

Summative Assessment

Position Paper

INTRODUCTION

Students demonstrate what they have learned over the course of the unit by identifying and justifying their personal position regarding their own participation in a real clinical trial. Students evaluate a trial using a decision-making model to consider ethical protections, the scientific and social value of the trial, and the potential risks and benefits of their possible participation in the trial. Students then write a paper detailing how their decision to participate or not reflects their position on research involving humans.

CLASS TIME

Two class periods of 55 minutes each are needed for students to choose a study and work through the decision-making framework.

Additional time, inside or outside of class, will be needed for students to complete their position papers.

KEY CONCEPTS

- Involving humans in medical research is a complex issue that requires careful and deliberate thought.
- Students may agree with some aspects of human participation in research but not others, and the ability to identify and justify these positions allows for continued growth and discussion about complex issues.

LEARNING OBJECTIVES

Students will:

- Demonstrate their understanding of the ethical involvement of humans in research.

MATERIALS

Materials	Quantity
Student Handouts SA-1a-f— <i>Summaries of Clinical Trials</i>	Several copies of each summary for students to look through to make a choice; plus enough copies so that each student can work with the trial of his or her choice.
Student Handout SA-2— <i>Guidelines for Choosing Your Own Clinical Trial</i>	1 per student
Student Handout SA-3— <i>Decision-Making Framework</i>	1 per student
Student Handout SA-4— <i>Decision Paper Rubric</i>	1 per student
Completed <i>Silent Chalk Talk Posters</i> from RARE Film Guide activity	6 posters

FRAMING THE LESSON

Use the *Summative Assessment* to assess student understanding of concepts presented in the lessons in this curriculum.

Vocabulary words used in each lesson are in **bold**. Definitions can be found at the end of each lesson and in the *Master Glossary* in the *Appendix*.

TEACHER PREPARATION

- Make copies for each student of *Student Handouts SA-2*, *SA-3*, and *SA-4*.
- Make a several copies of each of the clinical trial summaries (*Student Handouts SA-1a-f—Summaries of Clinical Trials*) for students to share while considering which trial they would like to explore. After that point, there should be enough copies so that each student can work with the trial of his or her choice.
- Read through the clinical trial summaries (*Student Handouts SA-1a-f*) to assess vocabulary and readability for students. Some of these trials are more technical than others and therefore may be more appropriate for advanced students. [**Note:** The HPV study presented in *Student Handout SA-1c* is only applicable to females.] Teachers may decide to:
 - o provide information about specific clinical trials using the *Student Handouts*,
 - o have students choose a clinical trial from <http://www.clinicaltrials.gov>, or
 - o combine the two methods depending on individual student preferences.

NOTE TO THE TEACHER

The provided clinical trials (*Student Handouts SA-1a-f*) are real but have been abbreviated, and may not be currently recruiting participants. However, these trials do provide students with the information necessary to complete the assessment. Some students may prefer to do a web search to look for trials relating to a specific condition due to a personal connection or interest. Complete trial descriptions are much more detailed than those provided in the *Student Handouts*. To make these trial descriptions more accessible, encourage students to focus on the **purpose**, **detailed description**, and **eligibility criteria** of the trial, and to skim all other information.

Students may struggle with some of the medical vocabulary found in the clinical trial summaries in *Student Handouts SA-1a-f*. The summaries are authentic examples of studies found in the U.S. National Institutes of Health's database for trials conducted in the U.S. and worldwide (<http://www.clinicaltrials.gov>), and represent a real-world culmination of the lessons in this curriculum.

Remind students that they are not being assessed on their understanding of the specific details of a particular clinical trial, but on the broader questions posed during this unit, such as: Why would I choose to (or choose not to) participate in this trial? What ethical protections are in place for me? Does this research have social value? Does the study design seem scientifically valid? What are the risks and benefits? And finally, how does my decision to participate or not reflect my position on research involving humans?

PROCEDURE

Teacher Background

Before students begin working on their position papers, teachers may wish to read the directions aloud to the class and answer any questions. Teachers may also choose to request rough drafts before students begin their final drafts.

Activity One: Setting the Stage

1. Explain to students that they will be demonstrating what they have learned over the course of the unit by identifying and justifying their personal positions regarding their own participation in a real clinical trial.
2. If students participated in the *RARE* Film Guide *Silent Chalk Talk* activity, review the main ideas covered in the unit, ending with the poster focusing on the knowledge/likelihood that students would participate in a clinical trial.
3. Invite students to briefly share with the class their ideas and concerns about personal involvement as a human subject, and then transition into the introduction of the assessment.

