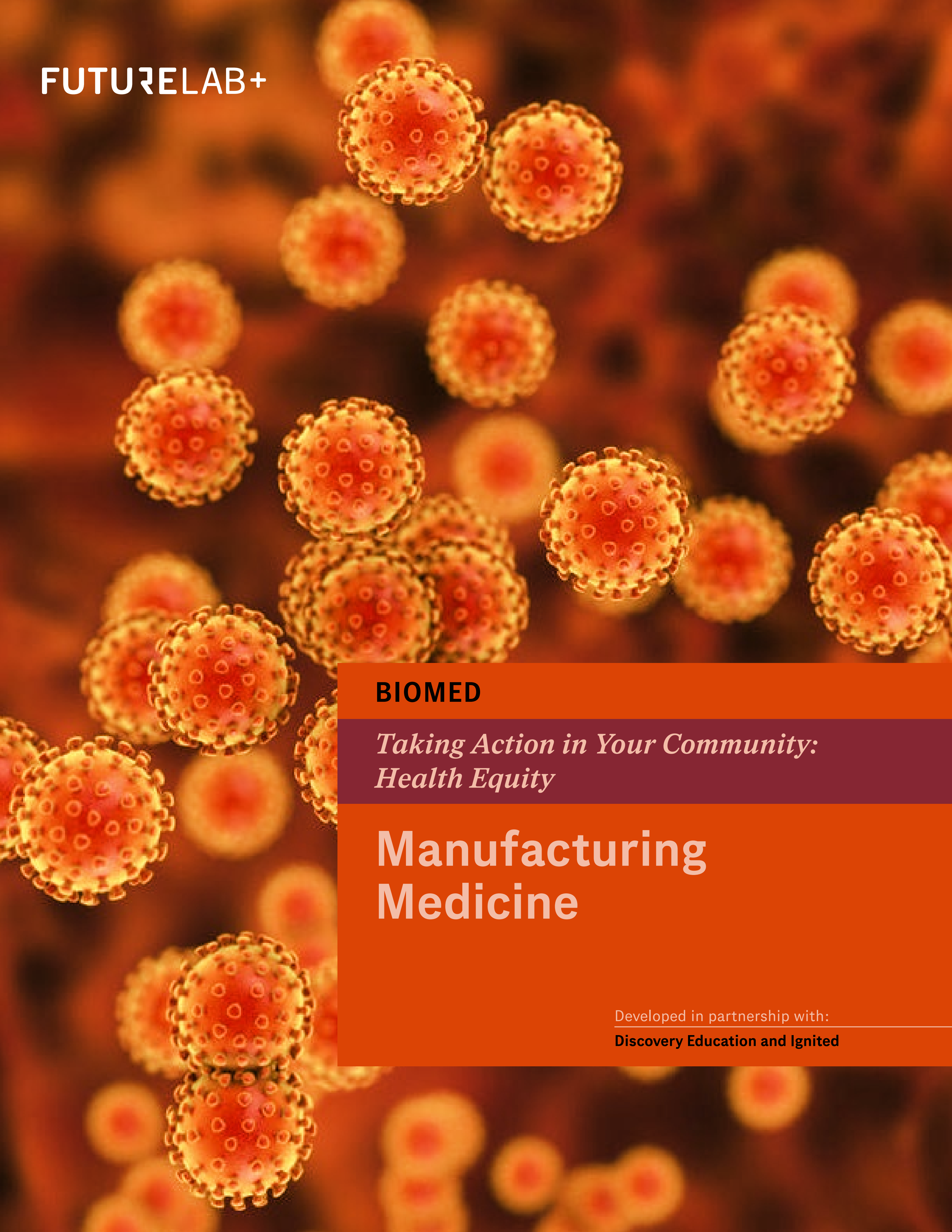


FUTURELAB+

BIOMED

Taking Action in Your Community: Health Equity

Manufacturing Medicine

Developed in partnership with:

Discovery Education and Ignited

In this Lesson Plan:

Print the **Teacher Section** →

Print the **Student Section** →

Medication
Packaging of dosage forms.
—
Cover Image
This is an illustration of coronavirus particles.

