot benefit directly.	Low (Studies focus on symptoms and conditions for humans.)

Scientific Models Used in Biomedical Research 2.4

Name	Uses	Benefits	Limitations	Dependence on Animal Models
In Vitro Diagnostics (Using cells in test tubes to investigate the effects of drugs or compounds on a specific aspect of normal functions.)				
Non-Human Tissue Culture Methods (Using cells or tissues from non-human organisms to test new drugs or therapies.)				
Human Tissue Culture Methods (Using cells or tissues from humans to test new drugs or therapies.)				
Computer-Based Modeling (Using computers to simulate how drugs may be absorbed by or react in living organisms.)				
Animal Studies (Using animals to evaluate procedures for efficacy and/or safety.)				
Clinical Studies (Using humans as test subjects.)				
Epidemiological Studies (Studying characteristics of certain human populations)				

Handout 2.5 Research Process Cards



Finding Candidate Drugs:

Rational Drug Design

Computers are used to design candidate drugs that will 'fit' with a target, such as an enzyme involved in a disease pathway.

Combinatorial Chemistry

Chemistry and robotics are used to generate many possible candidates to test randomly and rapidly.

'Discovery' Drug Methods

Researchers use what is known about a disease process or previously discovered drugs to identify potential candidates.

In Vitro ('in glass') Tests

Candidate drugs are tested on cells or tissues in test tubes or flasks to determine their effectiveness.

In silico ('in computer') Tests

The interaction of a candidate drug with the body may be modeled on a computer.

Final Approval

The drug has been approved and is ready to be marketed and sold!

Sometimes, the FDA will require additional human clinical testing after the drug has been marketed.

File Investigational New Drug Application

Investigational New Drug (IND) applications must be filed with the Food and Drug Administration (FDA) in order to proceed.

The application includes information on:

- results of animal tests that show the safety of the drug
- manufacturing information
- procedures for upcoming human trials

Most drugs take 6.5 years to reach this point!

Animal Testing

Animal tests are used to see how the drug will act in a living organism. They are conducted according to federal laws and are carefully reviewed and monitored by special groups designed to oversee experiments. Experiments should be designed based on the 3R's:

- Reduction-using the minimum number of animals necessary.
- Refinement-enhancing animal welfare and ensuring the best conditions possible.
- Replacement-using other models when appropriate.

Handout 2.5 Research Process Cards



Human Clinical Trials

Drug is tested on a small number (20-80) of healthy volunteers to see how the drug acts in the body and to determine safety and dosage.

This process usually takes 1.5 years.

Human Clinical Trials

Drug is tested on a large number (1000-3000) patient volunteers in clinics and hospitals to confirm its effectiveness and to continue to look for risks and side effects from longer use.

The drug is used in the way it would be administered when marketed.

This process usually takes 3.5 years.

Human Clinical Trials

Drug is tested on a relatively small number (100-300) of patient volunteers with the disease to determine the drug's effectiveness in treating the disease and to look for side effects.

This process usually takes 2 years.

File New Drug Application (NDA) with the Food and Drug Administration (FDA) for Final Approval.

Most NDAs are about 100,000 pages long!

The final approval process at the FDA takes approximately 1.5 year.

ANSWER KEY

1. Finding Candidate Drugs
2. In vitro and In silico tests
3. Animal Testing
4. IND
5. Clinical Trials (Phase I, 20-80 individuals)
6. Clinical Trials (Phase II, 100-300 individuals)
7. Clinical Trials (Phase III, 1000-3000 individuals)
8. NDA
9. Final Approval

Handout 2.6

Research Process for New Drug Development

On average, it costs a company \$500 million to get one new medicine from the laboratory to U.S. patients, according to a January 1996 report by the Boston Consulting Group.

	Early Research / Preclinical Testing	File IND at FDA			File NDA at FDA		
		Clinical Trials			FDA		
		Phase I	Phase II	Phase III			Phase IV
Years	6.5	1.5	2	3.5	1.5	15 Total	
Test Population	Laboratory and animal studies	20 to 80 healthy volunteers	100 to 300 patient volunteers	1000 to 3000 patient volunteers Evaluate effectiveness, look for side effects	Review process/ approval		Additional post- marketing testing required by FDA
Purpose	Assess Safety and biological activity	Determine safety and dosage	Evaluate effectiveness, look for side effects	Confirm effectiveness, monitor adverse reactions from long-term use			
Success Rate	5,000 compounds evaluated	5 enter trials			1 approved		

Research Process for New Drug Development

Early Research (6.5 years)



5000 compounds

Laboratory, computer, and animal studies

**File Investigational New Drug (IND)
Application at Food and Drug Administration
(FDA)**

Clinical Trials (7 years)



5 drugs enter human trials

Phase I 20-80 healthy volunteers

Phase II 100-300 patient volunteers

Phase III 1000-3000 patient volunteers

File New Drug Application (NDA) at FDA

FDA (1.5 years)



1 medicine approved

Review process/approval

Lesson 3



Lesson 3

Models in Ethics

Why are decision-making tools so vital to citizenship in a democratic society? How can ethical models be used to address controversial issues?

Purpose:

Students will understand the need for a structured, logical approach to addressing ethical questions. Students will learn the use of ethical models through the application of an ethical decision-making framework.

Understandings:

- Citizens in a democratic society need effective tools for ethical analysis, so that their arguments are based on logic, reason, and principles.
- Decision-making frameworks provide tools for studying complex ethical questions.
- Individual views and values shape approaches to utilizing ethical frameworks.
- Biomedical research raises questions that require both science and ethics to address.

Assessment:

- Students demonstrate their understanding by completing the ethical-decision making model and identifying ethical principles involved.

Materials and Preparation:

- Copies/overheads of OVERHEAD 3.1/3.2, Introduction to Bioethics/Ethical Concepts
- Copies/overheads of HANDOUT 3.3, The Ethical Decision-Making Model
- Copies/overheads of HANDOUT 3.4, 4-Page Ethical Decision-Making Model discussion.

Lesson Plan

1. Introduce Lesson 3 as a chance for students to focus on another kind of model - an ethical decision-making model. Indicate that such models are tools for studying complex ethical questions and have wide applicability for addressing ethical issues.

2. If there has been a recent news story featuring ethics or bioethics, it may make a useful 'hook' for this lesson. Provide the 'big picture' by discussing the following with students:

- What are the rights and responsibilities of citizenship?
- Why are informed and reasoned decision-making necessary?
- What roles do laws, values, and principles play in a democratic society?

Refer back to the Four Corners activity and the justifications people made for their decisions. Share the idea of analyzing different options in a logical, reasoned way in order to come to a decision rather than relying on pure emotion or 'gut-level' reactions. Introduce the idea of a commonly agreed-upon framework for reasoning.

Lesson 3

3. Introduction to the language of ethics

Ask students whether cheating is 'unethical', and if so, why?

Gather answers and group them based on the concepts on Overhead 3.2. For example, some students will bring up rules, some consequences, etc. Use these groupings as a vehicle to discuss morals, values, ethics, and the main ethical concepts.

Introduce ethics as a study of the rational process for determining the best course of action in the face of conflicting choices (H.Brody),

Webster online defines ethic(s) as a *discipline or organized system of thought* that reflects on and studies the moral life.

a) The discipline dealing with what is good and bad and with moral duty and obligation.

b) A set of moral principles or values, a theory of conduct governing an individual or a group, a guiding philosophy.

Review Overheads 3.1 and 3.2

Refer to the appendix for a more complete review of ethical theories.

4. Improvisation on Ethical Principles. Within the field of ethics, there are many different systems (summarized in the appendix), but principle-based approaches have been widely used, especially in biomedical ethics, and are a helpful starting point for learning about bioethics.

Choose pairs or small groups of students to improvise 30-second role-plays for the rest of the class, demonstrating ethical principles in a simulated interaction between a parent and child. Do not explain what the principles are; simply allow the students to observe each dramatization. The 'parents' could, for instance, wonder out loud about what they 'should' or 'should not' do as a result of their child's actions.

Possible examples:

- Parent respecting the privacy of child's bedroom. (respecting autonomy)
- Parent refraining from belittling a child out of anger. (nonmaleficence)
- Parent helping child with their homework. (beneficence)
- Parent being fair between siblings. (justice)

Point out that these scenarios themselves bring up other issues that require balancing of principles:

- What if the child is hiding something in their room that could harm others?
- What if the parent is doing too much of a child's homework?
- Does treating siblings fairly mean treating them equally?

Lesson 3

• **Autonomy- ‘Respect the Individual’**

The word autonomy comes from the Greek *autos* (self) and *nomos* (governance). Autonomy emphasizes the responsibility individuals have for their own lives. Individuals have the right to self-determination and to make their own decisions and choices. The rules for informed consent in medicine derive from the principle of autonomy.

• **Nonmaleficence- ‘Do no harm’**

Nonmaleficence relates to one of the most traditional medical guidelines, the Hippocratic oath (*First of all, do no harm*). It requires individuals to not intentionally or directly inflict harm upon others.

• **Beneficence- ‘Do good’**

This principle stresses directly helping others, acting in their best interests, and being a benefit to them. It requires positive action.

• **Justice- ‘Be Fair’**

This principle relates to ‘*Giving to each that which is his due*’ (Aristotle). It dictates that persons who are equals should qualify for equal treatment, and that resources, risks, and costs should be distributed equitably.

Some ethicists also add:

• **Care** – Focus on the maintenance of healthy, caring relationships between individuals and within a community. The principle of care adds context to the traditional principles and can be used in a complimentary way alongside them.

5. Ethical Frameworks

Suggest that an organized approach, coupled with knowledge of ethical approaches, can be helpful when addressing ethical issues. In addition, a logical, structured approach to addressing controversial or difficult ethical issues is of broad applicability.

Introduce the Decision-Making Model, HANDOUT 3.3, and tell students you will go through it with a familiar example before addressing the use of animals in research.

Have students identify a common ethical issue encountered in their lives, or choose one for them. Then work through the model, drawing on the ethical concepts and principles.

Possible examples include:

- A friend asks you to lie to their parents about his/her whereabouts.
- You haven’t done your homework and your friend offers you hers to copy from.

Walk through the 4-page Decision-Making Model, HANDOUT 3.4, using the hypothetical example, or have students complete it as homework.

6. Closure

End of activity reflection or journal questions:

- Compare and contrast ethical and scientific models. What similarities do they share? What is unique and different about them?
- The last time you were confronted with an emotional or controversial issue, how did you make your decision?
- How can an ethical decision-making model help you with the process in the future?

Lesson 3

Extension

- The appendix provides in-depth information about additional ethical theories and systems. Have students research the various ethical systems, compare their merits and drawbacks, and provide examples of each.
- Also included in the appendix is a comparison chart that summarizes some of the differences between theories. Advanced students could be given a blank or partially blank chart similar to this one to fill out based on their readings.
- More information about bioethics is available at the NWABR website:
<http://www.nwabr.org/education/bioethresc.html>

Handout 3.3

Ethical Decision-Making Model Overview

I. Identify the Bioethical Issue

WHAT is the Ethical Question?

II. Formulate the Facts

KNOWN: What facts are known? What are the essential biological, ethical, economic, social or political considerations? How do you know that the facts are significant, relevant, and accurate?

UNKNOWN: What additional facts, information, or evidence would be useful?

III. Stakeholders and Values

WHO are the stakeholders? Which individuals or groups have an important stake in the outcome?

For each group, identify the claims they hold and the VALUES associated with their claims.

IV. Address Alternatives

Generate Alternative Options

Identify different possible options.

Compare Options

Which ethical perspectives are addressed by each option?

What costs and benefits are associated with each option?

- a. Which options would help support a good general rule for people to follow in similar situations? (MORAL RULES)
- b. Which options would help support or develop the character traits we value most as individuals? (VIRTUE)
- c. Which options would produce the most good and do the least harm? (OUTCOMES)
- d. Which principles are granted priority (autonomy, nonmaleficence, beneficence, justice) for each option? (PRINCIPLES)
- e. Which options are most responsive to the individual needs of those involved and consider the relationships among those individuals? (CARE)

V. Decide

a. What is your decision and how do you justify it?

b. How are the many perspectives, facts and principles thoroughly and fairly considered by your decision?

VI. Act and Evaluate

Act on your decision. Evaluate your decision over time, assessing whether the solution results in the desired outcome. If it doesn't, repeat the process and make adjustments.