A note about Student Handout SA-1f—Safety of an Oral HIV Vaccine in HIV Uninfected

Volunteers: Students may be interested to know that this study never opened. Despite significant preparations for a **Phase I trial**, the study vaccine did not live up to expectations and it never progressed beyond pre-clinical research.

A note about eligibility: For the purposes of this activity, students should consider joining the trial based only on the merits of the study itself. This is not “real world” in that students would be ineligible for many trials due to their age, and many would find the commitment of being in a trial challenging due to their school schedule, extracurricular activities, or access to transportation. For this assessment, students should make their decision as if they are eligible and have no competing obligations.

Activity Two: Position Paper

4. Tell students they will have the opportunity to demonstrate their understanding of humans in clinical research by investigating a current clinical study. They will make an argument about whether or not they would be willing to enroll and explain why or why not.
5. Share with students copies of Student Handouts SA-1a-f—*Summaries of Clinical Trials*. Allow them time to review the *Student Handouts*.
6. Answer any questions after students have reviewed the studies, and then ask them to choose a clinical trial to write about.
7. If students decide instead to research a clinical trial using the internet, have them follow the guidelines provided in Student Handout SA-2—*Guidelines for Choosing Your Own Clinical Trial*.
8. Students will use Student Handout SA-3—*Ethical Decision-Making Framework* to organize the information from the clinical trial summary and begin formulating a justification for their decision about whether they would choose to enroll in the study. Walk through the *Student Handout* to make sure students understand where to find the necessary information in the clinical trial summary. Assist with any vocabulary or content questions.
9. Give students time to individually work through Student Handout SA-3—*Ethical Decision-Making Framework*.
10. Before students begin to write their papers, give them a copy of Student Handout SA-4—*Decision Paper Rubric*.

Name _____ Date _____ Period _____

Breath Test for Early Detection of Lung Cancer

Purpose

To demonstrate and validate a breath test for detection of early stage lung cancer that could potentially reduce lung cancer deaths.

Condition:	Lung Neoplasms
Study type:	Observational
Study design:	Observational Model: Cohort
Official title:	Breath Test Assay for the Detection of Lung Cancer
Primary outcome measures:	Sensitivity and specificity of the breath test as compared to CT and pathology to support primary lung cancer diagnosis.
Estimated enrollment:	600

Groups/Cohorts

1. Asymptomatic High Risk Subjects. Smokers aged ≥ 18 undergoing chest CT
2. Symptomatic High Risk Subjects Without a Tissue Diagnosis. This group will consist of patients who are undergoing medical evaluation for a pulmonary symptom such as chronic unexplained cough or hemoptysis.
3. Symptomatic High Risk Subjects With a Tissue Diagnosis. This group will be found to include a. lung cancer, and b. diseases other than lung cancer (e.g., sarcoidosis, COPD, or pulmonary infection).
4. Apparently healthy individuals having no signs or symptoms of lung carcinoma.

Detailed Description

This is a multicenter study comparing several groups of subjects with and without lung cancer by CT scan, biopsy, and the breath test. The breath test will be performed to make sure that the previously developed methods and procedures are valid.

Eligibility

Ages Eligible for Study:	18 and older
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	Yes

Criteria for Group 4—Apparently healthy subjects

- | | |
|---------------------|--|
| Inclusion criteria: | <ul style="list-style-type: none">• Willingness to follow protocol requirements as evidenced by written, informed consent.• Healthy, male or females, ages 18 and older.• Non-smokers having no signs or symptoms of lung carcinoma. |
| Exclusion criteria: | <ul style="list-style-type: none">• Any active ongoing medical problems. |

ClinicalTrials.gov processed this record on July 12, 2012.

Citation: <http://clinicaltrials.gov/ct2/show/NCT00639067?term=Breath+Test+for+Early+Detection+of+Lung+Cancer&rank=1>.