This document is separated into two sections, For Teachers [T] *and* Student Resources [S]*, which can be printed independently.*

Select the appropriate printer icon above to print either section in its entirety.

Follow the tips below in the Range field of your Print panel to print single pages or page ranges:

Single Pages (use a comma): T3, T6

Page Range (use a hyphen): T3–T6

BIOMED / TAKING ACTION IN YOUR COMMUNITY: HEALTH EQUITY

Manufacturing Medicine

DRIVING QUESTION

What are the methods used to reproduce a virus and produce a vaccine efficient enough to protect against the associated disease?

OVERVIEW

Every day, more than four million doses of vaccines are administered worldwide. To meet these requirements, industrial-scale manufacturing of the vaccines requires complex methods of production that include introducing the virus to fertilized eggs or serum-free culture media. Processes must follow strict guidelines to ensure safety and avoid contamination.

In this lesson, students will review the methods used to replicate a virus and produce the vaccine. They will identify the challenges associated with vaccine production. Taking on the role of Quality Assurance Engineers, students will produce a revised vaccine manufacturing process.

ACTIVITY DURATION

Three class sessions
(45 minutes each)

ESSENTIAL QUESTIONS

What are the cells used to reproduce a virus?

How can we avoid contamination by the active virus and still produce a vaccine containing the antigen of the virus?

OBJECTIVES

Students will be able to:

Identify the stages in the manufacturing of vaccines.

Apply their knowledge of cell division to the production of viruses.

Examine what cells can be used for mass production of viruses of interest for vaccines.

Understand the risks bound to each step in vaccine making.

Develop techniques to maximize quality control and assurance during the manufacturing of a vaccine.

BACKGROUND INFORMATION

In this lesson, students will learn about the method of production of a vaccine. They will make a connection between the different antigen types, the cells used to replicate the virus, and the industrial-scale manufacturing stages of the vaccine. It would be helpful if students have basic knowledge of immunity and what causes an immune response in a human body when in contact with a virus or a bacteria.

Materials
Computers with Internet Access
Career Profile
Butcher Paper
Markers
Vaccine Project Scenario
Failure Modes and Effects Analysis (FMEA) Capture Sheet
How Are Pathogens Grown? Capture Sheet
Stages of Vaccine Production
Scissors
Glue or Tape
What Can Go Wrong? Capture Sheet
Revised Vaccine Manufacturing Process
Design Journal

Pedagogical Framing

Instructional materials are designed to meet national education and industry standards to focus on in-demand skills needed across the full product development life cycle—from molecule to medicine—which will also expose students and educators to the breadth of education and career pathways across biotechnology.

Through this collection, educators are equipped with strategies to engage students from diverse racial, ethnic, and cultural groups, providing them with quality, equitable, and liberating educational experiences that validate and affirm student identity.

Units are designed to be problem-based and focus on workforce skill development to empower students with the knowledge and tools to be the change in reducing health disparities in communities.

SOCIAL-EMOTIONAL LEARNING

Students will develop their social awareness by discussing the vaccination rates in different communities. They will assess challenges associated with vaccine preparation in developing countries and therefore, work toward a culture of empathy. They will need to engage with others and show open mindedness while working in pairs and small groups throughout the activities, which will provide opportunities for social management.

CULTURALLY AND LINGUISTICALLY RESPONSIVE INSTRUCTION

This lesson allows students to look at equal access to vaccines. Systemic and institutional barriers to access include transportation, labor policies, working conditions, and monolingual information dissemination. They are being challenged to keep vaccines at freezing temperatures to avoid spoilage, while living in countries with extremely hot temperatures. As an exercise, this will provide students to consider the challenges of diverse cultures and conditions around the world. They will assess the direct impact of costs in vaccine production on low-income communities, which could be a personal factor for some students. The lesson provides for a culturally and linguistically responsive approach in order to validate and affirm cultural differences, while building content connections to the real world.

ADVANCING INCLUSIVE RESEARCH

The issue of access is at the core of health disparities. When it is challenging or impossible for people to join clinical trials and/or afford medication, they have little incentive to participate. In order to help as many people as possible, it is important that the scientific community develops outreach programs that connect patients with the medicines they need. Due to the exploitative history of testing on people of color without their knowledge, the medical community must use more of its power, resources, and finances to allay these genuine concerns in communities of color.