Introduction to Bioethics

Values are principles or qualities that signify what is important and worthwhile. Values serve as the basis for moral codes and ethical reflection.

(‘Life is sacred, therefore killing is wrong’)

Each individual has their own values based on many aspects including; family, religion, peers, culture, race, social background, gender, etc. Values guide individuals, professions, communities, and institutions.

Morals are codes of conduct governing behavior. They are an expression of values reflected in actions and practices.

(‘Thou shalt not kill’)

Morals can be held at an individual or communal level.

Ethics provide a systematic, rational way to work through dilemmas and to determine the best course of action in the face of conflicting choices.

(‘If killing is wrong, can one justify the death penalty or kill in self defense?’)

Ethics attempts to find and describe what people believe is right and wrong, and to establish whether certain actions are actually right or wrong based on the all the information available.

Ethical Concepts and Approaches

Rules

An action is right if it follows certain fundamental moral rules (such as ‘don’t treat people as a means to an end’).

Virtues

An action is right if it conforms to a model set of attributes that is inherent in a particular community.

Outcomes/Consequences

An action is right if good consequences outweigh bad consequences.

Principles

An action is right if it follows the principles:

1. *Autonomy*: Respecting the individual
2. *Beneficence*: Being of benefit to others
3. *Non-maleficence*: Not intentionally harming others (Hippocratic oath: ‘First, do no harm’)
4. *Justice*: Acting fairly

Handout 3.4: Ethical Decision-Making Model

Name: _____

Period: _____

Date: _____

I. Identify the Bioethical Issue:

WHAT is the ETHICAL QUESTION?

II. Formulate the Facts

KNOWN: What facts are known? What are the essential biological, ethical, economic, social or political considerations?

UNKNOWN: What additional facts, information, or evidence would be useful?

III. Consider the Controversy

WHO are the stakeholders? Which individuals or groups have an important stake in the outcome? Identify the concerns and **VALUES** associated each stakeholder.

stakeholder	stakeholder	stakeholder	stakeholder
↓	↓	↓	↓
values	values	values	values
stakeholder	stakeholder	stakeholder	stakeholder
↓	↓	↓	↓
values	values	values	values

IV. Address Alternatives

	Pros	Cons
Option 1		
Option 2		
Option 3		



Which options would help support a good general rule for people to follow in similar situations?
Which options would help support or develop the character traits we value most as individuals?
Which options would produce the most good and do the least harm?
Which principles are granted priority for each option?
Which options are most responsive to the needs of individuals and their relations with others?

V. Decide

What is your decision?

Justify your decision, using ethical concepts and principles.

1.

2.

3.

VI. Act and Evaluate

Act on your decision. Evaluate your decision over time, assessing whether the solution results in the desired outcome. If it doesn't, repeat the process and make adjustments.

Lesson 4



Lesson 4

For the Greater Good

How does considering different perspectives promote an understanding of the many dimensions of an ethical issue?

Purpose:

Students will appreciate the importance of considering different perspectives when considering ethical questions. Students will apply the ethical decision-making framework to the essential question of the unit.

Understandings:

- Citizens in a democratic society need effective tools for ethical analysis, so that their arguments are based on logic, reason, and principles.
- Decision-making frameworks provide tools for studying complex ethical questions.
- Individual views and values shape approaches to utilizing ethical frameworks.
- Biomedical research raises questions that require both science and ethics to address.

Assessment:

- Students demonstrate their understanding of the issue by applying the ethical-decision making model and identifying the various viewpoints and ethical principles involved.
- Students share their summaries of the various viewpoints with each other and the class.

Materials and Preparation:

- Copies of HANDOUT 4.1, For the Greater Good Article Summary Sheet, 1 for each student.
- *Copies of For the Greater Good Articles, 1 per student. Distribute the 5 articles evenly among students. Alternatively, provide each student with the set of articles.*

Lesson Plan

1. In Lesson 4, students will have an opportunity to apply the decision-making model to the essential question posed at the outset of the unit.

Revisit the differences in position among students made evident through the 'Four Corners' activity, and stress again the importance of rigorous and disciplined justifications of arguments in the decision-making process.

Regardless of whether students alter their stance or position, they should be able to demonstrate their consideration of multiple sides of the issue and present a structured, logical defense of their conclusions.

Lesson 4

2. Stress to students that they will have the opportunity to examine both sides of the issue surrounding the use of animals in research. They will have the opportunity to look at the responses that followed the publication of the articles (both pro and con) in Lesson 5, as well as share their own perspectives in their 'Letter to the Editor' at the end of the unit.

Describe the historical context of the For the Greater Good Series:

- *The series ran in the Seattle Post-Intelligencer in April 2000.*
- It consisted of five segments, each portraying a different viewpoint of a person involved in animals and research.
- Editor Samuel Sperry introduced the series in the following way: *Most of what we know about using animals in medical research comes from people who oppose it. Today the Post-Intelligencer begins a five-part series looking at the issue from the other side.*

3. Distribute the articles and ask students to take out a piece of paper (or HANDOUT 4.1 if desired) and assign each student one of the five stakeholder perspectives featured in the articles:

- Physician
- Veterinary Oncologist (Animal Cancer Specialist)
- Biomedical Researcher
- Spiritual Leader
- Laboratory Animal Veterinarian

4. Allow all students assuming the same stakeholder role to meet as groups. BEFORE reading the articles, have students read the BIOGRAPHICAL information and reflect on their **assigned** perspective in writing:

- How might your stakeholder describe their perspective about the relationship of animals and humans in general and the use of animals in research in particular? Explain your reasoning.
- What issues might be of concern to your **assigned** stakeholder?

5. Allow quiet reading time.

6. After reading, students should summarize in writing the main points of the article, and take note of the degree to which they anticipated the important issues.

- What was the overall position of the **assigned** stakeholder?
- What were the 2-3 main points of the **assigned** stakeholder and how did they support their points with examples or evidence?
- How closely did you anticipate the issues of concern to the stakeholder?

7. Ask students to discuss the 2-3 main points of their stakeholder in their small group.

8. 'JIGSAW': Form groups composed of each stakeholder. Allow each stakeholder to assume the 'role' and share their 2-3 important points with others in their group from their perspective. If time permits, allow others to ask questions of that stakeholder.

Lesson 4

9. Distribute Handout 3.4 (the 4-page version of the decision-making template) to each student. You may also wish to distribute or review with students the scoring guide for the template found in Lesson 5.

In their groups, have students identify the issue and the stakeholders together. They will also begin to collect examples and factual information from the articles and record that information on their sheets.

10. Instruct students to keep their handouts (or papers upon which similar information is written, if they have used their own paper) until the end of the unit, to be turned in as a package with their final decision-making template and Letter to the Editor.

Closure

- Indicate that the final lesson will allow students to follow the responses to the article series, both pro and con, and to finish their decision-making model to come to their own conclusions about the issue.

Reflection/journal question:

- Why is understanding different perspectives important within society?

Alternatives and Extensions:

Have each stakeholder group designate a spokesperson to share their position with the class, rather than meeting in a jigsaw.

Have each student read all 5 articles and summarize the main points of each perspective as homework the previous night. Use class time to review the perspectives, research additional information about the use of animals in research, and allow students to begin filling out the decision-making template.

Have students research the use of the animals in research as homework. The NWABR website, <http://www.nwabr.org/research/resources.html>, has additional information and resources on the topic.

Alternate Culminating Activity Lessons 4 and 5: Mock Congressional Hearing

1. Have students conduct preliminary research as homework, each bringing in an article related to animals in research.
2. Identify key concepts that need to be clarified/explored, and additional information required.
3. Have students identify stakeholders and values, including congressional panel (moderate / liberal / conservative representation).
4. Randomly assign students to stakeholders.
5. Have students gather information on stakeholder perspectives, including providing them with the 'For the Greater Good' Articles as well as the Pro/Con responses.
6. Allow each stakeholder to write their main points on an index card, and allow them a brief time to present to the panel and answer questions from the panel/audience.
7. After all stakeholders have spoken, the panel deliberates and shares their decision.

For the Greater Good Handout 4.1

Name: _____

Period: _____

Date: _____

Stakeholder Assigned:

- | | |
|---|---|
| <input type="checkbox"/> Physician - Eschbach | <input type="checkbox"/> Spiritual Leader - Luedke |
| <input type="checkbox"/> Animal Cancer Specialist - Gavin | <input type="checkbox"/> Laboratory Animal Veterinarian - Pekow |
| <input type="checkbox"/> Biomedical Researcher - Corey | |

First, read the biographical sketch of your stakeholder at the end of the article.

Before reading the article itself, answer the following:

1. How might your stakeholder describe their perspective about the relationship of animals and humans in general and the use of animals in research in particular? Explain your reasoning.

2. What issues might be of concern to your stakeholder?

After Reading:

3. Summarize in one sentence the 'position' of the stakeholder.

4. What were the 2-3 main points of the stakeholder? Describe the examples or evidence that the stakeholder used to support these points.

5. Look back at the pre-reading questions 1 and 2. How closely did you anticipate the issues of concern to the stakeholder?

OTHER ARTICLES / STAKEHOLDERS	
Stakeholder: Main points: 1. 2. 3.	Stakeholder: Main points: 1. 2. 3.
Stakeholder: Main points: 1. 2. 3.	Stakeholder: Main points: 1. 2. 3.

Lesson 5



Lesson 5

Pro & Con Responses to Series

How does considering different perspectives promote an understanding of the many dimensions of an ethical issue?

Purpose:

Students will appreciate the importance of considering different perspectives when considering ethical questions. Students will apply the ethical decision-making framework to the essential question of the unit and justify their own decisions.

Understandings:

- Citizens in a democratic society need effective tools for ethical analysis so that their arguments are based on logic, reason, and principles.
- Decision-making frameworks provide tools for studying complex ethical questions.
- Individual views and values shape approaches to utilizing ethical frameworks.
- Biomedical research raises questions that require both science and ethics to address.

Assessment:

- Students demonstrate their understanding of the issue by applying the ethical decision-making model, weighing different options, and justifying their conclusions. The culminating assessment is a Letter to the Editor of a newspaper or journal.
- Information on the extent to which the unit has impacted student perspectives can be gauged by the use of the Four Corners activity.

Materials and Preparation:

- Obtain copies of *For the Greater Good: Pro & Con Responses to Series*, 1 pairing per student. Distribute the letters evenly among students. Alternatively, provide each student with the full set of letters.
- Handout 5.1, Letter to Editor Guide (one per student)
- Handout 5.2, Letter to Editor Checklist (one per student)
- Handout 5.3, Letter to Editor Scoring Guide (for teacher use but can be shared with students)
- Handout 5.4, Decision-Making Model Scoring Guide (for teacher use but can be shared with students)

Lesson Plan

1. In Lesson 5, students continue to apply the decision-making model to the essential question posed at the outset of the unit. They will read some opposing viewpoints regarding the use of animals in research. Finally, they will use the decision-making model to clarify their position in a rational, logical way and will summarize their position in a *Letter to the Editor*.

Lesson 5

2. Distribute the articles and assign students to one of the five ‘article partnerships’.

Article groupings ★ longer and more content-rich articles.	
<p>Group 1</p> <p>Con: Series ‘props up powerful rather than supports the truth’, Lenz Abberation of medicine grows under guise of helping humans, Papy</p>	<p>Pro: Cancer survivor got to know puppies that helped save her life, Coulter Four-footed friends important in development of new drugs, Connolly</p>
<p>★ Group 2</p> <p>Con: Human lives not saved by lab animals, Cohen</p>	<p>Pro: Four-footed friends important in development of new drugs, Sprugel</p>
<p>Group 3</p> <p>Con: In search for cures for human illnesses, leave animals alone, Guillermo</p>	<p>Pro: Honor animals: All of God’s creatures deserve our respect, Turner</p>
<p>Group 4</p> <p>Con: Experiments prove we don’t hold all life sacred, Wilkins</p>	<p>Pro: Penicillin’s success came from tests on rats, Speth</p>
<p>★ Group 5</p> <p>Con: Why veterinarians go to one school, medical doctors to another, Greek and Greek (could add <i>The whole story of research on animals has yet to be told,</i></p>	<p>Pro: Flaws in anti-animal research argument, Burke (could add <i>Submitted Letter, Botting</i>)</p>

3. Form groups of 5, with one student from each ‘article grouping’.

4. Provide quiet reading time.

5. Ask students to take out their decision-making templates (HANDOUT 3.4) and add to the ‘formulate the facts’ section any information gleaned from reading their articles.