STUDENT HANDOUT SA-1b

Summaries of Clinical Trials

Name _____ Date _____ Period _____

Connection Between Sleep and Athletic Performance

Purpose

In the last few decades much knowledge has been accumulated on the connection between healthy, sufficient sleep, and overall health, cognitive function, memory, and job or school performance, motor vehicle accidents, and work accidents. There has been growing awareness recently of the connection between physical activity and competitive sports performance, and the amount and quality of sleep. Despite the shortage of scientific studies, there is a constant effort to improve understanding in this field.

Athletic activity includes not just competitions but also training toward competitions. Since it is difficult to control for influences of competitions and other occasional events, in this study the investigators focus on evaluating the connection between sleep and athletic performance in training.

Toward the end of adolescence, youth are busy in multiple activities related to studies, social obligations, and athletic activities. This is also the age they learn to drive. This is an age at which physiologically a person needs more sleep relative to other ages (9.25 hours of sleep a day), and paradoxically, due to the multiple obligations, these youths' actual sleep time may be lower than needed.

In light of this, there is sound basis for the presumption that athletic performance is connected to the influence of sleep directly and indirectly.

Condition	Intervention
Quality Sleep Time Athletic Performance	Behavioral: Sleep extension

Study type:	Interventional
Study design:	Randomized
Official title:	Connection Between Sleep Quality and Duration and Performance in Young Athletes
Estimated enrollment:	50

Detailed Description

Aim: The purpose of this study is to evaluate the connection between sleep quality and duration and athletic performance among young athletes.

Participants and their parents will be asked to give informed consent.

The proposed study will have two stages:

1. Baseline assessment: In the first stage there will be an evaluation of the athletes' sleep quality and duration over the course of two weeks, and in parallel their athletic performance will be evaluated using accepted measures such as: swimming times over set distances, running times over set distances, etc.
2. Assessment of intervention's effect of prolonging the duration of nighttime sleep on the athletic performance of the participants, using the same measures as above. This stage will take four weeks.

Stage 1:

- a) Before beginning the study, each participant will fill out a general health questionnaire.
- b) Each participant will receive a heart monitor belt to wear for two weeks when sleeping. Each participant will be asked to wear the belt before going to bed and remove it upon waking in the morning. Heart rate data stored on the belts will

be transferred to a computer each morning. Sleep data will be analyzed and each participant will receive a personalized sleep analysis. At this stage, the investigators will evaluate the baseline characteristics of the participants including their sleep duration, sleep efficiency, and presence and duration of the different sleep stages. In particular, investigators will assess slow wave sleep (during which a growth factor is released that is important for muscle recovery), time and duration of training sessions, and athletic performance.

- c) Evaluation of athletic performance will be done using standard tests that are routinely carried out as part of athletic training in every branch of sports. Also, general parameters will be measured like standing heart rate and reclining heart rate, and heart rate at awakening in the morning.

Stage 2:

- a) At this stage the participants will be divided randomly into two groups. In the course of an additional training cycle of two weeks, one group labeled "A" will be given additional sleep time of one to two hours. The second group (group "B") shall continue with no change. In the course of the two weeks, sleep parameters of both groups will be assessed and analyzed, and athletic performance during routine training will continue to be measured and tabulated. After these two weeks, the two groups will be crossed over, group "A" will return to a routine sleep schedule, i.e., the extra sleep time will be removed, and group "B" will get additional sleep time. All the aforementioned measures will be collected during the next two weeks (sleep quality, athletic performance during training).
- b) During the entire study there will be close monitoring of injuries among participants. Events will be defined as injuries (according to the number of treatments by a physiotherapist or visits to a doctor) or near-injuries and will be quantified. Correlations will be sought between performance, injuries, and sleep duration.
- c) In both stages, in addition to wearing a heart monitor belt, participants will be asked to fill out a questionnaire before and after sleep during the entire study.

- Expected benefits:
- Better understanding of the physiology associated with sleep among adolescents involved in regular, competitive physical activity.
 - Improved performance by building a sleep program, optimal wakefulness, and training.

Eligibility

Ages eligible for study:	13 Years to 20 Years
Genders eligible for study:	Both
Accepts healthy volunteers:	Yes

Criteria

- Inclusion criteria:
- Age: 13–20 years old, male and female athletes.
 - Generally good health.
 - Willingness to participate in the study.
 - Healthy heart rate.
- Exclusion criteria:
- Arrhythmia.
 - Chronic or acute illness.
 - Unwillingness of the subject or his parents to allow participation in the study.

ClinicalTrials.gov processed this record on July 12, 2012.

