LESSON 5:
Putting it all Together

INTRODUCTION

In this lesson, students consider the case of a young doctor hired by a U.S. pharmaceutical company to test a new antibiotic in Nigeria during a meningitis epidemic. Students work through a ***Decision-Making Framework*** in small groups, in which they identify the ethical question, determine which facts are known or unknown, consider the values of different stakeholder groups, generate possible solutions, and then make and justify a decision about the case. This is a jigsaw exercise, in which students first meet in "like" stakeholder groups to become experts in the values and concerns of that group. Teams are then rearranged into "mixed" stakeholder groups so that each new group has students from different stakeholder viewpoints. After sharing the views and values of each stakeholder group with their peers, groups work together to generate options for solutions to the case study. Lastly, students come to individual decisions about the case and write a thorough justification.

KEY CONCEPTS

- A decision-making framework provides a structured format for logical student thought.
- Difficult decisions can be "reasoned through" in a systematic way, even if the different solutions are not without challenges for diverse stakeholder groups.
- Not all of the Principles of Bioethics will be equally relevant to any one situation.

LEARNING OBJECTIVES

Students will be able to:

- Reason through a case study using a decision-making framework.
- Apply bioethical principles to a case study.
- Create a strong justification for their decision about the case study.

CLASS TIME

One class period of 55 minutes.

MATERIALS

Materials	Quantity
Student Handout 2.1—*The Principles of Bioethics* (handed out in *Lesson Two*)	1 per student
Student Handout 4.3—*Justify The Answer* (from *Lesson Four*)	1 per student
Student Handout 5.1—*Case Study: The Time and the Place?*	1 per student
Student Handout 5.2—*Ethical Decision-Making Framework*	1 per student
Possible Answers for Student Handout 5.2—*Ethical Decision-Making Framework*	1
Student Handout 5.3—*Elements of a Strong Justification*	1 per student

TEACHER PREPARATION

Make copies of the *Student Handouts*, one per student

NOTE TO THE TEACHER

Although the case study presented in this lesson highlights what might be considered a questionable action by a pharmaceutical company, please note for students that we have all benefitted enormously from the drugs and therapies developed by the pharmaceutical industry. Pharmaceutical companies are regulated by the Food and Drug Administration (FDA). A number of regulations are in place regarding appropriate actions and behavior in testing and marketing new drugs.

FRAMING THE LESSON

Students are ***not introduced*** to any new concepts in this lesson but ***put into practice*** what they have learned throughout the unit. They apply to a new case study their knowledge of ethical questions, bioethical principles, stakeholders, generating options, and writing a thorough justification.

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As students read the case study, it may be helpful for them to color code elements of the decision-making framework. For example, ***facts*** could be highlighted in yellow, and ***stakeholders*** could be highlighted in green.

PROCEDURE

Part I: Ethical Question, Facts, and Stakeholders

Activity Time: 15 minutes

1. Distribute copies of Student Handout 5.1—*Case Study: The Time and the Place?*, one per student. Allow time for students to read the case study.
2. Distribute copies of Student Handout 5.2—*Ethical Decision-Making Framework*, one per student. As a class, decide the ethical question. Guide the class to this question:

   "Should Rezip conduct this clinical trial research?

3. Give students approximately five minutes to write down the facts from the case and any questions that they have on Student Handout 5.2—*Ethical Decision-Making Framework*.
4. Have individual students brainstorm a list of stakeholders in the case.
5. Ask for student volunteers to provide names of stakeholders.

Field test teachers suggest using the term ***developing country*** rather than ***third world***.

6. List the stakeholders on the board. They could include:
   - You (the doctor)
   - Rezip
   - The children
   - The families of the children
   - Other sick people in Kano
   - The U.S. government
   - The Nigerian government
   - *Doctors without Borders*
   - Rezip shareholders
   - Other pharmaceutical companies
   - Other doctors employed by Rezip
   - Kano ethics committee
7. Choose the top four stakeholders that are most affected by the decision and have students list these on their decision-making framework. Four groups that work well are:
   - You (the doctor)
   - The sick children (and their families)
   - Rezip
   - Kano

Part II: "Like" Stakeholder Groups

Activity Time: 10 minutes

8. Divide the class into groups of four and assign one stakeholder to each small group (more than one group can represent the same stakeholder, if needed).
9. First, students should consider the values and concerns of that stakeholder group and record them on Student Handout 5.2—*Ethical Decision-Making Framework*. What are their concerns? What do they care about?