6. Allow students time to share information from the articles with each other and to add additional facts presented by other students.

7. Provide students time to complete the decision-making model, weighing different options and the implications of each. Have students use the justification of their final decisions as a basis for writing their letters.

8. Review guidelines for the Letter to the Editor (HANDOUT 5.1) as well as the accompanying checklist (HANDOUT 5.2), and allow students to complete as homework.

9. When collecting Letters to Editor, also collect completed decision-making model templates (HANDOUT 3.4), as well as student summary sheets (HANDOUT 4.1).

Lesson 5

Ethical Theories and Their Relationship to Animal Research Issues

• **Opposition to research:** Ethical arguments against the use of animals in research have focused primarily on **outcome-based** (Singer) and **rights-based** (Regan) perspectives. Outcome-based (or 'consequentialist') arguments against animals in research propose that the interests of other animals deserve equal consideration with those of humans, and that valuing humans above other animals is 'speciesism' - on par with racism and sexism. Strict consequentialists support research if on balance the benefits outweigh the harms. If humans and other animals have equal interest in being free from suffering, then only that research which could also be conducted on humans would be supported. Rights-based arguments against animal research postulate that all animals, including humans, possess inherent value. Animals that, according to this perspective are 'subjects of a life' (with desires, memories, a sense of the future, etc.) have the moral right to be treated in the same way as humans and other 'subjects of a life'. These rights are inherent and the decision to use animals should not rest on what the potential benefits might be to others.

• **Support of research:** Contemporary ethical arguments supporting the use of animals in research have focused primarily on **outcome-based perspectives** (Fuchs/Rollins/Tannenbaum), pointing to great benefits of such research for both humans and other animals. Strict outcome-based calculations can be difficult, however, because the direct utility of experiments cannot always be predicted, and basic research that seems unrelated to direct human interests may later drive many discoveries. In refuting rights-based views, proponents of research point out that nonhuman animals lack the capacity for moral judgment, but they have moral rights not to suffer undue pain. Animals should be treated humanely, and their interests should be maximized to the extent possible, but that does not mean they cannot be used appropriately in research. Historically, (after human experimentation in Nazi Germany) the Nuremburg Principles set the foundation for the use of non-human animal experiments prior to experimentation on humans. Proponents of the use of animals in research consider it unethical to experiment on human subjects prior to conducting animal experiments.

Closure

If time permits, have students do a **SECOND FOUR CORNERS ACTIVITY** (see Lesson 1) on the use of animals in research. Compare the number of students in each category (strongly agree, etc.) for pre- and post- unit using the overhead graph. Have students share any change in perspectives.

Extension:

- Spread the letter writing activity over several days, allowing for multiple drafts and peer review.
- Allow more time for students to obtain additional information about the use of animals in biomedical research.

Alternative Options:

1. Choose 5 'con' letters to provide a counterpoint to the 5 articles in lesson 4.
2. Examine viewpoints not directly related to the series. One possible resource is: Roleff, T., ed., *The Rights of Animals* (Current Controversies Series), Greenhaven Press, San Diego, 1999.
3. Mock Congressional Hearing, see Lesson 4: Alternate Culminating Activity.

Letter to the Editor Writing Guide

Background

A Letter to the Editor is a short essay that expresses a writer's views on a topic, and tries to persuade others to accept or understand that view based on logical arguments. It is an effective way of participating in the dialogue surrounding an issue in the media.

Your Letter to the Editor will provide you a chance to demonstrate your understanding of the issues surrounding the use of animals in research and allow you to present your opinions in a well-reasoned and thoughtful way. Your Letter should build upon the conclusions you come to as a result of completing the Ethical Decision-Making Model.

You will not be graded on what your opinion is, but rather in how well you support your points and present your case. Your message will be influenced by the vocabulary that you use and by the way your letter is presented, so these will also contribute to your score. Be sure to check your final draft against the checklist for the Letter to the Editor requirements.

Writing the Letter

1. Write a single sentence that sums up your position (sometimes called your **THESIS STATEMENT**).
This sentence will often contain the words *should* or *should not*. Make the statement as specific as possible. Explain what should be done, who should do it, and any other particulars that will clarify your position.
2. Identify the basic **BIOETHICAL CONCEPTS** involved and describe **HOW** they relate to your position.
3. Using the information from your Ethical Decision-Making Model, develop reasons that will support your position. How convincing your position is depends largely on the reasons you choose to support it.
 - a. Your Letter to the Editor should have at least **THREE** reasons, each with its own paragraph.
 - b. Each reason should be clearly **DIFFERENT** from the other.
 - c. Each reason should **RELATE** directly to the position statement.
 - d. Each reason should also have some **EXAMPLES** or **EVIDENCE** (facts, statistics) behind it.
 - e. Your letter should include an explanation of 'scientific models' and a discussion of how they relate to your position.
4. Pick what you believe to be your opponent's strongest arguments and be sure to address each of those opposing reasons with evidence. Counter them in either a separate paragraph or as part of a preceding paragraph.
5. Conclude the letter in a way that ties things together. You may want to end your letter with a suggestion of some kind of action that the reader should take.
6. Consult the Letter to the Editor Checklist for specific writing and presentation requirements. In addition, consider the following:
 - a. Put your full name, address, phone number, and email at the top of the letter so that the newspaper can contact you.
 - b. Identify by headline and date of publication any reference to a letter or article published previously
 - c. Address your opponents' arguments instead of attacking your opponents personally.
 - d. Incorporate personal experience to your letter only if it is relevant.

Letter checklist 5.2

Letter to the Editor Checklist

IDEAS and REASONING (50 pts)

- ☐ THESIS statement clearly stated.
- ☐ Bioethical concept(s) involved clearly defined.
- ☐ Relationship of bioethical concept(s) to position described.
- ☐ Minimum of 3 reasons clearly stated.
- ☐ Each reason is clearly different from the other.
- ☐ Each reason relates directly to the position statement and is relevant.
- ☐ Each reason has appropriate and credible examples or evidence supporting it.
- ☐ Opponent's position analyzed and evaluated.
- ☐ Effective closing statement provided.
- ☐ Scientific models discussed

LOGIC and ORGANIZATION (25 pts)

- ☐ THESIS statement and description of bioethical concepts involved.
- Reason 1** – Evidence/Examples
- Reason 2** – Evidence/Examples
- Reason 3** – Evidence/Examples
(Opponents' position addressed, either as separate paragraph or part of a preceding one)
- ☐ Closing and/or Call to Action
- ☐ Sequence of the writing builds to a high point (has momentum)
- ☐ Smooth transitions

WRITING (20 pts)

- ☐ **Voice:** personal voice, aware of audience
- ☐ **Vocabulary:** strong, natural, and avoids repetition and clichés
- ☐ **Sentence fluency:** writing flows, sentence lengths are varied
- ☐ **Conventions:** accurate spelling, grammar, and evidence of proofreading

PRESENTATION (5 pts)

- ☐ Appropriate letter format: name and contact information, date, and signature
- ☐ Appropriate use of fonts (10 or 12 point, Arial, Helvetica, Times, or similar)
- ☐ Standard 1 inch margins
- ☐ Presentation enhances the writer's message.

<h1>Letter to the Editor</h1> <h2>Scoring Guide</h2>		5 STRONG Shows control and skill in this trait; many strengths present.	4 COMPETENT Strengths outweigh the weaknesses; a small amount of	3 DEVELOPING Strengths and need for revision are about equal.	2 EMERGING Need for revision outweighs	1 NOT YET A bare beginning; writer not yet showing any control.	Score
Ideas and Reasoning <ul style="list-style-type: none"> • Thesis statement clearly stated. • Bioethical concepts involved defined and relation to position described. • Minimum of 3 reasons clearly stated. • Each reason is distinct, relevant, and has appropriate and credible examples/evidence supporting it. • Scientific models discussed. • Opponent's position analyzed and evaluated. • Relates to outcome determined by decision-making model. • Effective closing statement provided. • Shows thoughtfulness and insight into topic. 							__X 10 =
Logic and Organization <ul style="list-style-type: none"> • Follows overall suggestion for organization. • Effective and logical sequence, good pacing, and smooth transitions. • Builds to a high point, has momentum. • Sense of resolution. 							__X 5 =
Voice Awareness of audience. Commitment, involvement, and conviction conveyed. Text is lively, personal, and individual.							__X 1 =
Word Choice <ul style="list-style-type: none"> • Strong vocabulary used. Word choice is natural, not forced. Minimal use of repetition, clichés, or abstract language. 							__X 1 =
Sentence Fluency <ul style="list-style-type: none"> • Natural sentences with a variety of lengths and structures. No run-ons. 							__X 1 =
Conventions <ul style="list-style-type: none"> • Accurate spelling, punctuation, capitals, paragraphs, grammar. • Readable to a wide audience. • Evidence of proofreading. 							__X 1 =
Presentation <ul style="list-style-type: none"> • The form and presentation enhance the writer's message. • The presentation is consistent with a letter format. • Appropriate use of fonts and font sizes, margins, spacing. 							__X 1 =
Total Score							____/100

Lesson 5

<i>Ethical Decision-Making Model Scoring Guide</i>	Points Possible	Points Received
Ethical question clearly identified 5 pts: Question that relates to an ethical dilemma clearly identified. 4 pts: Question suggests an ethical dilemma but is ambiguous, vague, or not clearly identified. 3 pts: Question does not clearly relate to an ethical dilemma or is inappropriate for topic. 0 pts: Question not identified.	5	
Sufficient factual information gathered 10 pts: Factual information gathered reflects good use of the time and resources available to student. 8 pts: Factual information gathered reflects adequate use of the time and resources available to student. 6 pts: Factual information gathered reflects poor use of the time and resources available to student. 0 pts: Factual information is missing.	10	
Additional (unknown) information necessary for decision-making identified 10 pts: Additional information necessary for decision-making is thoroughly considered, clear explanation of what is lacking is provided. 8 pts: Additional information briefly considered, and explanation conveys what is lacking overall. 6 pts: An attempt to identify additional information is made, but explanation is unclear or not present. 0 pts: Additional information not considered.	10	
Stakeholders clearly identified 5 pts: Major stakeholders clearly identified, and their claims, values, and assumptions are explored. 4 pts: Major stakeholders clearly identified, but without corresponding clarification of their position. 3 pts: Major stakeholders not clearly identified, or irrelevant stakeholders mentioned. 0 pts: Description of stakeholders is missing.	5	
Basic bioethical concepts involved identified and explained 5 pts: Concepts clearly identified and their logical relation to the ethical question is explained. 4 pts: Concepts are identified, but their relationship to the question is illogical or not explained. 3 pts: Inappropriate concepts are identified, and no explanation is provided. 0 pts: Concepts are neither identified nor explained.	5	
Minimum of 3 alternative options generated 5 pts: 3 alternative options described 4 pts: 2 alternative options described 3 pts: 1 option described 0: Description of options is missing	5	

over
→

Lesson 5

<i>Ethical Decision-Making Model Scoring Guide (continued)</i>		Points Possible
Option 1 10 pts: Option thoroughly evaluated based on principles, consideration of perspectives, implications, concessions, and costs/benefits. 8 pts: Evaluation of option is adequate, but certain aspects lack depth. The discussion of principles, implications, concessions, and cost/benefits would benefit from further exploration and development. 6: Evaluation of option is attempted, but Important aspects may have been missed or are incorrectly interpreted. 0 pts: Option is not described.	10	
Option 2 10 pts: Option thoroughly evaluated based on principles, consideration of perspectives, implications, concessions, and costs/benefits. 8 pts: Evaluation of option is adequate, but certain aspects lack depth. The discussion of principles, implications, concessions, and cost/benefits would benefit from further exploration and development. 6: Evaluation of option is attempted, but Important aspects may have been missed or are incorrectly interpreted. 0 pts: Option is not described.	10	
Option 3 10 pts: Option thoroughly evaluated based on principles, consideration of perspectives, implications, concessions, and costs/benefits. 8 pts: Evaluation of option is adequate, but certain aspects lack depth. The discussion of principles, implications, concessions, and cost/benefits would benefit from further exploration and development. 6: Evaluation of option is attempted, but Important aspects may have been missed or are incorrectly interpreted. 0 pts: Option is not described.	10	
Decision clearly identified 5 pts: Final decision is readily identified. 4 pts: Final decision is identified, but may be unclear or vague 3 pts: Final decision is alluded to, but may be incomplete or fragmentary. 0 pts: Final decision is not identified.	5	
Justification provided based on comparison of options 25 pts: Thorough reference made to the consideration of perspectives, facts, and principles involved. Clear articulation of the rationale behind the decision. Explanation is logical and presents at least 3 supporting examples. 22 pts: Reference made to the consideration of perspectives, facts, and principles involved. Articulation of the rationale behind the decision is mostly complete. Explanation is logical and presents at least 3 supporting examples. 19 pts: Partial reference is made to the consideration of perspectives, facts, and principles involved, but key points may be missing. The rationale behind the decision may be incomplete. The explanation may not follow logically, or less than 3 supporting examples are present. 16 pts: The consideration of perspectives, facts, and principles involved is incomplete. The rationale behind the decision is not clearly explained. Evidence of a logical justification for the decision reached is scant or absent, or less than 2 supporting examples are present. 15 pts or less: The consideration of perspectives, facts, and principles involved is attempted. Evidence of a logical justification for the decision reached is scant or absent. Supporting examples, if provided, are insufficiently developed or do not relate to the decision made.	25	
TOTAL		100

Appendix

Ethical Theories

Scientific Models

Ethical Theories

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These theories all represent efforts to understand, organize and structure moral life. Each one provides a framework that helps human beings determine what human actions are morally right or morally wrong.