Citation: <http://clinicaltrials.gov/ct2/show/NCT01364831?term=Connection+Between+Sleep+and+Athletic+Performance&rank=1>.

STUDENT HANDOUT SA-1c

Summaries of Clinical Trials

Name _____ Date _____ Period _____

Immunogenicity of Off-Schedule Dosing of HPV Vaccine

Purpose

The purpose of this study is to gain a better understanding of the body's response to a human papillomavirus (HPV) vaccine and booster shot. The study will also investigate factors related to adolescents not following vaccination schedules. The HPV vaccine requires three doses (shots). Girls sometimes receive the three shots at the recommended times, and sometimes receive the shots at non-recommended times. This study will evaluate whether getting the shots at non-recommended times affects the level of protection provided by the vaccine. Participants will include about 1,400 girls 9–17 years old receiving a third dose of HPV vaccine from their primary care clinician. Study procedures include: medical history, questionnaires, and blood draws. Participants will be involved in the study for about six months from time of enrollment.

Condition:	Human Papillomavirus
Study type:	Observational
Study design:	Observational Model: Cohort
Official title:	Immunogenicity of the HPV-6, 11, 16, 18 Vaccine Among Adolescent Girls Who Receive Vaccine Doses at Non-recommended Intervals and Factors Related to Non-adherence
Estimated enrollment:	1,400

Groups/Cohorts

Experimental/Primary Arm 1:	This will consist of subjects receiving the second dose on time/third dose substantially late.
Experimental/Primary Arm 2:	This will consist of subjects receiving the second dose substantially late/third dose on time.
Experimental/Primary Arm 3:	This will consist of subjects receiving the second dose substantially late/third dose substantially late.
Alternate Arm:	This will consist of subjects who meet eligibility requirements but do not fit into any of the primary experimental arms.
Control Arm:	This will consist of subjects with an on-time interval between dose one and two, and an on-time interval between dose two and three.

Detailed Description

The immune response to the Gardasil® human papillomavirus (HPV) vaccine in non-clinical trial settings is unknown. In addition, the immune response following administration of the vaccine at substantially prolonged intervals is unknown. Early indications suggest that many girls will receive the vaccine at prolonged intervals and that this timing may affect immunogenicity. The lack of knowledge about the immunogenicity of prolonged intervals between vaccine doses precludes evidence-based recommendations for patients who are substantially late for their second or third dose. Currently, some clinicians restart the series while others give the doses at the incorrect interval without being able to counsel their patients as to their expected level of immune response or protection. Examining the immune response before the third dose and at one and six months after the third dose will allow a better understanding of the immunogenicity of this vaccine, and of the immune response to booster doses. Furthermore, determining factors related to non-adherence in the adolescent age group is important and timely. As an increasing number of vaccines are being recommended to the adolescent age group, understanding factors involved with non-adherence to the recommended dosing schedule is now critical. This information can guide interventions that aim to increase adolescent adherence

to the recommended schedules. Eligible girls 9 to 17 years old receiving the Gardasil HPV vaccine from their primary care provider will be enrolled into this study on the day of, but prior to, receiving their third HPV vaccine dose or at approximately 28 days after HPV dose two. Blood for immunogenicity testing will be obtained up to three times during the study: one month and six months after the third dose for all subjects, and just prior to the third dose for subjects on time for their third dose (regardless of the time interval between the first and second dose). In addition, on Study Day 0, patient- and parent-related factors known to impact healthcare utilization may be measured using a questionnaire given to parents/legal guardians and to 14 to 17 year old subjects. Initially, all subjects meeting eligibility criteria will be enrolled regardless of timing of the second and third vaccine doses.

Eligibility

Ages eligible for study:	9 years to 17 years
Genders eligible for study:	Female
Accepts healthy volunteers:	Yes
Sampling method:	Non-probability sample
Study population:	Girls 9 to 17 years old receiving a third dose of the Gardasil HPV vaccine from their primary care clinician. Parent/legal guardians will participate by answering a questionnaire to determine factors related to non-adherence to recommended vaccine schedule.