Students may want to refer to Student Handout 1.2—*Values Definition Table* and Student Handout 2.2—*The Principles of Bioethics*.

10. Next, each group should also consider the Principles of Bioethics from the perspective of that stakeholder. How does Respect for Persons relate to the group? Maximize Benefits/Minimize Harms? Justice? Do all the principles apply equally to each stakeholder group?
11. Allow about five minutes for each stakeholder group to delve into the values and concerns of that stakeholder.

Part III: "Mixed" Stakeholder Groups

Activity Time: 10 minutes

12. Rearrange the class into groups of four, so that each new small group has one representative from each stakeholder set. If there are extra students, two students can represent the same stakeholder in the same group, if needed.
13. Each stakeholder should share, in turn, their values and concerns with the other students in the group until each stakeholder has reported.
14. Students should record basic information about each stakeholder group on Student Handout 5.2—*Ethical Decision-Making Framework*.

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15. While staying in the stakeholder roles, have students proceed to "Generating Options" on the handout. What are the options for the case? What would each stakeholder group do, if the decision were only up to that group?

16. Tell students to drop their stakeholder roles and explore, as a group, any additional options, if available. Have the extreme positions been expressed? Have the middle-ground options been expressed?

17. Each team member should come to an individual decision. This does not have to be a group consensus, nor does the student have to share his or her decision.

Part IV: Student-Written Justification

Activity Time: 20 minutes

18. Each student should write a thorough justification for his individual decision, using the decision chart found on Student Handout 5.3—*Elements of a Strong Justification*. Note for students that a good justification will touch upon all parts of the Decision-Making Framework. Student Handout 5.3—*Elements of a Strong Justification* is organized the same way as the framework, beginning with the question and ending with the solutions.

19. If time permits, have students discuss their justifications in pairs. Students can give each other feedback on the strength of their justifications based on the justification template. Students should ***not*** critique each other's positions directly, but focus on the strength of the reasoning.

20. Collect the justifications.

21. Ask students to reflect on their experiences by asking, "Do you have a better ability to make a well-justified decision?" and, "Were you able to listen to and respect other viewpoints?"

Part V: Variations on the Story (*Optional*)

22. Once students have come to a decision about the case and have justified their decision, have them consider the following variations to the story. In pairs or small groups, have students discuss whether any of these additional pieces of information would change their decision. Why or why not?

Would students feel differently if they knew…

A. The outcome of the trial?

- Eleven children died during the drug trial—five of whom had been given Trovan, six of whom had been given the other approved antibiotic.
- Families of the children who received Trovan claim that many of them suffered serious side effects from the drug, such as brain damage and organ failure. Rezip claimed that these effects were from the meningitis itself.
- Rezip claimed that Trovan clearly saved lives since the survival rate from the epidemic went from 80% at the beginning to 94% after the trial.

B. Some doubts existed as to the legitimacy of the ethics committee?

- Some documents suggest that the ethics committee referenced by Rezip was actually set up a year ***after*** the doctors conducted the trial.

C. Trovan is now banned?

- The "blockbuster antibiotic" Rezip was testing did not live up to expectations. The European Union later banned the drug and it is no longer in production or for sale in the U.S.

The Rest of the Story

[**Note:** Share *The Rest of the Story* ***only if*** the students have finished writing their own decisions and justifications.]

Each of the variations to the story (above in *Part V*) is true. In April 2009, the pharmaceutical company that is featured in this case agreed to pay a $75 million out-of-court settlement to the families of the children who participated in the drug trial. In August 2009, the company and Kano State reached an agreement in which Kano State dropped all claims, and the company denied any wrongdoing or liability in connection with the Trovan study. Under terms of the settlement, the pharmaceutical company agreed to establish a healthcare/meningitis fund to support study participants, provide $30 million in healthcare initiatives for Kano State, and reimburse Kano State government for legal costs.