Rules and Duties: Deontological Ethics

Deontologists focus on the act. This theory holds that there is something about an act, independent of its consequences – or at least not totally dependent on its consequences – that makes it right or wrong. The rightness of an act depends on the nature of the act itself, not on the consequences.

One well known version of this type of ethical theory is called “Kantian” ethics because the German philosopher Immanuel Kant (1724-1804) was a major proponent and developer of this approach to ethics. Kant emphasized the need for persons to act from moral duty. Deontologists also argue that persons must act not only in accordance with obligation or duty but for the sake of obligation or duty – persons must be motivated to act out of duty for the act to be moral. Kant offered a “categorical imperative” – a command that is absolutely binding, without exception – as the fundamental principle grounding morality. He stated it in several different ways:

1. “One must act only in such a way that one could will one’s act to become a universal law or rule (maxim)”.
2. “I ought never to act except in such a way that I can also will my maxim should become a universal law”.
3. “Act in such a way that always the action treats humanity never simply as a means, but at the same time as an end”.

From Kant we gain a focus on autonomy and respect for persons. Kant does hold that some of our duties to ourselves and others are perfect and must always be done – do not commit suicide, do not kill innocents, do not lie, etc. Whereas other duties are imperfect and therefore must only sometimes be done – develop our talents and ourselves, contribute to the welfare of others.

Terms associated with deontological ethics

Duty, Immanuel Kant, categorical imperative, rules, autonomy

Contributions

- Offers consistent principles or rules
- Relatively clear and simple guide
- Recognizes certain role-related duties
- Incorporates past action into reasoning
- Persons must be treated as ends in themselves and never solely as a means to an end
- Recognizes individual rights

Constraints

- Does not offer a way to deal with conflicting obligations
- Perfect obligations permit no exceptions and sometimes this dictate is not in accord with our experience of the moral life
- Sometimes neglects the importance of relationships
- Does not offer much guidance about forming and applying moral rules in a real life setting

Virtue-Based Ethics

Virtue theory is an ancient theory from classical Greek ethics. Virtue theory focuses on the character of the moral agent and his or her attitudes, dispositions, or character traits. These traits or dispositions are evaluated by comparing them with the traits or virtues that enable us to be and to act in ways that fully develop our human potential. Examples of virtues are honesty, courage, integrity, trustworthiness, wisdom, temperance, justice. It is the virtue - the character trait or persistent disposition to act in a certain way - that makes an act right or wrong. The agent must work to cultivate virtuous traits - education, role models, habitual exercise or attitude and behavior - to ensure that he or she will act morally rightly. He or she needs to develop discernment, emotional attunement, sympathetic insightfulness to act in the proper manner.

Contributions

- Compatible with principles
 - Broadens the perspective of ethical concern beyond that of moral action to include the moral agent
 - Encourages the identification and cultivation of human excellence, a prerequisite for good living.
- Specific virtues are identified as prerequisite for the practice of good medicine, good nursing, good science, etc.

Constraints

- Lack of consensus regarding the essential virtues
- Needs a prior theory of the right and the good and of human nature in which the virtues can be anchored and defined
- Skeptics question whether good character or virtue can be taught
- Virtue is of a very personal nature
- An agent can be of good character and do wrong - or be of bad character and do right - virtue theory does not explain this fact very effectively

Outcomes: Consequentialist Ethics

The focus of consequentialist theories is on the consequences of the action or policy on all persons directly or indirectly affected. The morally appropriate act is one that maximizes the amount of whatever outcome is deemed good and identified as intrinsically valuable, useful, or good. Consequentialists seek to bring about the greatest good for the greatest number of people.

English philosophers Jeremy Bentham and John Stuart Mill were crucial in the development of utilitarianism as a form of consequentialist ethics. In its most simplistic and traditional form, utilitarianism identifies “pleasure” as the good that must be maximized and “pain” as the evil that must be minimized. Utilitarians want to maximize happiness so they determine which actions will have the best outcome in terms of happiness or pleasure, and act so as to bring it about. Moral action is that which results in good or desirable consequences. The rightness of the act is measured by the good or bad consequences it brings about – more good is better. Contemporary utilitarian philosophers identify other values as “good” such as friendship, health, knowledge, etc.

Terms associated with consequentialism:

Utility, consequences, ends, outcomes, cost/benefit analysis, “the ends justify the means”

Contributions

- Considers the interest of all persons equally
- Directs attention to the consequences of actions
- Offers a familiar form of reasoning – thinking about consequences to guide actions
- Can be used to establish public policy

Constraints

- Appears to permit consequences to drive the determination of what is or is not a moral action, so that bad acts with good consequences might be permissible
- Ignores or does not do justice to the particular and morally significant relationships that make up our lives – the highly personal nature of “duty”
- Interests of majority can override the rights of minorities
- Can lead to unjust social distributions
- Makes people responsible for too much; requires too broad a view – ALL people and ALL consequences
- Hard to determine what counts as a benefit or a harm
- Difficult to quantify certain goods in terms of benefits and harms
- Difficult to compare goods or harms

Principle-Based Ethics

The focus of principlism is on identifying the principles supported by or compromised by the question or issue at hand. Philosophers Thomas Beauchamp and Jim Childress identify four principles, namely respect for autonomy, justice, beneficence, and nonmaleficence. These principles form a commonly held set of pillars for moral life.

Respect for Autonomy	Acknowledge a person's right to make choices, to hold views, and to take actions based on personal values and beliefs
Justice	Treating a person fairly or appropriately in light of what is due or owed him or her; many different forms of justice and different principles provide the conditions for justice – equal share, need, effort, contribution, merit, free-market exchange, etc.
Nonmaleficence	Obligation not to inflict harm intentionally; In medical ethics, the physician's guiding maxim is "First, do no harm". Discussions in bioethics involve issues ranging from letting die, withholding or withdrawing medical treatment, physician-assisted suicide, etc.
Beneficence	Requires us to provide benefits to persons, to contribute to persons welfare, refers to an action done for the benefit of others, prevent harm, etc.

Terms associated with principlism

Principles, respect for autonomy, justice, beneficence, nonmaleficence

Contributions

- Draws on principles or pillars that are a part of American life – familiar to most people, although not by their philosophical term
- Compatible with both consequentialist and deontological theories
- Provides useful and fairly specific action guidelines
- Offers an approach that is appropriate for general bioethics and clinical ethics
- Requires weighing and balancing – flexible, responsive to particular situations

Constraints

- Lacks a unifying moral theory that ties the principles together as a systematic, coherent, and comprehensive body of guidelines
- The principles can conflict and the theory provides no decision procedure to adjudicate these conflicts
- Runs the risk of being applied without thought – "mantra"
- Requires weighing and balancing – difficult, no clear guidance provided

Summary of Main Ethical Theories

Ethical Theory	Moral Rules (Act)	Virtues (Agent)	Consequence	Principles (Context)
	Duty-based (Deontological) Ethics	Virtue-based Ethics	Consequentialist Ethics	Principle-Based Ethics
Description	Actions independent of consequences make the actions right or wrong. We are universally obliged to fulfill our duties and to act to fulfill these duties.	Attitudes, dispositions, or character traits that enable us to be and to act in ways that develop our human potential (for example, honesty, trustworthiness, integrity, faithfulness, etc.)	Consequence of actions or policies must uphold well-being of all persons directly or indirectly affect by action or policy	Four principles form a commonly held set of pillars for moral life. They are respect for autonomy, justice, beneficence (do good), and nonmaleficence (do no harm).
What would a person from such an approach say?	<p>"Whenever I am , I shall . Whenever anyone is , he or she will ".</p> <p>"The ends do not justify the means."</p>	<p>"What is ethical is what develops moral virtues in ourselves and our community."</p> <p>"It takes a virtuous person to act in a virtuous manner; if you always act in a virtuous manner, you are a virtuous person."</p>	<p>"Of any two actions, the most ethical one will produce the greatest balance of benefits."</p> <p>"The ends do justify the means."</p>	<p>"Uphold the pillars whenever possible according to the situation."</p> <p>"Take the agent, act, and consequence all into consideration and proceed in the path that follows the principles."</p>
Some Contributions	Offers consistent rules to follow Recognizes role-related duties in society	Encourage cultivation of human excellence	Directs attention to consequences Considers interests of all persons equally	Requires balancing Draws on principles familiar to American life
Some Constraints	Sometimes obligations conflict	Lack of consensus regarding essential virtues Circularity	Bad acts are permissible Interests of the majority can override minority Can't predict all outcomes	Principles can conflict

Scientific Models Used in Biomedical Research

In Vitro (in glass) Models

Description:

In Vitro diagnostics models typically use a biological component (such as bacterial cells, skin tissue, liver cells, etc.) as a model to test the effects of a new compound or drug on a specific aspect of the model's normal function, such as enzyme release, metabolism, programmed cell death activation, electrical conductivity, etc.

Uses:

Currently, In Vitro diagnostics models are generally used to evaluate whether a compound is toxic or irritating; in fact, some of these models are used as alternatives to the Ocular Irritation Test, or the Draize Test.

Benefits:

- For most of these models, the results are obtained very quickly.
- Most have specific sets of instructions, so they are relatively easy to use.
- The models are small in scale and allow researchers to repeat tests as often as necessary.
- These models are very specific; they allow the researcher to investigate very specific functions of cells or tissue.
- The environment and test conditions for these models are controlled so rigorously that they provide clear results; their specificity prevents most, if not all, outside influences from interfering with the results.
- Finally, they're easier to use and maintain than animals.

Limitations:

- The primary benefit of these models—their specificity—is also their primary limitation. In most cases, they are so specific for a particular biological function that they don't mimic what happens In Vivo (in life). Cellular functions In Vivo are extremely complicated; one particular function always affects dozens, if not hundreds, of other functions. Conversely, those other functions inevitably affect the function being tested with the diagnostic model. So obtaining a clear result for one specific function only provides a very small picture of what actually happens in the animal or human.
- More importantly, however, is that by eliminating all the normal variables that would make obtaining a clear result impossible, these models may not accurately predict what will happen in a living organism.

Dependence on Animal Models: Very High.

In Vitro diagnostic models rely heavily on animal models for two reasons.

- Most require cells or tissues from animals.
- In order to confirm that these tests are reliable, the results obtained from them are compared to results obtained from previous research studies using animal models.

Contributions to Biomedical Research:

As stated above, a combination of several of these tests is being investigated as an alternative to the Draize Test. Also, scientists sometimes use these models as the first step in investigating whether a new compound might eventually become an effective drug. Results from these tests help scientists determine if a new compound should be studied further.

Non-Human Tissue Culture Methods

Non-Human Tissue Culture Methods

Description:

Non-human tissue culture methods generally use normal or abnormal cells or tissues extracted from a wide range of organisms (bacteria, rodents, primates, etc.), which are maintained in rigidly controlled artificial environments. Researchers can insert new drugs or devices in these cultures, or apply new therapeutic procedures to the cultures, to evaluate their effects on the cells/tissues.