Criteria

Inclusion criteria:	Girls will be eligible if they are: <ul style="list-style-type: none"> • 9 to 17 years of age (defined as between 9 years 0 days and younger than 18 years of age) at time of receipt of third HPV dose; • Receiving the third dose of Gardasil human papillomavirus (HPV) vaccine as part of routine healthcare; • Able and willing to complete all study visits and evaluations; • Able and willing to participate in the study by providing written informed assent/consent; and • Parent or legal guardian provides permission.
Exclusion criteria:	Girls will be excluded from study participation if they: <ul style="list-style-type: none"> • Are unable to comply with the study protocol. • Have received more than three doses of human papillomavirus (HPV) vaccine. • Have received blood and or blood products (including immunoglobulin) in the past three months or anticipate receiving these products during the study period. • Have a history of any physical, mental, or developmental disorder that study personnel believe may hinder their ability to comply with the study requirements. • Have a history of malignancy or confirmed or suspected immunodeficiency condition, such as human immunodeficiency virus infection. • Are participating or have participated in HPV vaccine related research. • Have received an investigational or alternate (Cervarix) HPV vaccine.

ClinicalTrials.gov processed this record on July 12, 2012.

Citation: <http://clinicaltrials.gov/ct2/show/NCT01030562?term=Immunogenicity+of+Off-Schedule+Dosing+of+HPV+Vaccine&rank=1>.

Name _____ Date _____ Period _____

Natural History Study of the Development of Type I Diabetes

Purpose

TrialNet is an international network dedicated to the study, prevention, and early treatment of Type I Diabetes. TrialNet sites are located throughout the United States, Canada, Finland, United Kingdom, Italy, Australia, and New Zealand. TrialNet is dedicated to testing new approaches to the prevention of and early intervention for Type I Diabetes.

The goal of the *TrialNet Natural History Study of the Development of Type I Diabetes* is to enhance our understanding of the demographic, immunologic, and metabolic characteristics of individuals at risk for developing Type I Diabetes.

The Natural History Study will screen relatives of people with Type I Diabetes to identify those at risk for developing the disease. Relatives of people with Type I Diabetes have about a three to four percent chance of being positive for the antibodies associated with diabetes. TrialNet will identify adults and children at risk for developing diabetes by testing for the presence of these antibodies in the blood. A positive antibody test is an early indication that damage to insulin-secreting cells may have begun. If this test is positive, additional testing will be offered to determine the likelihood that a person may develop Type I Diabetes. Individuals with antibodies will be offered the opportunity for further testing to determine their risk of developing diabetes over the next five years, and close monitoring for the development of diabetes.

Condition:	Diabetes Mellitus, Type I
Study type:	Observational
Study design:	Time perspective: Prospective
Official title:	Natural History Study of the Development of Type I Diabetes
Estimated enrollment:	75,000

Detailed Description

- The study is conducted in two parts:
- Screening.
 - Monitoring (annual and semi-annual depending on risk).

A simple blood test is done to screen for the presence of diabetes-related biochemical antibodies. Islet cell antibodies are also measured in individuals positive for one or more biochemical antibodies. Participants can go to a TrialNet Clinical Center, or request a screening kit to have their blood drawn by a local physician or laboratory. Participants will be provided with their screening results within four to six weeks.

If antibodies are present initially and are confirmed by repeat testing, participants will be invited to have additional testing at a baseline monitoring visit to determine their average risk of developing diabetes over the next five years. The baseline monitoring visit will include an Oral Glucose Tolerance Test (OGTT), re-testing for biochemical and islet cell antibodies if needed, measurement of HbA1c, and HLA (genetic) typing.

Individuals with a less than 3% average risk will be asked to come for follow-up on annual basis; individuals with greater than average 32% risk will be asked to come for follow-up visits on semi-annual basis.

Participants will be monitored for possible progression towards Type I Diabetes and may be offered the opportunity to enter into a prevention study (e.g., oral insulin prevention study) or an early treatment study if they are diagnosed with Type I Diabetes while participating in the *Natural History Study*.

Eligibility

Ages eligible for study:	1 year to 45 years
Genders eligible for study:	Both
Accepts healthy volunteers:	Yes
Study population:	First, second, and third degree relatives of individuals with Type I Diabetes.

Criteria

- Inclusion criteria:
- Individuals 1 to 45 years old who have an immediate family member with Type I Diabetes (such as a child, parent, or sibling).
 - Individuals 1 to 20 years old who have an extended family member with Type I Diabetes (such as a cousin, niece, nephew, aunt, uncle, grandparent, or half-sibling).
- Exclusion criteria:
- To be eligible a person must not:
- Have diabetes already.
 - Have a previous history of being treated with insulin or oral diabetes medications.
 - Currently be using systemic immunosuppressive agents (topical and inhaled agents are acceptable).
 - Have any known serious diseases.