This pharmaceutical company also became the first to be accredited by the Association for the Accreditation of Human Research Protection Programs for ensuring the protection of human subjects taking part in early-stage clinical trials in four major sites across the globe. To earn this accreditation, the company participated in a rigorous, 15-month examination of the clinical research practices at these sites.

This case reportedly inspired the book *The Constant Gardener* by John Le Carre. The story was also made into a film of the same name, starring Ralph Fiennes and Rachel Weisz.

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CLOSURE

23. Share with students that the decision-making framework and bioethical analysis tools that students have learned over the week are conceptual models that will help them as they examine subsequent bioethical cases. They may also find them helpful as they consider dilemmas they may encounter in the future.

EXTENSION

Additional discussion points could include:

- The challenge of getting informed consent. (How do researchers conduct studies in populations with high rates of illiteracy? In cultures where the voice of a community leader might outweigh the voice of an individual?)
- Study design for international human clinical trials. (How do researchers control for the many variables inherent to the study? What if the amount of compensation in one region would unduly influence participants in another region?)

ADDITIONAL RESOURCES FROM *AN ETHICS PRIMER*

Additional information and discussion about using ethical decision-making frameworks in class can be found in the section *Decision Frameworks*. Alternate frameworks are also included.

SOURCES

"Pfizer to pay $75m after death of Nigerian children in drug trial experiment." Howden, Daniel. *The Independent*, April 6, 2009. http://www.independent.co.uk/news/world/africa/pfizer-to-pay-16350m-after-deaths-of-nigerian-children-in-drug-trial-experiment-1663402.html.

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STUDENT HANDOUT 5.1

Case Study: The Time and the Place?

Name_____ Date_____ Period_____

You have recently completed years of medical training—undergraduate work, medical school, internships, and residency—and are excited to have gotten a job with Rezip, one of the largest pharmaceutical companies in the world. Based in the United States but operating in 150 countries, Rezip discovers, develops, manufactures, and delivers prescription medicines to patients. Many Rezip drugs make life easier and healthier for millions on a daily basis.

You have been interested in global health since middle school, and chose to focus on infectious diseases during your medical training. It seems unbelievable to you that each year hundreds of thousands of people die from bacterial diseases like meningitis, cholera, and pneumonia, especially in developing countries. Your passion for global health and your new job at Rezip seem like the perfect match. Rezip has developed what it hopes will be a "blockbuster antibiotic" – an antibiotic that would fight a wide range of bacteria and could be taken in tablet form. The drug, called Trovan, is in the late stage of development and so far has been successfully tested on over 5,000 adult patients in the United States, Europe, and elsewhere. The results are very promising, and Rezip anticipates that the drug will receive approval for adult use. However, additional clinical trials with younger patients are needed to prove its effectiveness and safety for children; otherwise the drug will not receive approval for pediatric use. Rezip is sending you to Africa for two weeks to dispense Trovan to children as part of this needed clinical trial. If Trovan proves successful overall, millions of adults and children suffering from a variety of deadly bacterial diseases could be cured easily by taking a few pills. Rezip also projects its total sales could reach over a billion dollars a year as a result.

Drug clinical trials are heavily regulated by the FDA (Food and Drug Administration). In Phase I trials, the drug dosage must be proven to be ***safe*** in 20–80 healthy volunteers. Phase II trials then prove ***effectiveness*** of the drug in 100-300 patient volunteers sick with the disease the drug will treat. Finally, Phase III trials prove ***widespread safety and effectiveness*** of the drug in 1,000–3,000 patient volunteers. Clinical trials must be conducted in target populations – in other words, if the drug will be used on women, it must be tested on women; if the drug will be used on children, it must be tested on children. Certain drugs have been known to affect different populations differently, and therefore the FDA demands rigorous clinical trials on all target populations. In the United States, the full clinical trials cycle can take two to ten years depending on how many people sign up to be in the trial, the way the trials are conducted, and whether the results are decisive.

Your boss tells you that you are going to Nigeria, which is experiencing the most serious meningitis outbreak ever recorded—hundreds are dying each month. In the first weeks of the epidemic, only about 80% of those with the disease have survived. Understandably, this presents a severe public health crisis for the government of Nigeria. When you arrive at the Nigerian slum city of Kano, you are overwhelmed by the needs of the people—many of whom are children—and the huge crowds gathered at the Kano Infectious Diseases Hospital.