Uses:

Non-human tissue cultures are generally used to evaluate the toxicity and/or efficacy of a particular drug, device, or procedure on a specific type of cell or tissue. One of the most widespread uses is in cancer research, since new chemotherapeutic agents can be applied to cultured cancer cells to determine how effective they are in killing the cells.

Benefits:

The benefits of utilizing non-human tissue cultures are similar to the benefits of In Vitro Diagnostic models.

- The procedures used to test drugs, devices, etc. are fairly easy to use.
- These models offer strict environmental control, so they can be repeated with little variation from one test to another.
- The control over the environment allows the researcher to evaluate the results without concern for other “confounding variables” seen when conducting In Vivo experiments.
- One tissue sample can provide millions of cells, so many tests can be conducted using cells donated from a relatively small amount of tissue.

Limitations:

- The model might be so specific for a certain function that does not accurately represent what may or will happen In Vivo (in life).
- When specialized cells are cultured in artificial environments (a condition called de-differentiation), they tend to lose the functions and abilities that defined them as functional cells; for example, mouse hepatocytes (liver cells) may actually lose their ability to metabolize drugs In Vitro, which is one of the hepatocytes’ primary functions In Vivo.

(Scientists are attempting to reduce the effects of both of these limitations by creating tissue culture methods that mimic In Vivo conditions more closely.)

- These models utilize non-human cells/tissues, so the researcher must remember that they may not behave exactly as human cells, although in most cases, similarities between human and animal cells vastly outweigh the differences.

Continued on back

Scientific Models Used in Biomedical Research

Dependence on Animal Models: Very high.

- Any tissue culture method utilizing animal cells or tissue requires a donation from the animal itself. Since most animal cells/tissues are not capable of living and thriving on their own outside the body (they are not “immortal” cells/tissues), animal tissue donation is required regularly.
- Results obtained from these models must be compared to results obtained from previous research studies using animal models in order to validate their reliability.

Contributions to Biomedical Research:

Antibiotics are routinely tested on bacterial cultures to confirm their effectiveness In Vitro before they are tested In Vivo—penicillin was one of the first successful examples of the procedure. Virtually all chemotherapy agents are tested In Vitro on tumor cells obtained from mice to determine their ability to kill these cells. In most cases, these agents are subsequently administered to other mouse cells In Vitro (i.e. liver cells, cardiac tissue, etc.) to determine if they might be toxic to organs/tissues if administered In Vivo.



Scientific Models Used in Biomedical Research

Human Tissue Culture Methods

Description:

Human tissue culture methods generally use normal or abnormal cells or tissues extracted from a wide range of organisms (bacteria, rodents, primates, etc.), which are maintained in rigidly controlled artificial environments. Researchers can insert new drugs or devices in these cultures, or apply new therapeutic procedures to the cultures, to evaluate their effects on the cells/tissues.

Uses:

Human tissue cultures are generally used to evaluate the toxicity and/or efficacy of a particular drug, device, or procedure on a specific type of cell or tissue. Human tissue culture plays a very important role in cancer research—cancer cells are obtained from human hosts, maintained *In Vitro*, and used to evaluate new drugs.

Benefits:

There are two primary benefits to utilizing human tissue culture methods:

- The models offer strict environmental control, so they can be repeated with little variation from one test to another; additionally, they allow the researcher to evaluate the results without concern for other “confounding variables” seen when conducting *In Vivo* experiments.
- Since the cells/tissue used are human, it eliminates the concern that animal cells may not behave exactly as human cells. By utilizing human cells/tissue, the technique removes this potential source of variability.

Limitations:

Human tissue culture models have three primary limitations to their use.

- De-differentiation can and does occur in human tissue cultures. When specialized cells are cultured in artificial environments (a condition called de-differentiation), they tend to lose the functions and abilities that defined them as functional cells.
- Human cells/tissue can carry and transmit human diseases. In fact, transmission of diseases such as HIV and Hepatitis via contact with human tissue can occur with little difficulty if protective precautions are not taken. As a result, the use of human tissue for any biomedical research, including cultures, is highly regulated by federal and state agencies. If the tissue to be used has the potential to transmit diseases such as HIV and/or Hepatitis, laws and regulations require the use of special containment units (i.e. Biological Safety Cabinets) and personal protective equipment (i.e. face shields, goggles, HEPA-filtered air units, coveralls, and even spacesuits with independent air supplies).
- Human tissue is relatively difficult to obtain in sufficient quantities for research, and when there is enough tissue, it's usually quite expensive (due to supply problems and the number of regulations in place to use the material).

Dependence on Animal Models: Low.

Human tissue culture models are primitive compared to non-human models, so their continued development and validation as reliable models depend on how well they compare to non-human tissue culture and animal models.

Contributions to Biomedical Research:

Human tissue culture's most significant contribution to biomedical research has to be in cancer studies, since human cancer cells and novel chemotherapy drugs can be investigated *In Vitro*. Typically, the results seen *In Vitro* help the scientist determine if additional studies may be worthwhile.

Computer-Based Modeling

Description:

To create the computer simulation, vast amounts of data from tissue culture studies and animal studies on a particular type (or class) of drug must be compiled. This includes data from absorption, distribution metabolism, and excretion (ADME) studies conducted for several different drugs within the drug class being investigated. The information must include specific details on effects on many different tissue types and organs for the animal that will be simulated by the computer program. The compiled information/data is entered into a computer; from this, a computer simulation program is created that essentially produces a “virtual animal” that can predict how other drugs in that drug class will effect that particular animal.

1) **Toxicokinetics** is the field of biomedical research that investigates how a drug is absorbed by the body, metabolized in the body, distributed throughout the body, and excreted out of the body - otherwise known as a drug's ADME profile.

2) **Toxicodynamics** is the field of biomedical research that is the next logical step after toxicokinetics. Once a drug has been absorbed, metabolized, and distributed, and before it's excreted, it has to affect the cells/tissues/organs in the body in some way. Toxicodynamics investigates the effects of drug compounds on animal or human tissue In Vivo (in a living organism).

Uses:

Results from toxicokinetic and toxicodynamic models can be used to select optimum dosages for animal and/or clinical studies. They can be used to predict the optimum route of drug administration; for example, the model can provide the ADME profiles for oral and/or injected administration of a drug. They can also be used to predict the efficacy and/or the toxicity profile of slightly different structures of the same drug.

Benefits:

- Toxicokinetic models provide predictions for a drug's ADME behavior before it's actually administered to animals or humans. The information allows the researcher to select more appropriate dosages for future In Vivo ADME studies, or to design such studies with fewer treatment groups .
- Toxicokinetic and toxicodynamic models help to reduce the number of animals needed for studies.
- The animals used for these studies are less likely to experience toxic effects.

Limitations:

- Conditions In Vivo are vastly complex; because of this, computer models can provide fairly reliable, but not perfect predictions; the effects of a drug are never truly known until the drug is administered to a living organism.
- Toxicokinetic and toxicodynamic models can only work after the model has been established—the model can only be programmed after data from previous In Vitro and In Vivo studies have been entered into the computer.
- Each model only works for one particular class of drug—if the new drug has a novel structure that has never been seen before in any drug class, a new model must be created from scratch.

Dependence on Animals Models: Very High.

- Computer simulations such as these require data on ADME functions.
- The data can only come from In Vitro or animal studies conducted in the past.

Scientific Models Used in Biomedical Research

Animal Studies

Description:

In animal studies, drugs, medical devices, or surgical procedures are evaluated for efficacy and/or safety utilizing animals as study subjects.

Uses:

Animal studies can be used to determine how effective a new drug may be in treating a medical condition, whether a drug is toxic or harmful to a living organism, and even to determine the dose levels that may cause toxicity. Animal studies are critical for cancer research, because they represent the only research model (other than clinical studies) that allows the scientist to investigate the effectiveness of a new chemotherapy agent and its safety profile at the same time. They are also indispensable in reproductive studies; in fact, the guidelines for administration of most drugs to pregnant women are based on results obtained from animal studies.

Benefits:

- Animal studies are much easier to conduct than clinical studies, and cost far less.
- Animal studies provide much more reliable predictions about a drug's potential behavior in human beings than any other biomedical research model (except for clinical studies).
- Organizations that specialize in providing laboratory animals for biomedical research have exceptional breeding programs that are conducted in facilities that are more sanitary than most hospitals; as a result, scientists can rely on ample supplies of healthy animals.
- Breeding programs are able to provide populations of animals with wide genetic diversity (Outbred stocks) or populations of animals that all have the same genetic makeup (Inbred strains).
- With the development of "transgenic" and "knockout" technology (genes that cause or prevent disease conditions can be inserted into or removed from an animal's normal DNA), scientists can investigate new treatments and therapies using animal models that actually mimic specific disease conditions found in animals and humans.

Limitations:

Animal studies have two general limitations compared to other biomedical research models:

- They require more time, effort, money, and expertise than In Vitro studies or modeling programs. Because the use of animals is never to be taken lightly, their health and well-being must be considered at all times. In addition, unhappy, unhealthy animals will produce poor study results.. So scientists must take the greatest care possible when planning and performing studies with animals.
- Animals may be very similar to human beings, but they are not identical to them; because of this, results from an animal study may not always reliably predict the results in clinical studies. With continued research, scientists continue to learn more about the ways animals are similar to humans, and the ways they differ from humans. The most current information on animals must be learned and considered by the scientist in order to select the most appropriate animal model for their research.

Contributions to Biomedical Research

Too numerous to count. Animal studies have contributed to almost every breakthrough or discovery in biomedical research.

Scientific Models Used in Biomedical Research

Clinical Studies

Description:

Clinical studies utilize humans as the test subjects. They represent the last step in the biomedical research pathway before a drug, device, or surgical procedure ("treatment") is approved for widespread use.

Uses:

Clinical studies investigate the safety and/or efficacy of drug administration, medical device function, or surgical procedures. There are four types or "phases" of clinical studies: (1) Phase I studies determine the safety profile of the treatment; (2) Phase II studies continue to evaluate the safety profile, but also begin to examine the efficacy of the treatment; (3) Phase III studies enroll a large number of test subjects, and are designed to provide a detailed, accurate efficacy profile of the treatment in human beings; (4) Phase IV studies are conducted after the treatment has been approved for widespread use - they provide even more detail about safety and efficacy profiles.

Benefits:

- The primary benefit of clinical studies is simple - drugs, devices, or procedures intended for widespread use in humans are actually being tested on humans, so results from these studies obviously provide the most reliable indication of how the treatment will work once it's approved.

Limitations:

- Enrollment in clinical studies is usually quite low, even in the larger Phase III and IV studies. The reasons include: rigid government laws regulating the conduct of such studies; time (most clinical studies require a lengthy commitment from the test subjects); enrollment requirements (most studies have strict enrollment requirements, so most applicants are rejected); money (clinical studies are far more expensive than any other type of biomedical research study).
- Because of low enrollment, some characteristics of the drug, device, or procedure may not become evident until after it has been approved, when it's provided to a much larger population. Even though the treatment has been tested in humans, it hasn't been tested in every human, so it may produce adverse effects in a small percent of the population.
- The other primary limitations are time (clinical trials are quite lengthy) and money.

Dependence on Animal Models: High.

For ethical and practical reasons, a drug, device, or procedure can't be administered on a human being until its potential effects are already understood. This is only possible by investigating the effects using every tool available to researcher. This includes animal models, which almost always proceed clinical trials.

Contributions to Biomedical Research:

Clinical trials have been essential for almost every discovery or breakthrough in biomedical research.



Epidemiological Studies



Description:

Epidemiological studies investigate the causes of, and progression of, public health problems or epidemics. Most of these studies resemble large-scale detective investigations; public health officials may conduct detailed interviews with people experiencing identical medical problems, or take samples of the environment common to a group of people experiencing the same infection or medical condition, or conduct detailed review of patient histories for people who have seen physicians for a particular ailment or set of symptoms. The epidemiologist looks for common traits among the interviewees/patients; detailed investigation of these common traits eventually leads to a common cause for the medical problem experienced by the community.

Uses:

Epidemiological studies can determine the origin of an infectious agent (Example: finding the first patient, or index case, to be infected with the Ebola Virus), or determine how an infectious agent is spread (Example: Legionnaires' Disease). These studies can also be used to determine the presence of hazardous material exposure in a community (Example: Three Mile Island), or can be used to link particular sets of health problems to a common practice (Tobacco Consumption).