COMPUTATIONAL THINKING PRACTICES

This lesson focuses on how medicine is manufactured, and thus gives students experience with the computational thinking strategies of developing algorithms and decomposition. These skills are important elements of designing effective manufacturing and supply chain operations.

CONNECTION TO THE PRODUCT LIFE CYCLE

This lesson is centered in the **manufacturing** phase of the product life cycle, during which drugs are made and tested.

Have you ever wondered…

How is the influenza virus incubated in preparation for the production of its vaccines?

Chicken eggs have been used to reproduce the influenza virus and produce enough viruses for vaccine use.

Are all vaccines administered by injection?

A few vaccines are given orally, such as the vaccine against polio. This is due to the fact that orally given vaccines have shown to procure a broader immune response.

What was the first method used to protect against disease?

The first vaccination method was used to control the smallpox infection and is called variolation. People infected by the virus would develop pustules. The inoculation consisted of exposing someone who never had smallpox by infecting them with substance from the pustules or scabs of someone previously infected. This method would still give symptoms to the person, however, people "immunized" this way would have a much better chance of survival at the end of the 18th century, when 3 out of 10 would die from the disease.

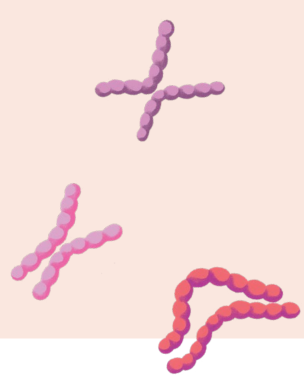
MAKE CONNECTIONS!

How does this connect to the larger unit storyline?

Vaccines prevent diseases from spreading from one individual to another and therefore, control pandemics. However, there have been safety concerns of people becoming infected by diseases through vaccination due to contaminated vaccines. Nevertheless, effective protection by the vaccines outweighs the risk of contracting and spreading disease itself if strict preparation guidelines are being followed.

How does this connect to careers?

Supervisor at a Pilot Plant understands the different stages of production and maintains records clearly while following protocol and analyzing data. This person is responsible for supervising processes, safety, and providing information about changes at any stage of the production.



How does this connect to our world?

For centuries, smallpox was a very serious disease and the only way to combat it was variolation, also called inoculation. Edward Jenner inoculated a boy with the cowpox virus using the blister of an infected person, and then purposefully exposed the boy to the smallpox virus. The boy never felt sick and was declared immune to smallpox. Jenner produced the first effective vaccine! Nowadays, scientists from all over the world are working on guidelines and methods to produce vaccines that are effective enough to keep the population safe from current and future pandemics.

Day 1

LEARNING OUTCOMES

Students will be able to:

Examine different types of vaccines.

Link the disease to the virus' antigen responsible for causing the disease.

Learn the antigen of the virus or bacteria used in vaccine preparation.

Investigate the risks associated with a vaccine's production.

Organize data from an article.

INDUSTRY AND CAREER CONNECTION

In this activity, students will be tasked with using a Pilot Plant Supervisor's soft skills of openness to learning as they will need to identify the challenges in the process of vaccine production and find a solution to keep the vaccines at freezing temperatures during transport in hot countries. They will need to display an organized sense of commitment skills as they will be placed in groups.

COMPUTATIONAL THINKING IN ACTION

Here, students are using the computational thinking strategy of decomposition to break down the food supply chain into components.

Procedure

Small Group (10–15 minutes)

1 Divide students into small groups of three or four who will work together throughout this lesson. Distribute one *Career Profile* to each group and give them 4–5 minutes to review the information presented.

2 Give each group a piece of butcher paper and markers. Ask each group to come to a consensus as to what are the main responsibilities of a Quality Assurance Engineer. Instruct them to write on the butcher paper large enough for all students to see. When finished, have groups hold up their papers and read them aloud. Ask students what they notice (i.e., Were they all similar? Were there any outliers?). Address any misconceptions and make sure students have a firm grasp of the role of a Quality Assurance Engineer before moving on.