Nearby, an aid group called *Doctors Without Borders* has set up a medical station and is dispensing treatments to ease the epidemic. Despite their efforts, the lines at the medical station are overwhelmed with people needing treatment. You and your team have been instructed to set up camp close to the *Doctors Without Borders* station to aid in the relief efforts and collect data for the clinical research study. As a Rezip doctor, you will choose 200 children with serious symptoms. Half will be given doses of the experimental drug Trovan, while others will be treated with an antibiotic from a rival company for comparison (this rival drug has already gone through standard clinical trials and has been shown to be effective and safe). The children and their families will not know which of the two drugs they are receiving. If Trovan has a very negative effect on the children, the other drug can be administered. Given the chaos of the crowds gathered, it is decided that getting consent from individual families will be impractical, so it is agreed that permission from a Kano ethics committee will serve as consent for everyone. Rezip sought and received permission and consent for the study from a Kano ethics committee made up of local doctors, health officials, and tribal elders. Culturally, tribal elders often represent their communities.

You look around at the malnourished and severely ill children from the slum city raging with meningitis, cholera and measles. These are the children you will dispense medicine to and gather data from for the clinical trial. You have some concerns about how the trial will be conducted, but you also recognize the potential health benefits of the drug. Should Rezip conduct this clinical trial research?

This is a fictionalized account of a true story. Contributed by Rosetta Eun Ryong Lee, Seattle Girls' School.

HANDOUT

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STUDENT HANDOUT 5.2

Ethical Decision-Making Framework

Name_____ Date_____ Period_____

Part I: Ethical Question

Part II: Facts and Questions	
Relevant facts (known)	Questions that remain (unknown, need to know)

Part III: Stakeholder Values		
Stakeholders (people/entities affected by the decision)	Values/concerns of each stakeholder	Bioethical Principle(s) given priority
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____

HANDOUT

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5. Generating Options
(What are some possible options to resolve the ethical question?)

6. Write a strong justification paragraph for your decision on the topic. Make sure to answer the following questions while using the evidence (such as the facts and ethical considerations) to support your claim in a way that shows your reasoning.

a. What is your position on this issue?
b. What is the factual content to support your position that can be confirmed or refuted regardless of cultural or personal views?
c. What ethical considerations can be included to support the position? (Respect for Others, Maximize Benefits/ Minimize Harms)
d. What are the views and interests of the individuals or groups affected by the decision that you think are most relevant to your position?
e. What are the alternative options and why are they not as strong as your position?

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Possible Answers for STUDENT HANDOUT 5.2
Ethical Decision-Making Framework

Answers can vary widely. Possible answers are below.

Part I: Ethical Question

Should Rezip conduct this clinical research trial?

Part II: Facts and Questions

Relevant facts (known)	Questions that remain (unknown, need to know)
• *Rezip, a large pharmaceutical company, wants to test an experimental drug in Kano, Nigeria during a meningitis outbreak.* • *Hundreds of thousands of people die each year due to bacterial infections.* • *Trovan has already been successfully tested on over 5,000 adults.* • *Additional clinical trials are needed with children.* • *Millions of people could benefit from Trovan.* • *If approved by the FDA, Trovan could earn over a billion dollars a year for Rezip.* • *Clinical trials happen in three stages.* • *Clinical trials must be conducted on target populations to get FDA approval for the drug.* • *Children in the trial would be given either Rezip's experimental drug or a standard antibiotic.* • *200 children would be picked for the trial.* • *Rezip set up its camp meters from the DWB station.* • *An ethics committee gave permission for the trial to take place, but individuals were not asked for their consent.*	• *Were there any negative outcomes for the 5,000 adults who took Trovan during earlier testing?* • *How dangerous is meningitis?* • *How healthy does a child have to be to participate in a clinical trial?* • *Who gave consent for the children to participate? How?* • *How much will the drug sell for if it is approved? Will people in Kano be able to afford it, if approved?* • *Is two weeks enough to gather data on how effective a drug is?* • *What are the side effects from the standard antibiotic that had already been proven safe and effective?* • *What drug(s) was Doctors without Borders using?*