Benefits:

- The primary benefit of epidemiological studies is the study subjects are human beings. Human beings are able to speak, and they can remember places they've been and activities they've participated in, so interviews of these subjects provide vast amounts of information. As long as epidemiologists conduct thorough interviews with many study subjects, and as long as they thoroughly review each interview to discover common threads within the interviews, a root cause of the problem can usually be identified.

Limitations:

- The biggest limitation is simple - the damage has already been done. The goal of biomedical research is to improve the quality of life; results from epidemiological studies can only serve this purpose indirectly, and only after people have already suffered. For example, epidemiological studies linked severe birth defects in children to Thalidomide use by their mothers during pregnancy; however, this was discovered long after many babies had already been born with severe disabilities or missing limbs.

Dependence on Animal Models: Low.

Animal model studies may be conducted to support or confirm results from epidemiological studies, but for the most part, these studies focus on symptoms and conditions found in human beings and/or their environments. In cases like Thalidomide, perhaps if more animal studies had been conducted on the effects of Thalidomide use, the drug may have never been approved, and thousands of people that were born severely deformed may have had a chance to live normal lives.

Continued on back

Contributions to Biomedical Research:

Epidemiological studies have been most important in the identification and investigation of new infectious agents, such as Bolivian Hemorrhagic Fever, AIDS, Legionnaires' Disease, and Ebola. They have also been critical in linking cancer in Vietnam Veterans to exposure to Agent Orange, or the prevalence of cancer in residential communities linked to the use of drinking water contaminated with hexavalent chromium. Finally, epidemiological studies have been indispensable in linking heart disease, lung cancer, throat cancer, etc. to tobacco consumption.

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Diabetes Information courtesy of Phuong Oanh T. Stephan, Ph.D., Staff Scientist, Pacific Northwest Research Institute, August 2002.

Scientific Test Models courtesy of Scott Burke, Ph.D. Research Scientist, Cell Therapeutics, August 2002.

Case Studies

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Pro&Con Responses

Responses to

Animals & Research:

A Five-Part Series

Published by

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NORTHWEST ASSOCIATION for
BIOMEDICAL RESEARCH

GROUP ONE

A. Series 'props up the powerful rather than supports the truth'

SUNDAY, APRIL 23, 2000

I shouldn't be a bit surprised that in the controversial matter of animal research, you've chosen yet again to prop up the powerful rather than report the truth. How dare you insinuate that all who oppose animal research do so on moral grounds? A large and increasing number of people, including doctors, are becoming aware of the fact that animal research does not work and is, in fact, fake science.

The researchers themselves admit that it doesn't work — listen very carefully the next time they announce one of their "major breakthroughs." If it works on animals, they'll say we should be cautiously optimistic because we don't know if it works on humans yet. If it doesn't work on animals, they say, it might work on humans, we haven't really tested it yet. Of what value is a test that has to be repeated on humans because we can't be sure the results can be extrapolated? The real experiment takes place when a drug that has been tested only on animals is given to a human.

Vivisection is the science of similarity. The problem is, the concept of similarity has no place in real science.

If you were in need of a blood transfusion but only a substance similar to blood could be found, would you allow it to be pumped into your arm? There are, of course, a million other analogies I could draw, but I hope they're not necessary to help you see that the similarity of animals to humans is not a sound foundation upon which to proceed.



Animals are not only different from humans in every scientifically meaningful way, they're different from one another. Did you know that aspirin is perfectly safe for dogs but is toxic for cats? Did you know there are thousands of examples of how drugs affect different species differently?

One more thing: Please spare us the accounting of the budgets of those groups who oppose vivisection. They are puny in comparison to the billions of wasted dollars being poured into the fraudulent, financially motivated "science" of animal research.

**Nora Lenz
Bellevue**

B. Aberration of medicine grows under guise of helping humans

SUNDAY, APRIL 23, 2000

I am writing to express my disappointment in the P-I for being another cheerleader/mouthpiece for the incredibly well-funded animal experimentation industry. Under the guise of improving and protecting human health, this aberration of medicine continues to grow — in direct correlation with myriad diseases of the body and mind afflicting humans.

Animal experimentation is a doomed and fatally flawed research methodology, because it assumes that artificially re-creating the symptoms of human disease in healthy non-human animals is a process that has medical validity and predictive value for people. No amount of revisionist medical history concocted by vivisectionists and their ilk (which is then disseminated by supposedly neutral media entities such as the P-I) can change this fact. Neither can the deliberately deceptive animal rights vs. science style of presenting the issues involved. Playing on the fear humans have about their own mortality while asking for ever more research money to cure the diseases that conveniently remain uncured year after year is unconscionable.

Shame on the P-I for perpetuating this cycle of death that is antithetical to improving human health. I challenge you to print the writings of and/or interviews with some of the many doctors and scientists opposed to animal experimentation. The assertion that the practice is essential for medical progress is laughable — unless you ask the opinions only of those who profit directly from it.

**Robert L. Papy
Seattle**

C. Letter to the Editor: Cancer survivor got to know puppies that helped save her life

SATURDAY, APRIL 29, 2000

The series in the Post-Intelligencer about biomedical research using animals held special sway for me. It reminded me of the four-footed heroes who helped save my own life.

My nightmare encounter with acute myelogenous leukemia (AML) began in July 1992. Three months earlier, I had given birth to a son. But even after three months, I still felt tired and weak. And despite reassurances from family and friends, deep inside I knew something was really wrong.

The day my family doctor diagnosed me with AML, I became a warrior. I was blessed that my sister turned out to be a perfect bone marrow match, increasing my survival odds to 50 percent.

After weeks of radiation and chemotherapy, followed by my transplant, my stem cells began building healthy new blood cells. I left the Fred Hutchinson Cancer Research Center on Christmas Day 1992. It was the greatest Christmas imaginable.

I shall always feel gratitude to everyone who helped save my life. But there is one debt that can never be repaid: to the many beagles who contributed to enormous advances in cancer treatment. It's ironic that I had met some of these beagles myself years earlier at the University of Washington when helping to care for research animals. My duties included giving them food and water and making sure their cages were clean. During one short period, seven beagle puppies were in my care. After finishing my duties, I couldn't wait to go back and play with them.

But as the days went by, the beagles decreased in number. Soon, there were none left to play with. I was sad to see them gone, but I also understood that they were bred specifically for bone marrow research. Thanks to those animals, I am alive today and here for my son.

*Jennifer Coulter
Duvall*

D. Letters to the Editor: Series reminds us of benefits from our four-footed friends

WEDNESDAY, MAY 3, 2000

I am grateful for your animals-and-research series. With the many headlines in recent months pertaining to the violence caused by animal rights groups, it did seem that the opposition to animal testing was receiving much more press than its scientific counterpart. The P-I picked up on this and filled the gap with five essays by the very researchers and caretakers who find animal testing to be a necessity for the pursuit of medical research.

No one wants to cause animals to suffer, although this issue does often collapse into a debate between those who care about our furry friends and the cold-hearted scientists. It's easy to join the ranks of the former when one is not aware of the incredible importance of animal testing to the fight against human (and animal) suffering. It's also easy to regard the researchers as merciless and unfeeling, even though the success or failure of their experiments can mean the life or death of thousands of people.

The men and women who dedicate their lives to the search for cures for the diseases that plague us do not find it an

easy task to face each experiment knowing full well that they are administering injections and treatments that may cause pain and often death to their innocent subjects. But those men and women also get to experience the relief and satisfaction that comes from seeing people freed from AIDS, cancer, influenza or one of hundreds of other viral, bacterial and genetic diseases.

Thank you for addressing the other side of this issue and for reminding us of the astronomical benefits that have resulted from the sacrifice of our animal cousins.

*Colin Connolly
Woodinville*

GROUP TWO

A. OPINION: Human lives not saved by animals

APRIL 28, 2000

By MURRY J. COHEN

Original article available at:
<http://seattlepi.nwsourc.com/opinion/noanop.shtml>

NWABR did not receive permission from Dr. Cohen to include his article in this Curriculum Guide.

Copyright law allows a brief summary of his key points:

Summary of key points –

The use of animals has slowed progress in medicine and has put humans at risk.

Over 3 million people were taking Plavix, an anti-clotting medication, until it was found to cause a potentially lethal blood condition. This medication was considered safe after animal tests, but is now causing serious side effects in those taking it. Antibiotics such as Raxar, Trovan, and Omniflox, were also recalled or reissued with warnings due to side effects not apparent from animal studies.

The Handbook on Laboratory Animal Science points out that ‘uncritical reliance on the results of animal tests can be dangerously misleading and has cost the health and lives of tens of thousands of humans’. Dr. Richard Klausner has commented that researchers have ‘cured mice of cancer for decades, and it simply didn’t work in humans.’ Animal studies failed to establish a relationship between smoking and lung cancer. Our most valuable information has come through in vitro (test tube), clinical, and population studies.

There is no nonhuman model of HIV, and effective treatments such as protease inhibitors came not from animal studies, but from in vitro ones. Such treatments proceed directly to testing in humans because of a lack of effective HIV animal models.

Animals also do not develop cardiovascular disease as humans do, although attempts have been made to induce a similar illness at least twenty species. Progress in understanding such illnesses have come from population studies such as the Framingham Heart Study, autopsies and surgical techniques, and in vitro studies.

Both the identification of the pancreas as the organ involved in diabetes and the development of a polio vaccine were hampered by the contradictory evidence presented by animal research. For example, although physicians in 1700 noted that the pancreas was involved in diabetes, animal studies that did not support this observation slowed the search for treatments. Similarly, although pathologists noted in 1912 that polio entered the digestive tract in humans, studies in monkeys implied a nasal route of entry, hindering vaccine development for over thirty years.

Animals should not be used in medical research. Just as it is inappropriate to bring a child to a veterinarian for care, so animals should not be looked upon as models for disease research in humans.

Murry Cohen, M.D., practices in Northern Virginia and is a member of the Physicians Committee for Responsible Medicine, a nonprofit organization comprised of 5,000 physicians and 100,000 lay people.

B. OPINION: Four-footed friends important in development of new drugs

THURSDAY, MAY 18, 2000

By KATIE SPRUGEL

An April 28 headline on the Post-Intelligencer’s Op-Ed page took my breath away: “Human lives not saved by lab animals.” What could the author be thinking?

By presenting a few extreme examples and misunderstanding or misinterpreting the circumstances behind them, the author was trying to convince us that animals have no useful role in drug development. I think a little balance is in order.

I am a research scientist who works in the pharmaceutical industry. One of my primary goals is to protect patients from unsafe drugs. Specifically, I test whether a new drug is effective in animal models of human diseases and whether it is safe enough to be tested in people. How do animals fit into my work?

Animal studies help determine which compounds are most likely to succeed as a drug. Drug discovery and development is a winnowing process. We are constantly trying to separate the wheat (good drug possibilities) from the chaff (compounds that won’t succeed as drugs from some reason).

Current industry estimates are that for 5,000 compounds that start pre-clinical evaluation, only five will reach the point of being tested in humans. Of those five, only one is likely to be considered safe and effective enough to be approved as a drug.

Animal models of human disease provide the first indication of whether a new molecule will actually be useful in treating the disease. These animal studies also determine how the body eliminates

the drug and, thus, helps predict the appropriate doses and routes of administration.

Animal studies also are used to evaluate the safety of the molecules. Safety studies begin before a compound is ever administered to people, and continue during clinical trials with reproductive studies to determine whether the compound might cause infertility or birth defects if administered to a pregnant woman.

The animal safety evaluation may conclude with long-term studies to determine whether there is a risk of cancer or other problems associated with chronic exposure. All these animal-based studies help identify and eliminate compounds that do not have the characteristics needed to be safe and effective drugs.

Animal studies identify potential side effects before testing in people. All drugs have the potential to cause harm. The goal of drug development is to find molecules that improve a clinical condition at doses well below those that cause serious side effects. Knowing what some of the potential side effects are means physicians conducting clinical trials can be better prepared to recognize and deal with such side effects if they occur in people. Toxicity studies in animals identify potential side effects and also determine whether the effects will reverse if the treatment is stopped.

Animal studies keep really unsafe compounds from ever being given to people. Much publicity accompanies the withdrawal of a drug from the market after it has been approved by the FDA. That is a very rare event, however.

Between 1980 and 1998, 493 drugs have been approved by the FDA and only 13 (2.6 percent) have been removed from the market for safety reasons, according to the Journal of the American Medical Association, of May 1999.