3 Distribute or display electronically the *Vaccine Project Scenario*. Read aloud and explain that students will be taking on this role as they explore more about the vaccine manufacturing process.

Whole Group (10 minutes)

1 Ask students to think about how a food product goes from a farm to a grocery store or bodega. Ask them to summarize that process in four main steps with a *Train or Pass it On* discussion protocol. It is anticipated that students may respond with some variation of:

- **a.** growth/harvesting
- **b.** packaging/putting in a container
- **c.** storing/temperature control
- **d.** shipment

2 Tell students that there are also four critical stages in the production and distribution of a vaccine: the manufacture, the packaging, the storage, and the shipment.

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Day 1

Continued

Procedure

3 Ask students to consider what questions emerge as we think about the manufacturing and global distribution of vaccines. Use the instructional strategy *Snowball Fight* to increase student engagement and provide for a non-threatening way for students to respond. Ask a handful of students to read the "snowballs" they picked up and volunteer an answer if they wish. Anticipated questions include:

- How do we make enough vaccines to ensure the entire globe has access?
- Can we use plastic as a package for vaccines?
- Can we store vaccines at room temperature?
- Can we use refrigerators to transport vaccines?
- What if there is a power failure?

Teacher Note > *An optional activity is to show students a video about the COVAX Pillar in order to continue the conversation around equity and access.*

Individual (10 minutes)

1 Allow students to spend time reading *Manufacturing, safety, and quality control of vaccines* and watching embedded videos individually.

2 As students read the text, ask them to note required conditions for vaccine production and areas where steps of quality assurance may be necessary in the first column of the *Failure Modes and Effects Analysis (FMEA)* capture sheet. Remind them to look at this article as a Quality Assurance (QA) Engineer would. Review with students after they have completed reading.

Small Group (10 minutes)

1 Explain to students that actual Quality Assurance Engineers conduct a process known as *Failure Modes and Effects Analysis (FMEA)*. It is designed to evaluate a process or design for potential vulnerabilities and weak points. Before you begin a process, you think through risks and put corrective measures in place. A QA Engineer would ideally complete this step before the creation of a new product or process, but it can also be used to evaluate existing products or processes.

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Day 1

Continued

Procedure

2 Instruct students to complete a model *FMEA* by comparing and analyzing their list with a partner. Together, they can record potential corrective or control measures they would put in place as a QA Engineer to address the risks they noted.

Whole Group (5–10 minutes)

1 Facilitate a group discussion on the steps students noted and the various corrective measures they recorded. Challenge students to brainstorm extra challenges that might face in developing countries. How would this contribute to inequality in global health? How could we overcome these challenges?

Teacher Note > *Instructors may want to collect this as an Exit Ticket that serves as a formative assessment.*

Day 2

LEARNING OUTCOMES

Students will be able to:

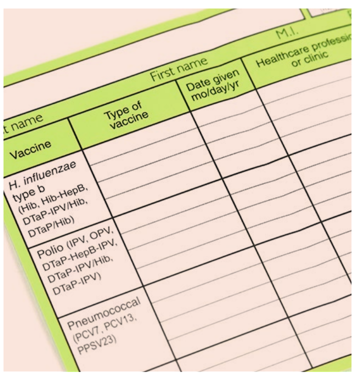
Identify the steps in manufacturing a vaccine.

Investigate the materials needed to produce the vaccine.

Create a logical sequence.

COMPUTATIONAL THINKING IN ACTION

By identifying the steps in creating a vaccine, students are using the computational thinking strategy of developing algorithms.



Procedure

Whole Group (10 minutes)

1 Ask for volunteers to list vaccines they know. Write them on the board as they name them. Some examples include vaccines for the flu, chickenpox, polio, measles, mumps, COVID-19, etc.