Part III: Stakeholder Values

Stakeholders (people/entities affected by the decision)	Values/concerns of each stakeholder	Bioethical Principle(s) given priority
You (and/or other doctors)	*You are concerned that the children not be treated as a means to an end but respected for their inherent worth. You also see the benefit of the drug and the need for clinical trials.*	*Respect for Persons* *Maximizing Benefits/ Minimizing Harms*
The sick children and their families	*Both value the children's health and well-being. Families may be concerned that their children are treated fairly, and that they are not bearing an unequal share of the risks.*	*Justice*
Rezip Pharmaceutical Company	*Rezip is being practical in finding a population who could potentially benefit from their experimental drug, while getting the trial results they need quickly.*	*Maximizing Benefits/ Minimizing Harms*
Kano State	*They are concerned that their citizens are protected and not being used as a "means to an end." They may also value positive relationships with U.S. corporations.*	*Respect for Persons* *Justice*

RESOURCE

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5. Generating Options
(What are some possible options to resolve the ethical question?)

The trial should not proceed at this time of intense need and the doctors should return to the U.S.

The trial should proceed as planned.

The trial should proceed only if the families of the children give their fully informed consented to participate in the clinical trial.

The trial should proceed under the oversight of the Nigerian government.

The trial should proceed but only if Rezip stays in Nigeria for longer than two weeks to offer ongoing medical care for the study participants and their families.

6. Write a strong justification paragraph for your decision on the topic. Make sure to answer the following questions while using the evidence (such as the facts and ethical considerations) to support your claim in a way that shows your reasoning.

a. What is your position on this issue?

b. What is the factual content to support your position that can be confirmed or refuted regardless of cultural or personal views?

c. What ethical considerations can be included to support the position? (Respect for Others, Maximize Benefits/ Minimize Harms)

d. What are the views and interests of the individuals or groups affected by the decision that you think are most relevant to your position?

e. What are the alternative options and why are they not as strong as your position?

Example justifications:

No, Rezip should not conduct this trial. Although hundreds of thousands of people die each year due to bacterial infections and the drug has already been successfully tested on over 5,000 adults, more studies are needed with children who are not already dangerously ill and living during a meningitis epidemic. Rezip will violate the principle "Respect for Persons" by not obtaining informed consent from the families of the children. Furthermore, they are not respecting the vulnerable population in Kano since they are scheduled to leave the area after only two weeks, even though the need for medical care will still be acute. The principle of Justice states that risks, costs, and resources should be equally distributed, but the children of Kano would take the risk of participating, while Rezip would benefit by collecting the needed data. Although the drug may prove to be beneficial to the children, the potential harms to the children in this population at this time outweigh the benefits to Rezip.

OR

Yes, Rezip should conduct this trial. The company has already undergone preliminary clinical trials that have shown the drug's effectiveness in adults. This drug could ultimately be beneficial in this geographical region and health situation—a meningitis outbreak—and the fatality rate may be lowered. Rezip could be "Maximizing Benefits" of study participants by testing an antibiotic that could potentially alleviate much pain and suffering. By having such a short trial period, the drug could be put on the market sooner and made available to the people who need it. Meningitis is a serious disease with devastating and sometimes deadly effects; all parties (stakeholders) should support the development of drugs against it.

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STUDENT HANDOUT 5.3

Elements of a Strong Justification

Name_____ Date_____ Period_____

A strong justification should have the following elements:

✔	A good justification includes:	Which means…
☐	A DECISION	A position (claim) has been clearly stated. The decision relates directly to the ethical question.
☐	FACTS	The facts and science content can be confirmed or refuted regardless of personal or cultural views. This can be used as evidence to support the claim.
☐	ETHICAL CONSIDERATIONS	Ethical considerations may include Respect for Persons, Maximize Benefits/ Minimize Harm, and Justice, in addition to others. This can be used as evidence to support the claim.
☐	STAKEHOLDER VIEWS	There are a variety of views and interests in the decision and more than one individual or group will be affected by the outcome.
☐	ALTERNATIVE OPTIONS and REBUTTALS	No one decision will satisfy all parties. A thorough justification considers strengths and weaknesses of various positions.
☐	REASONING and LOGIC	A logical explanation that connects the evidence to the claim is provided.

For our purposes, the justification for the decision is more important than the position on the decision.

HANDOUT

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