Much less visible is the large number of compounds that are never even tested in people because of unacceptable safety profiles in animals. This is a major failure point for many molecules (20-30 percent of them) and an important way that animal studies directly protect people from exposure to unsafe compounds.

If animal studies are so helpful, why are some drugs withdrawn for safety reasons after they are approved?

Many of the drugs that have been removed from the market had serious, but rare, side effects that were not evident during the clinical trials. Sometimes this is because of the rarity of the event. Most clinical trial programs treat a combined total of 1,500 to 4,000 people in all of the trials conducted. An effect that occurs in one in 10,000 patients may not be detectable under these conditions.

It isn't until the drug is in much wider use that enough incidents occur to enable the pharmaceutical firm, the medical community and the regulatory agencies to recognize a causal relationship between the drug and the side effect.

In other cases, the problems were not due to the drug per se but to the drug's interaction with other drugs that a patient takes. Although clinical trials are designed to study likely drug interactions, it is not possible to anticipate and test all possible drug interactions.

For some drugs that have been removed from the market, potentially serious side effects have been predicted by animal studies and clinical trials. Careful assessments of potential risks and benefits to patients were made by the Food and Drug Administration and if the drug was approved, the instructions for use were often quite specific to minimize the risks. For this type of drug, serious side effects began to appear, however, when its use in clinical practice differed from the instructions.

If additional education and strengthening the label did not reduce the problem, the drug was withdrawn from the market. Overall, industry scientists, the medical community, regulatory requirements and government reviewers have done a remarkably good job of providing patients with access to safe, effective drugs for their medical needs.

Put yourself in the shoes of a physician administering the first dose of an experimental drug to a person. Would you be comfortable doing this only on the basis of cell culture data and computer models that said the compound should be safe?

Would you be comfortable volunteering to take that first dose of drugs? I wouldn't. I'd be relying on the complete package of animal testing data that told me what happened to all of the major organs of the body when the compound was administered to animals at high doses.

I would want to know how severe the damage was, when it occurred relative to the administration of the compound and whether the changes reversed if treatment was stopped. That kind of information isn't available from cultured cells or computer models.

Like most of my colleagues, I am keenly aware of the ethical issues that are intrinsic in using animals in medical research. I do my best to reduce, refine and replace my use of animals whenever possible. That said, however, I firmly believe that new drugs need to be tested in animals before they are tested in people.

Drug development is a long, complicated, expensive and risky process. The role that animals play in defining which compounds are most likely to be safe and useful drugs is invaluable and, at the present time, irreplaceable.

Katie Sprugel, Seattle, holds a Ph.D. in pharmacology and toxicology from Michigan State University. She has spent the past 12 years evaluating the safety and efficacy of new drugs at local biotechnology companies. She is a former member of the board for the Washington Association for Biomedical Research.

GROUP THREE

A. OPINION: "In search for cures for human illnesses, leave animals alone"

By KATHY GUILLERMO

MAY 3, 2000

Original article available at:
<http://seattlepi.nwsourc.com/opinion/anmlop.shtml>

We did not receive permission from Ms. Guillermo to include her article in this Curriculum Guide.

Copyright law allows a brief summary of her key points:

Summary of key points –

Many of the comments made by authors of the P-I opinion pieces are incorrect or misleading.

The Animal Welfare Act is the only federal governing animal experimentation, and it does not limit what experimenters can do, even if their tests are painful. More than 90% of animals used in research are rodents, yet the U.S. Department of Agriculture does not interpret the act to rodents or birds. There are limited government resources to oversee animal research (85 inspectors covering 1500 research facilities, 1,800 animal exhibitors, and 4,400 animal dealers), leaving those who use animals to self-regulate.

Institutional Animal Care and Use Committees are intended to review experiments, but there are examples of cruel or redundant research projects taking place currently (including addicting monkeys to crack cocaine or nicotine, implanting cat brains with electrodes to study sleep deprivation,

severing nerves in the brain and ear of mice, and depriving monkeys of maternal care). Although \$6 billion of taxpayer money is provided to animal researchers, no governmental regulation exists to ensure that this money is only spent on research targeting fatal diseases.

Furthermore, years of animal experimentation targeted at diseases such as AIDS, Alzheimer's, and cancer have not produced cures. Richard Wragham, Harvard Professor, notes that all advances in AIDS research have come from non-animal approaches, and that early work diverted funds from more productive strategies.

The fundamental issue is whether it is right to use animals for research even if there are resulting benefits for humans. PETA joins others who believe that cures can come without harm to animals.

*Kathy Guillermo,
People for the Ethical Treatment of
Animals*

B. Honor animals: All of God's creatures deserve our respect

LOCAL NEWS : SATURDAY, SEPTEMBER 30, 2000

By Religion / The Rev. Dale Turner

(This article was not directly in response to the series, but presents another supporting view point).

Among the many things humans have in common is a love for animals. There are not many homes in our society where at one time or another there has not been some kind of pet.

Certainly, it has been true for me. A dog was one of my earliest companions, and I have treasured the company of dogs and other animals through the years. Animals are such agreeable friends. They ask no questions and pass no criticisms.

Walt Whitman said, "I think I could turn and live with the animals. They are so placid and self-contained. They do not swear and whine about their condition. Not one is dissatisfied. Not one is demented with the mania of owning things. Not one is disrespectful or unhappy over the world."

For many years we had a dachshund. I always loved the rhyme:

A dachshund is a long dog
That hasn't any notion
How long it takes his tail
To display an emotion
So when his eyes are filled
With tears and sadness
His tail goes on wagging
With previous gladness.

When I was a youngster, I heard a story about Robert Louis Stevenson and a dog that endeared the author to me before I ever began to read his wonderful stories. During one of Stevenson's walks, he encountered a man who was beating his dog. Stevenson, angered by the man's cruelty, interposed himself between the man and the dog and ordered him to stop. "It is my dog," replied the startled man. "I will do with it what I please." "No, it is not your dog," said Stevenson. "It is God's dog, and I am here to protect it."

Stevenson was right. We do not own animals anymore than we can own another human being. The Bible affirms that humans were given dominion over animals, but this does not mean we own other creatures or that we have the right to exploit them or deny them their rights. The recent protests against Ringling Brothers and Barnum and Bailey's use of circus animals for the entertainment of humans made clear the feelings of many in regard to the treatment accorded animals.

Thoughtful people today are asking if we have the right to experiment on animals and sacrifice their lives to discover ways to improve the lot of humans. I have thought about that question for years but was forced to think more deeply years ago when I became a member of the animal-

care committee at the University of Washington. The 21-member committee had many responsibilities, but central was the monitoring of animal experimentation to assure that all national regulations were met and animals were tested humanely. No experiments were conducted except those approved by the committee. There were regular meetings where the total program was discussed before decisions were made. Opening the meetings was a step in the right direction. Closed meetings only arouse suspicions and deny the committee insights that others had to offer. We honored the 10 to 30 people who usually attended what were more often than not protests against animal experimentation and procedures within the program. Our committee listened attentively to comments.

The visitors also listened to those involved in the experiments. The experimenters were highly trained, competent and compassionate people. They had entered their field of study because they loved animals and were committed to working for cures to both human and animal ills. I appreciated what the opponents of animal experimentation had to say, and at several points I shared their conclusions. But my support for experimentation at the university continued.

What are the alternatives, imperfect though they may be? To ban all medical research using animals would be to abandon millions of human beings, now living and not yet born, to suffering and premature death that might be prevented through supervised animal research. Many famed surgeons attest to the fact that millions of lives have been prolonged and improved through research on kidney disease, cancer, diabetes, Alzheimer's disease, blindness and many other maladies to which humans are subject.

The deadly AIDS virus was isolated in monkeys. There is an acceleration of experiments with primates with the hope that a vaccine may be discovered to counter the scourge of AIDS.

Many maintain that vital medical research can be done with computers and cell cultures, making the use of animals unnecessary. Experimenters believe those are useful in several ways but are not substitutes for testing a drug or procedure on a complex living creature.

As I left the University of Washington Medical Building after each meeting, I would often pause and read the words of American author Henry Beston that were enclosed in a large frame on the wall of one of the offices in the medical school: "We need another and wiser, and perhaps a more mystical concept of animals they are not brethren, they are not underlings, they are other nations, caught with ourselves in the net of life, fellow prisoners of the splendour and the travail of the earth."

GROUP FOUR

A. Letters to the Editor: Experiments prove we don't hold all life sacred

SUNDAY, MAY 14, 2000

I am happy that the P-I is raising people's awareness to the animal research controversy, but I strongly disagree with the April 20 article, "Ethics of using animals in research."

Contrary to the expressed opinion, Americans are not taught that all life is sacred. If we were, we would not sit down at a table each night to eat an animal that had his/her life taken away. We would not test products on animals and justify it by saying that it was all for the sake of improving life for humans. What we are actually taught is that it's OK to eat meat and it's OK to test on animals because animals are inferior to our species.

When Delmas Luedke wrote that euthanasia was used to minimize suffering, he forgot to mention that this is only if it won't interfere with the results of the test.

An example is the lethal dose test, where a group of animals is given a chemical until a certain percentage of the group dies. In those tests, euthanasia is not used and pain killers are not used, either, for fear of affecting test results. The law doesn't require the lethal dose test, but it's still used.

Even beyond the moral issues are the ones of reliability. Animals might be similar to humans, but they are not identical. There have been cases where drugs that were proven to be very effective on animals went on the market for human use and caused humans to become sick or even die.

There are also cases where things that are toxic to animals are effective in humans. If we had relied on animal tests, we would not have penicillin, which was toxic to the guinea pigs upon which it was tested.

There are effective, non-animal tests such as single-cell tests and computer models that are often cheaper. Why do we still use animals when cheaper, more reliable methods are available? It's because we don't attach enough value to what we consider to be "inferior" species. As a result, we often overlook the possibilities of more economical and effective tests.

Victoria Wilkins
*Eighth Grade, Eckstein Middle School
Seattle*

B: Letters to the Editor: Penicillin's success came from tests on rats

SUNDAY, MAY 21, 2000

The animal rights movement has made schoolchildren primary targets of their anti-research propaganda. The letter (May 14) from Victoria Wilkins, an eighth-grader at Eckstein Middle School is an example of how the animal rights movement is victimizing children. The letter, which no doubt she took great pains to write, is founded in the litany of inaccurate information used by the animal rights movement to disparage animal research.

While each of the arguments she poses against animal research can be rebutted, her comment regarding penicillin is so inaccurate as to require immediate correction.

When penicillin was discovered in the 1870s, it was tested on humans. Its effects were so erratic and unpredictable that it was ignored as a drug until 1940 when Sir Howard Florey tested it on eight mice injected with a lethal dose of bacteria. Only the mice that got penicillin lived. The experiment was so compelling that it quickly led to the use of penicillin in World War II, saving thousands of soldiers' lives.

Florey used mice because he had so little penicillin he could not test it on humans. Indeed, attempts to use penicillin in humans after Florey's discovery were still inconclusive. But, because the results in mice were so convincing, Florey and his chemist purified their crude penicillin extract to obtain a grade that worked reliably in humans.

When animal rights activists tell children that penicillin kills guinea pigs and, therefore, "If we had relied on animal research we would not have penicillin" they are lying to our children.

That is why teachers must be extremely vigilant with regard to the materials distributed by animal rights groups for their curriculum. Children's schooling should not be a means for the animal rights movement to spread their false propaganda.

Bob Speth, Ph.D.
*Professor of Pharmacology and
Neuroscience
College of Veterinary Medicine
Washington State University*

GROUP FIVE

A. Why veterinarians go to one school, medical doctors another

SUNDAY, MAY 14, 2000

By RAY GREEK and JEAN GREEK

As students in veterinary and medical school, we often compared notes on how we treated the same disease in different species. We were surprised to learn that while penicillin is effective in humans it causes death in hamsters and guinea pigs.

We also learned that thalidomide, the infamous birth defect-causing drug of the 1950s, could be given with impunity to most animals but that morphine and aspirin actually caused birth defects in some animals. Clearly, parity between species was not always present.

Animals and humans do have similarities on the gross or macroscopic level. We all have hearts that pump blood, lungs that breathe and immune systems that fight off disease. But, animals do not suffer from coronary artery disease or AIDS or get lung cancer from smoking. Disease occurs at the cellular level and it is the very small differences at the cellular level that prohibit us from getting reliable data about humans from animal models.