2 Inform them that some vaccines, such as the one for measles, include weakened live virus cells that force your body to “fight” and could make you feel sick. Because they are living, they must be kept cool. Other “inactivated vaccines,” such as the vaccine for polio, include killed versions of the virus. Because they are not as strong, they usually require “booster” doses over time. mRNA vaccines, such as some of those for COVID-19, do not contain the virus at all, but instead contain mime proteins that trigger similar immune responses. These shots almost always require booster doses to remain effective.[1]

3 Remind students that cells produce antibodies in the human body. The B lymphocytes produce antibodies in our bodies in response to an antigen. An antigen is a foreign substance in our bodies that triggers our immune system. Antigens are produced outside the body so they can be used in vaccines. How are scientists able to do that?

4 To help students discern the answer, distribute or have students access *Cell-Based Flu Vaccines* and provide the following close reading strategy written on the board:

- Circle ideas or facts that you already knew.
- Underline ideas or facts that are new learning for you.
- Write questions that you still have along the margins.
- Summarize how antigens are produced outside the body on the back side.

5 Summarize for students that antigens responsible for the immune response in a human body are produced to use in vaccines and are replicated in cells, media, and chicken eggs.

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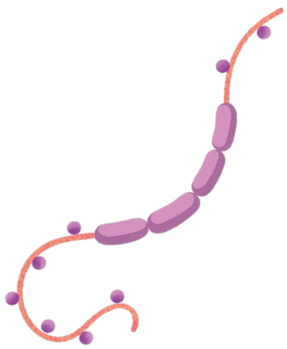
[1] https://www.hhs.gov/immunization/basics/types/index.html

Day 2

Continued



Procedure

Individual (5 minutes)	
1	Give one *How Are Pathogens Grown? Capture Sheet* to each student.
2	Instruct students to reference Table 5.1 from *Vaccine Manufacturing* to fill in the boxes with the name of each pathogen in the relevant column.
3	Use the *How Are Pathogens Grown? answer key* as your reference during the activity.

Small Group (30 minutes)	
1	Distribute one *Stages of Vaccine Production Capture Sheet* to each student. Instruct them to cut out the boxes and rearrange them to show the correct order of events.
2	Ask students to consult, using *Turn to Your Partner*, to agree or disagree with the other's sequence. They may change their order if presented with new information or an argument they find convincing.
3	At the end of the task, provide students with the correct sequence, using the *Stages of Vaccine Production answer key* as a reference. Instruct students to glue or tape each step into the correct box on page two of their capture sheets.
4	Organize students back into their original groups and distribute one *What Can Go Wrong? Capture Sheet* to each group. Prompt students to discuss Figure 5.2, which can be found in *Vaccine Manufacturing*.
5	Remind students of the scenario in which they have been hired as Quality Assurance Engineers. Read or display it again if necessary. They are going to demonstrate their understanding by completing their own *FMEA* on the vaccine production provided.

Teacher Note > *In order to enhance diversity and inclusion in this field, students need the opportunity to envision themselves in these roles with authentic scenarios and relevant skill development. To add more weight to this role and task, instructors may take an added step of providing clipboards, work badges and official files, as well as referring to student teams with the QA title.*

6	Read the directions of the *What Can Go Wrong? Capture Sheet* aloud and encourage your class of QA Engineers to begin brainstorming potential risks, required conditions, areas for quality control, or steps that could be improved. Following the examples provided, students can record their ideas directly on the capture sheet.

Day 3

LEARNING OUTCOMES

Students will be able to:

Understand the techniques used to produce a vaccine.

Organize data from a source.

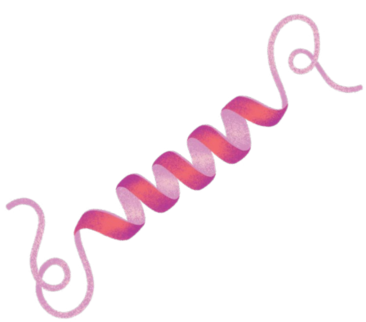
Evaluate and **annotate** current processes.

Revise processes to show understanding of quality control.