ClinicalTrials.gov processed this record on July 12, 2012.

Citation: <http://clinicaltrials.gov/ct2/show/NCT00097292?term=Natural+History+Study+of+the+Development+of+Type+1+Diabetes&rank=1>.

STUDENT HANDOUT SA-1e

Summaries of Clinical Trials

Name _____ Date _____ Period _____

Pharmacokinetics Study of HT-2157 in Healthy Subjects and in Patients With Major Depressive Disorder

Purpose

This is a two-part study. The objective of Part 1 is to evaluate the safety, tolerability, and pharmacokinetics of HT-2157 in healthy normal volunteers.

Part 2 is a randomized, double-blind, placebo-controlled, multiple (21-day) ascending-dose evaluation of the safety, tolerability, and pharmacokinetics of HT-2157 in patients with major depressive disorder.

Condition	Intervention
Healthy volunteers (Part 1)	HT-2157
Major depressive disorder (Part 2)	HT-2157 or a placebo

Study type: Interventional

Study design: Randomized

Official title: A Two-Part Study: Part 1 is a Multiple-dose (7-day), Open-label Evaluation of the Safety, Tolerability, and Pharmacokinetics of HT-2157 in Healthy Subjects. Part 2 is a Randomized, Double-blind, Placebo-controlled, Multiple (21-day) Ascending-dose Evaluation of the Safety, Tolerability and Pharmacokinetics of HT-2157 in Patients With Major Depressive Disorder.

Estimated enrollment: 28

Arms	Assigned Intervention
Experimental: HT-2157	Drug: HT-2157 QD oral dosing
Placebo comparator: Placebo	Drug: Placebo QD oral dosing

Detailed Description

This is a two-part study. The objective of Part 1 is to evaluate the safety, tolerability, and pharmacokinetics of HT-2157 administered for seven days in healthy normal volunteers.

Part 2 is a randomized, double-blind, placebo-controlled, multiple ascending-dose evaluation of the safety, tolerability, and pharmacokinetics of HT-2157 administered for 21 days in patients with major depressive disorder. The primary objective of Part 2 is to assess the entrance of HT-2157 into cerebrospinal fluid in the central nervous system. In addition, the potential activity of HT-2157 in this patient population may be assessed using exploratory biologic and pharmacokinetic markers of potential efficacy.

Criteria

- Main inclusion criteria (Part 1):
- No clinically relevant abnormalities.
 - Ages 18 to 55 years, inclusive.
 - Body Mass Index (BMI) of 18.5 to 32 kg/m².
- Main inclusion criteria (Part 2):
- No clinically relevant abnormalities.
 - Ages 18 to 55 years, inclusive.
 - Body Mass Index (BMI) of 18.5 to 32 kg/m².
 - Mild-to-moderate major depressive disorder.
- Main exclusion criteria (Part 2):
- Any disorder that would interfere with the absorption, distribution, metabolism, or excretion of drugs.
- Main exclusion criteria (Part 2):
- Any disorder that would interfere with the absorption, distribution, metabolism, or excretion of drugs.
 - Current and primary Axis I disorder other than MDD.

ClinicalTrials.gov processed this record on July 12, 2012.

Citation: <http://clinicaltrials.gov/ct2/show/NCT01413932?term=Pharmacokinetics+-+Pharmacodynamic+Study+of+HT-2157+in+Healthy+Subjects+and+in+Patients+With+Major+Depressive+Disorder&rank=1>.

STUDENT HANDOUT SA-1f

Summaries of Clinical Trials

Name _____ Date _____ Period _____

Safety of an Oral HIV Vaccine in HIV Uninfected Volunteers

Purpose

This study will test the safety of and immune response to an oral HIV vaccine in healthy volunteers. The vaccine in this study uses a weakened bacterium called *Salmonella typhi* to deliver an HIV gene into the body through the mouth. The body then produces an HIV protein from the gene; this protein stimulates an anti-HIV immune response. The vaccine contains only one of the many substances that HIV needs to make more copies of itself, so the vaccine itself cannot cause HIV or AIDS.