Experimenting on animals has achieved religious significance in our society. We are told that any new medication, surgical procedure or vaccine must first be tested on an intact animal. We are told that without such testing on intact systems, we will never know how the medication will affect the whole living human.

We doubt someone with a vested interest in animal models would be happy with a testing system that does not use animals. The fact is the success rate for predicting what will occur in humans is much better for the results obtained from in vitro research, epidemiology, computer and mathematical modeling, and research with human tissue than any test using

intact animals. Animals may be intact systems but they are not intact human systems.

The great breakthroughs in biomedical research came from non-animal-based research. It was in vitro research that gave us penicillin and the protease inhibitors. Epidemiology linked heart disease and cancer to smoking, spina bifida to folic acid deficiency and high blood pressure to strokes. Computer modeling gave us one of our current breast cancer treatments. Research on human tissue taught us about HIV and AIDS. Human clinical observation gave us drugs to treat leukemia.

The results of using animals as models for human disease have also resulted in many deaths.

Smoking was thought not to cause cancer, based on the results from experiments on animals, so many continued to smoke. Asbestos was thought non-carcinogenic so many continued to be exposed. Animal models of heart disease failed to show that a high-cholesterol/high-fat diet increased the risk of coronary artery disease. Animal models of stroke and sepsis resulted in patients receiving medications that were dangerous, harmful and not efficacious. Animal models of transplant surgery, cardiopulmonary-bypass surgery, radial keratotomy, artificial heart surgery and many others led to disaster when applied to human patients.

There are far too many examples of good medications, i.e., penicillin, beta-blockers, furosemide and digoxin, that were delayed because of adverse reactions in animals that did not occur in humans.

Anti-rejection medications now used for transplant patients were delayed because they did not work in animals. Conversely, side effects from medications such as Fialuridine, Practolol, Opren, fenfen, Clotrimazole, DES, Rezulin and others that tested safe in animals went on to kill or maim humans.

AIDS research is perhaps the most striking example of where small dissimilarities on the cellular level result in major differences in the cause and treatment of a disease. Because SIV replicates slowly in monkeys, HIV was thought to do the same. It does not.

We now treat HIV much sooner than we did when we modeled the treatment after experiments on primates. AIDS research is impossible in animals because HIV and AIDS are uniquely human. Animal models of AIDS also misinformed researchers about how HIV enters the human cell.

Animal experiments have wasted time, money and resources that could have gone to research modalities that historically have yielded results that benefited humans.

Ray Greek, M.D., is president of Americans for Medical Advancement. Jean Greek is a doctor of veterinary medicine. They are the authors of "Sacred Cows and Golden Geese, the Human Cost of Experiments on Animals," published by Continuum.

B. Letters to the Editor: The whole story of research on animals has yet to be told

SUNDAY, APRIL 23, 2000

Regarding your series "Animals and Research," some believe animal research is humane. Anyone reading your series should attend Animal Care Committee meetings at the University of Washington to see what's being done to animals behind laboratory doors. You'll hear of head-smashing experiments on everything from ducks to rabbits — supposedly to learn about head injury in humans.

The Animal Welfare Act does not protect animals in National Institutes of Health-funded experiments. Anesthetics aren't required. The ACC is just a bunch of researchers who put the stamp of approval on one another's experiments.

What about the harm animal research has done? Thalidomide tested safe on thousands of pregnant animals, yet caused women to give birth to deformed children. Humans were undergoing surgery without anesthetic long after chloroform had been discovered because it

excited rather than sedated dogs. Morphine causes maniacal excitement in mice and cats.

We might not have penicillin if animal tests had been used because it's toxic to many species. Humans have gall bladders; rats don't. Rats can synthesize their own vitamin C; humans can't. In England, doctors are not allowed to practice on animals because it leads to erroneous data. Here, grants through government agencies make this a multibillion-dollar business.

Darlene Kaiser
Lynnwood

C. OPINION: Flaws in anti-animal research argument

PRINTED WEDNESDAY, AUGUST 2, 2000

By SCOTT BURKE

I recently read the article "Why Veterinarians Go To One School, Medical Doctors Another," written by Ray and Jean Greek, published in the Seattle Post-Intelligencer on 5/18/00. The article speaks out against the use of animal models in biomedical research by citing examples where animal research failed the public, and by claiming that alternatives to animal use provide more reliable information. I'm very discouraged that such an unbalanced and misleading article was published in a respected source of journalism. For one, many of its "facts" are either wrong or fail to tell the whole truth. Secondly, it argues against animal research without presenting accurate information about the research process or the ways that "more reliable" alternative procedures work.

Let's start by examining "the facts" behind two well-known examples presented in the article—penicillin and thalidomide.

First, penicillin wasn't discovered because of rigorous tissue culture research. Penicillin was discovered by accident, because Alexander Fleming carelessly left the lid off one of his culture dishes, which

allowed the dish to become contaminated with the mold that makes penicillin! Secondly, animal research did not delay the approval of penicillin for human use; rather, it was delayed because it was an extremely difficult drug to make. Because of this, Fleming's discovery was largely ignored for 11 years, until 1939. But by 1941, scientists had figured out how to make it in large batches; had completely demonstrated its safety and effectiveness in mice, and then conducted successful tests in humans. In just two years.

Third, penicillin can cause death in guinea pigs and hamsters, but only in large doses. Scientists know this, and they know why, as well—they know that both species have large amounts of bacteria living in their gut. The bacteria digest the animals' food, so killing bacteria with penicillin leads to starvation and death in those animals. Scientists know this, which is why they don't use guinea pigs and hamsters to test large doses of antibiotics like penicillin. However, scientists also know that small doses are safe; in fact, scientists working today are studying allergic reactions to penicillin by giving small doses to guinea pigs. It is hoped that this research will lead to the reduction or elimination of severe allergic reactions to penicillin that many humans experience.

Fourth, the thalidomide birth defect tragedy was caused by a lack of well-controlled, comprehensive reproduction studies in animals, and not because animal models were worthless. You see, certain breeds of rabbits are very susceptible to birth defects caused by drugs (including thalidomide), and that is why rabbit reproduction studies are now required before a drug is approved for widespread use. Unfortunately for thousands of babies and their families, rabbit tests were not required by European and Canadian agencies in the 1950's. Had those tests been conducted, the drug would never have been approved, and the terrible tragedy would have been avoided.

As you can see, animal models perform essential functions in research; they demonstrated the safety and effectiveness of penicillin, and their use could have prevented the thalidomide tragedy. And while alternative techniques help to improve our

understanding of medicine, they have serious drawbacks that aren't present in animal model use. Let me illustrate this by looking at each alternative procedure in turn.

In vitro (tissue culture) research involves growing cells (i.e. bacterial, liver, brain, tumor) on dishes or in jars. New drugs can be given to these cultured cells to determine how well they work or how safe they are. However, these cells are often very different from the same cells found in a living system, because they're in an artificial environment. Furthermore, cells are very dependent on their relationship with other neighboring cell types in the body. Therefore, cells in vitro may not respond to drugs the same way they would in a living system. I have personal experience with this—I have worked with hundreds of potential chemotherapy drugs that successfully killed tumor cells in vitro, but were useless on tumors in animals and humans.

And do you know where scientists get those liver, brain, and tumor cells they use for in vitro research? The only place most of them can get animals. Scientists are also improving in vitro techniques every day, making them resemble living systems more and more. They're doing this by studying the living systems themselves—the animals.

Human tissue use is essentially the same as conventional in vitro research, using human tissue rather than animal. As a result, scientists can test human cells without putting a human at risk. However, this technique has the same drawbacks as conventional in vitro research—artificial living conditions may alter the cells' normal behavior. There are other serious drawbacks, as well; human tissue may contain and transmit disease. Government regulations for its use are very strict (as they should be), which makes it impractical or impossible for most researchers to adopt the technique. Finally, human tissue use is just as controversial as animal model use, if not more so.

In computer modeling, all available information on a specific living system and specific drug is programmed into a computer. With the press of a button, the computer provides a mathematical model

suggesting the probable effects of administering that drug to that living system. But in order for this system to work, it needs complete and detailed information on the drug and the system; without it, the computer is useless. So where does this information come from? Animal research.

Epidemiology has provided biomedical research the causes of heart disease, cancer, Ebola, Plague, Legionnaire's Disease, Malaria, and countless other maladies. But epidemiology works by collecting information from a large number of humans who either have had a disease or have taken a certain drug. By compiling this information, epidemiologists can determine the cause of a disease, or the percentage of people who experience side effects after taking approved drugs. In other words, epidemiology predicts what will happen in people by gathering information on what has already happened in people! Biomedical researchers are required to demonstrate that a drug is safe before it's given to people-not discover that it's unsafe after it's been given.

Animal models provide a reliable method to study new drugs or procedures on a living system before they are tested in human beings. Animal models provide reassurance to the scientific community, the government, and the general public that a drug can be given safely to a human being. A drug is not approved by the Food and Drug Administration (FDA) until it's been thoroughly tested in humans (clinical trials). And clinical trials do not occur until the FDA is satisfied that the drug is safe to give to living beings. This can only be done effectively in animal models.

The Greeks' article points to examples where the system didn't work perfectly. Many of those examples are wrong or misleading (i.e. penicillin and thalidomide). What's not mentioned is that for every example it lists, there are literally thousands upon thousands of experimental drugs or treatments that never even reached the attention of the FDA. Current industry estimates say that for every 5,000 new drugs created, only 5 are deemed safe and effective enough to petition for formal FDA review-of those 5 review candidates, only 1 will be approved. And the process of weeding out useless or dangerous drugs

is dependent on all available research methods, including animal research.

Alternatives research methods are available, but they're nowhere near as reliable, because one works only after the drug or treatment has been approved, while another is controversial, expensive, and hazardous. The other two alternatives provide minimal reliability, and are actually dependent on information gathered from animal research.

For every single problem encountered with anti-rejection medications, there have been many successes in the field of transplant surgery (Organ transplant procedures were perfected in animals long before they were performed in humans). When discussing coronary artery disease, AIDS, or Lung Cancer, we should also discuss bypass surgery techniques, AZT, and chemotherapy, which were all determined to be safe and effective through animal research long before human exposure.

The general public deserves the truth about the need for animal models in biomedical research. It can ill afford to be exposed to misleading, false, and incomplete testimony such as that in Ray and Jean Greek's article.

D. Submitted Letter

The article by J & R Greek (Why veterinarians go to one school, medical doctors to another; more debate about using animals in medical research) abounds with the misrepresentations of scientific fact commonly found in antivivisection literature. A complete analysis would necessitate many pages so I will restrict comment to a few examples.

Penicillin produces in guinea pigs and hamsters exactly the same condition that occurs in humans on long-term penicillin therapy, namely antibiotic-induced colitis. This is due to the destruction of the resident gut bacteria allowing the consequent infection, in both guinea pigs and humans, of the pathogen *Clostridium difficile*. This is a life threatening condition but can be treated in both species by the antibiotic metronidazole. To me this is an outstanding example of the similarity between humans and an animal species.

There is no difference in the reaction

of animals or humans to thalidomide. Thalidomide was never tested in pregnant animals before its therapeutic use, but within 5 months of the first report of the teratogenic action of the drug a report of a similar action in rabbit was published, and soon after thalidomide was also shown to be teratogenic in rats, mice, hamsters and 4 species of monkey.

The doctors Greek would do well to read the relevant papers before repeating the hoary old story of aspirin causing birth defects in animals but not in humans. The dose of aspirin needed to produce birth defects in rats is equivalent, on a weight basis, to administering 46 tablets a day to a woman of average size throughout the 9 months of pregnancy. Not surprisingly, this experiment has not been attempted in humans, but I would confidently predict it would produce some ill effects of the fetus.

Finally, I cannot resist comment on the claim that "animal models of heart disease failed to show that a high cholesterol/fat diet increased the risk of coronary artery disease", since the precise nature of the development of atheroma, from fatty streak to large, occlusive plaques, was clearly demonstrated in monkeys placed on high cholesterol diets. Indeed, the exact genetic defect in the inherited disease familial hypercholesterolaemia, where death occurs from acute coronary occlusion in youth, was established in the rabbit; an observation that earned a Nobel prize for the researchers.

No one can, or would wish to, dispute that epidemiology has contributed to medical advances. However animal experiments are the only means to resolve some remaining problems and hence provide effective treatments for disease.

Yours sincerely,
Dr Jack Botting
London SW16
UK

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