Procedure

Small Group (35 minutes)	
1	Prompt students to review their *FMEA Capture Sheet* and share with their group from the previous session. Considering the initial corrective actions the group noted on their *What Can Go Wrong? Capture Sheet*, are there any that can be added, removed, or modified based on their *FMEA* notes?
2	Distribute a *Revised Vaccine Manufacturing Process Capture Sheet* to each group. Read the instructions aloud and answer any questions as they arise. Students may choose to write their new process as a list, to mimic the initial process with the use of arrows, or to use computer software to create a flowchart.
3	Provide students with the remainder of the session or a predetermined amount of time to finish their revised processes.
4	If time allows or if you desire to stretch the activity into an extra session, students can present their final products to the class.

Individual (10 minutes)	
1	Ask students to capture how vaccines prevent diseases in their **Design Journal** and continue making connections between what they have learned and the social awareness campaign project.



National Standards

Next Generation Science Standards	**Science and Engineering Practices** Developing and using models Develop and/or use a model (including mathematical and computational) to generate data to support explanations, predict phenomena, analyze systems, and/or solve problems. **HS-ETS1-1: Engineering Design** Analyze a major global challenge to specify qualitative and quantitative criteria and constraints for solutions that account for societal needs and wants. **HS-ETS1-2: Engineering Design** Design a solution to a complex real-world problem by breaking it down into smaller, more manageable problems that can be solved through engineering. **HS-ETS1-3: Engineering Design** Evaluate a solution to a complex real-world problem based on prioritized criteria and trade-offs that account for a range of constraints, including cost, safety, reliability, and aesthetics as well as possible social, cultural, and environmental impacts.
Career and Technical Education (CTE)	**A9.1** Describe the major steps of a product's move through a company's product pipeline. **A9.2** Identify several products obtained through recombinant DNA technology. **A9.3** Outline the steps in production and delivery of a product made through recombinant DNA technology.

How Are Pathogens Grown? Capture Sheet

ANSWER KEY Do not share with students

Directions
Reference Table 5.1 from Vaccine Manufacturing to fill in the boxes with the name of each pathogen in the relevant column.

Medium	Human cells	Yeasts	Chicken eggs	Animal cells
Anthrax	Hepatitis A	Hepatitis B	Influenza	Japanese encephalitis
Haemophilus influenzae	Rubella			Measles
Meningococcal	Varicella			Mumps
Pneumococcal	Polio			Rabies
Typhoid fever				Yellow fever

Stages of Vaccine Production

ANSWER KEY | **Do not share with students**

Directions
Cut out each box and rearrange them to form the correct order of events.

1 Research Development	2 Assembling Raw Material
3 Producing the Antigen in Large Quantities	4 The Coupling Process for Conjugate Vaccine
5 Combining all Ingredients	6 Filling and Intermediate Approval
7 Packaging	8 Final Lot Release
9 Distribution	

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Career Profile

Quality Assurance (QA) Engineer
Our world depends on manufacturing, and the average consumer was awakened to its importance during the COVID-19 pandemic. The speed and quality of vaccine production became a central focus of governments and medical professionals around the world. Mistakes in vaccine manufacturing could mean human casualties, so overseeing every step of the process was essential.

What is a quality assurance engineer?

Quality assurance engineers are in charge of guaranteeing the quality of whatever is produced by their company. They oversee the manufacturing of the product at every stage from research at the very beginning until it is packaged, transported, and distributed to consumers.

Career outlook

A resurgence of industrial and manufacturing careers means there will be a need for QA Engineers into the future!

Projected job growth	8% (2018–2028)
Average salary range	$84,497–$87,568/year

Is quality assurance engineer a good career for me?

QA Engineers are:
— Analytical
— Confident team players
— Good communicators
— Organized

How do I become a quality assurance engineer?

You will need to:
— take classes in math, science, statistics, and technology.
— develop your communication and teamwork skills.
— study engineering in college.
— get job experience working with industrial or mechanical engineers.

Adapted from: Quality Engineer Job Description, Duties and Career Outlook

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Vaccine Project Scenario

Congratulations on being hired as the company's newest Quality Assurance Engineers! Your first project will be to analyze and provide suggestions for bettering our vaccine manufacturing process. Over the next few days, you will have the opportunity to learn the science behind producing a vaccine as well as our manufacturing process from research to distribution. It is our hope that by critically analyzing our process, you will be able to identify risks and potential outcomes that can go wrong...before they do! We cannot wait to hear your suggestions for how to improve our process. Good luck!