Condition	Intervention	Phase
HIV infections	Biological: SCBaL/M9	Phase I

Study type:	Interventional
Study design:	Randomized
Official title:	Development of an Oral Prime-Boost AIDS Vaccine to Elicit Broadly Neutralizing Antibodies Against HIV-1
Estimated enrollment:	38

Arms	Assigned Intervention
Experimental: All participants will receive oral vaccine at study entry, although dosage will vary.	Biological: SCBaL/M9 Oral recombinant <i>Salmonella typhi</i> HIV-1 gp120 vaccine

Detailed Description

The transmission of HIV-1 by both sexual and parenteral (directly through the blood via IV needle) routes makes it likely that a successful preventive vaccine against this virus will need to induce protective immunity in both mucosal and systemic compartments. The long-term objective of this program is to develop an HIV-1 vaccine that elicits protective immunity in both the mucosal and systemic compartments.

The study will evaluate the safety and immunogenicity of an oral recombinant *Salmonella typhi* HIV-1 gp120 vaccine in healthy human volunteers. This will be the first study in volunteers to use a bacterium to deliver a recombinant vector vaccine mucosally. The study will also develop an Env immunogen that elicits a broader spectrum of neutralizing antibodies than gp120 and that can be delivered by *Salmonella typhi* or as a soluble protein immunogen.

This is a Phase I dose-escalation study of two vaccine components that will be combined in a larger prime-boost protocol should the desired safety endpoints be obtained. Both components use a constrained gp120 that expresses epitopes recognized by broadly neutralizing antibodies. The priming immunogen will be the conformationally constrained gp120 gene delivered orally by live attenuated *Salmonella typhi*. The boosting immunogen will be a soluble subunit protein made up solely of the conformationally constrained gp120.

All participants in this study will receive the vaccine. Participants will be randomized to different vaccine doses. Participants will have eight study visits over 20 weeks. Study visits will include a brief medical interview, physical exam, blood and urine tests, and counseling on avoiding HIV infection and pregnancy. Participants will be tested for HIV infection three times during the study.

Eligibility

Ages eligible for study: 18 years to 55 years

Genders eligible for study: Both

Accepts healthy volunteers: Yes

Criteria

Inclusion criteria:

- HIV uninfected.
- Sexual behavior that is indicative of low risk for HIV infection.
- Negative for Hepatitis B surface antigen.
- Negative for Hepatitis C viral sequences and antibody.
- Availability for follow-up during the study (five months).
- Willingness to use acceptable methods of contraception during study period.

Exclusion criteria:

- Receipt of HIV vaccines or placebo in a previous HIV vaccine trial.
- History of immunodeficiency, chronic illness, autoimmune disease, or use of immunosuppressive medications.
- History of cancer unless there has been a surgical excision followed by a sufficient observation period to give a reasonable assurance of cure.
- Medical or psychiatric condition or occupational responsibilities that preclude compliance with the protocol.
- History of suicide attempts, recent suicidal ideation, or psychosis.
- High-risk behavior for HIV infection as determined by screening questionnaire.
- History of injection drug use within 12 months of study entry.
- Use of experimental agents within 30 days of study entry.
- Receipt of blood products or immunoglobulin within six months of study entry.
- Active syphilis.
- Active tuberculosis.
- History of anaphylaxis or serious adverse reactions to vaccines.
- Pregnant or breastfeeding.

ClinicalTrials.gov processed this record on July 12, 2012.

Citation: <http://clinicaltrials.gov/ct2/show/NCT00062530?term=healthy+volunteers&recr=Open&cond=vaccine&age=1&phase=0&rank=8>.

STUDENT HANDOUT SA-2

Guidelines for Choosing Your Own Clinical Trial

Name _____ Date _____ Period _____

1. Go to <http://www.clinicaltrials.gov> and click on **Search for clinical trials**.
2. Enter "healthy volunteers" "(location)" "(condition)." Omit condition if you would rather browse all types of studies.
3. At the top of list, click **Hide studies that are not seeking new volunteers** and look through the list of current studies to find one that seems appropriate.
4. Click on the link and read through the eligibility criteria to make sure the study is appropriate for this assessment. To work for the assessment the study must:
 - a. Accept healthy volunteers in your approximate age group.
 - b. Be located in your region (traveling long distances for participation as a healthy volunteer is not realistic).
 - c. Have inclusion requirements you meet. (Some studies require blood work or other testing to determine whether respondents are eligible. You may still use the study if you meet all of the inclusion requirements other than those for such tests.)