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Failure Modes and Effects Analysis (FMEA) Capture Sheet

Directions
Read the article Manufacturing, Safety, and Quality Control of Vaccines. Record your notes in the chart below.

Required conditions or areas for quality assurance	Potential control measures or corrective actions
Ex: Vials must be refrigerated.	Ex: Check and record min/max temperatures at the start of each workday.

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How Are Pathogens Grown? Capture Sheet

Directions
Reference Table 5.1 from Vaccine Manufacturing to fill in the boxes with the name of each pathogen in the relevant column.

Medium	Human cells	Yeasts	Chicken eggs	Animal cells
			Ex: Influenza	

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Stages of Vaccine Production
1 of 2 pages

Directions
Cut out the boxes and rearrange them to show the correct order of events.

Distribution	Research Development
Filling and Intermediate Approval	Combining all Ingredients
Producing the Antigen in Large Quantities	Final Lot Release
Assembling Raw Material	Packaging
The Coupling Process for Conjugate Vaccine	

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Stages of Vaccine Production

2 of 2 pages

Directions
Place the Stages of Vaccine Production cards in the correct order of events.

1	2
3	4
5	6
7	8
9	

What Can Go Wrong? Capture Sheet

Directions

For each step of the vaccine process, work with your group to predict something that could go wrong and record it next to the step. Two examples have been provided for you.

Adapted from Vaccine Manufacturing Fig.5 [2]

<table>
<tr><th colspan="3">Vaccine Process Steps</th><th>Potential Error</th></tr>
<tr><td colspan="3">Embryonated chicken eggs inspected and components (raw materials) sampled/tested</td><td></td></tr>
<tr><td colspan="3">Certified influenza monovalent seed virus suspension inoculated into eggs</td><td>Virus provided is cross contaminated with another virus</td></tr>
<tr><td colspan="3">Inoculated eggs are incubated</td><td></td></tr>
<tr><td colspan="3">Eggs inspected and viable eggs refrigerated</td><td></td></tr>
<tr><td colspan="3">Allantoic fluid from eggs harvested (contains the live virus)</td><td></td></tr>
<tr><td colspan="3">Virus concentrated, purified, and inactivated</td><td></td></tr>
<tr><td colspan="3">Whole virus reduced to subunit particles by adding disrupting agents</td><td></td></tr>
<tr><td colspan="3">Purification of split virus</td><td></td></tr>
<tr><td colspan="3">Preservative and stabilizers added (if required)</td><td></td></tr>
<tr><td colspan="3">Sterile filtration of split virus concentrate</td><td></td></tr>
<tr><td colspan="3">Monovalent split virus concentrate</td><td></td></tr>
<tr><td>Type A monovalent H1N1 split virus concentrate/ concentrate pool</td><td>Type A monovalent H3N2 split virus concentrate/ concentrate pool</td><td>Type B monovalent split virus concentrate/ concentrate pool</td><td rowspan="2"></td></tr>
<tr><td>CBER and QC potency testing (CBER assigned potency)</td><td>CBER and QC potency testing (CBER assigned potency)</td><td>CBER and QC potency testing (CBER assigned potency)</td></tr>
<tr><td colspan="3">Final bulk-trivalent types A and B influenza split virus vaccine</td><td></td></tr>
<tr><td colspan="3">QC and CBER release</td><td>Errors in quality control detection and method</td></tr>
<tr><td colspan="3">Bulk aseptically filled into final containers</td><td></td></tr>
<tr><td colspan="3">100% inspection for particulated and other defects</td><td></td></tr>
<tr><td colspan="3">Final containers labeled</td><td></td></tr>
<tr><td colspan="3">Containers packaged</td><td></td></tr>
<tr><td colspan="3">QA/QC release</td><td></td></tr>
<tr><td colspan="3">Ship to customer</td><td></td></tr>
</table>

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Revised Vaccine Manufacturing Process

Directions

As a team of Quality Assurance Engineers, consult your notes on potential risks and areas for corrective action as well as your FMEA *list of control measures to revise the vaccine manufacturing process to maximize quality control.*