Additional Resources

1. Centerwatch (<http://www.centerwatch.com/clinical-trials/overview.aspx>) provides a good overview of clinical trials and what you should know before you volunteer.
2. Other clinical trial sites include <http://www.centerwatch.com> and <http://www.cancer.gov/clinicaltrials>. You may also search local university or hospital websites for current trials.

STUDENT HANDOUT SA-3

Decision-Making Framework

Name _____ Date _____ Period _____

Part I: Question – Should I volunteer to participate in a clinical trial?

Name of trial:

Part II: Facts and Questions

Use the study details to answer the following:

What is the purpose of the study? Does it appear to have social value?

In what ways does the study plan seem scientifically valid? (Study type and design, eligibility, treatment/intervention received, **inclusion/exclusion criteria**, etc.)

What does the study require of me?

What ethical protections are in place for me? (Knowledge gained through historical clinical trials, **Belmont principles**, **IRB** involvement, etc.)

What other information do I need to know about this study or **clinical trial** before making a decision?

Part III: Stakeholder Values

Stakeholders (people/entities affected by the decision)

Values/concerns of each stakeholder

Belmont principle(s) given priority



HANDOUT

Part IV: Pros and Cons

(What are the possible benefits and risks of participating in the study?)

Possible benefits of participating	Possible risks of participating

Part V: Write a strong justification paragraph for your decision on the topic. Make sure to answer the following questions:

- a. What is your decision about enrolling in this study?
- b. What is the factual content (both from the clinical trial and other facts you learned in this unit) to support your decision that can be confirmed or refuted regardless of cultural or personal views?
- c. What ethical considerations can be included to support this decision? (Respect for Persons, Maximize Benefits/ Minimize Harms, Justice)
- d. What are the views and interests of the individuals or groups affected by the decision that are most relevant to your decision?
- e. Why is the alternative choice not as strong as your choice?

STUDENT HANDOUT SA-4

Decision Paper Rubric

Name _____ Date _____ Period _____

Throughout this unit we have discussed the involvement of humans in research. We have covered historical events, the **Belmont Report**, the **IRB** process (including **informed consent**), and **clinical trial phases**, including the challenges involved in recruiting participants. Using what you have learned about these aspects of human involvement in research, **identify and justify your personal decision regarding your possible involvement in a clinical trial**. In your answer, be sure to discuss **why you have/have not** chosen to participate in the trial. Provide justification for your decision by using facts (from what you have learned concerning historical cases, IRBs, etc., and those from your clinical study summary), various perspectives (multiple individuals on both sides of the issue from multiple backgrounds), and ethical considerations using the Belmont principles. Proficient or exemplary answers will demonstrate your understanding of classroom discussions, activities, and readings covering material spanning the entire unit. Use the rubric below to guide you in completing this assignment.

Exemplary	Proficient	Partially proficient	Developing
Student is able to identify her <i>personal decision</i> regarding her involvement in research that is...			
<ul style="list-style-type: none"> • Consistent with the nature of involving humans in research. • Authentic, clear, and easily understood. • Related to multiple issues outside of humans in research. 	<ul style="list-style-type: none"> • Consistent with the nature of involving humans in research. • Authentic, clear, and easily understood. 	<ul style="list-style-type: none"> • Consistent with the nature of involving humans in research. • Lacking authenticity and/or contains minor errors in understanding 	<ul style="list-style-type: none"> • Consistent with the nature of involving humans in research. • Lacking authenticity and/or contains major errors in understanding
Student is able to justify his personal position regarding his involvement in research through...			
<ul style="list-style-type: none"> • Multiple facts from his chosen clinical study and past studies. • Multiple perspectives from various backgrounds. • Multiple ethical considerations. • Providing examples of how this justification is based in social issues. 	<ul style="list-style-type: none"> • Multiple facts only from his chosen clinical study. • Multiple perspectives from various backgrounds. • Multiple ethical considerations. 	<ul style="list-style-type: none"> • Few facts, but they are only from his chosen clinical study. • Multiple perspectives, but predominantly from the same background. • Multiple ethical considerations. 	<ul style="list-style-type: none"> • Few to no facts. • A single perspective. • A single ethical consideration.