Activity Name

Manufacturing a Vaccine

Broad Area of Learning

Health and well-being
Career planning and entrepreneurship

Targeted Competency

Competency 1: Seeks answers or solutions to scientific or technological problems

Components of the Targeted Competency

- Defines a problem
- Carries out the plan of action

Curricular Concepts

- Vaccine fabrication (biotechnology component)
- pH scale, acidity, and basicity
- Molar concentration
- Mole concept
- Binomial nomenclature

Grade Level

- Secondary 4 (Grade 10)

Instructional Strategies

- Case study, evidence-based decision making
- Role play
- Place scientific discoveries in local & international contexts

Required Materials

- Student document “Manufacturing an antifungal vaccine”
- Computer or other electronic device (to conduct research)

Approximate Duration

-150 minutes

Activity Context and Rationale

Vaccination is the best way to control epidemics and diseases in a large population. Although it is widely recognized as the most effective method of disease control, there is still public debate as to the risks associated with its use. Public health authorities and doctors unanimously agree on the efficacy of vaccination, but some people hesitate to vaccinate themselves and their families because of a perceived health risk. As a result, education is needed in order to present the personal, social, and medical benefits of vaccination.

At the same time, secondary chemistry students often fail to appreciate the relevance of their classroom activities in their daily lives. This activity is designed to provide context to several topics in secondary chemistry, in particular pH and the use of acid/base indicators, concentration, mole concept, and molecular models. By simulating the manufacture of a new antifungal vaccine, students will have to use their chemistry knowledge in order to solve the problems that are presented to them. They will need to consider some of the same conditions and criteria that the pharmaceutical industry must abide by, and in so doing will better understand the usefulness of the chemistry concepts discussed during in their previous courses.

*To best integrate this lesson, it should be initiated once the concepts of pH, acid/base indicators, and molar concentration have been taught.

Sequence of Activities

1- Introduction (15-20 minutes)

The teacher presents the video found in the "Context" section in order to introduce the activity. Students can progress through the "Context" and "Your Role" sections individually, or it can be read as a group. Alternatively, the teacher can guide the students through the completion of Activity 1 by posing each question aloud first and highlighting important points to record from the ensuing discussion. Refer to the answer key below for some essential ideas that should be discussed.

2- Activity Completion (45-60 minutes)

Students complete, individually or in teams, the two other sections of the student document. They may refer to their notes or to any other appropriate reference material.

3- Group Discussion and Additional Information (10-15 minutes)

As a class, the teacher asks students to justify their conclusions about the choice of adjuvant and stabilizer, addressing incorrect answers as appropriate. To conclude the lesson, the teacher can introduce the controversy around the use of aluminum salts as adjuvants. Links are provided at the end of the student document to provide some background and context to the discussion. Questions the teacher could ask students include:

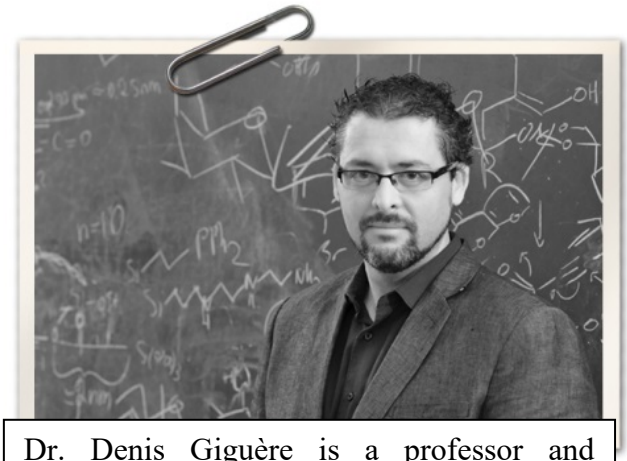
1. Should the authorities require an individual to be vaccinated for the benefit of public health?

2. Although the vast majority of faiths worldwide accept or promote the use of vaccines, some parents still seek to opt out of pre-kindergarten vaccinations for their children on religious grounds. Do you think parents should have this right?

3. In your own words, why is it important for a vaccine to have a precise pH and the right mix of ingredients?

4. How can the field of glycomics help advance vaccine research?

Context



Dr. Denis Giguère is a professor and researcher in the chemistry department at l'Université Laval.

Currently, a team of researchers at L'Université Laval is working on the development of a vaccine based on a sugar molecule (glucosamine hydrochloride) that could be used to treat certain fungal infections. Indeed, just like viruses or bacteria, some fungi cause serious infections in humans. Currently, only post-infection treatment is available on the market to help infected people treat their symptoms. If successful, the team of Dr. Denis Giguère, an organic chemistry researcher, could be among the first to create a vaccine capable of preventing fungal infections. To learn more about fungal infections and their current treatments, you can watch the following video:

https://www.youtube.com/watch?v=_de4qZpwP8Q

Your Role

If effective, the molecule being developed in Dr. Giguère's lab has the potential to become the basis of a commercial vaccine. Your task is to determine what other components need to be included in this future antifungal vaccine.

A vaccine comprises several components other than the *antigen*, the foreign molecule that triggers a response from the immune system (which may include the production of *antibodies*). You will have to select a *stabilizer* and an *adjuvant* to incorporate into your future vaccine. Both of these additives will need to meet strict criteria to ensure that they are safe for human use.

First, check your prior knowledge of vaccines and how they work by answering the questions on the next page.

Activity 1: Introductory Questions

1- What is a vaccine?
A vaccine is a mixture of several substances that, when administered to a patient, will trigger an immune response and allow the patient to develop antibodies against the disease without causing illness. Thus, the person is protected against future infection thanks to the immune response during the vaccination.

2- How are vaccines administered?
Most vaccines are given as *subcutaneous* (under the skin) injections. Other ways to administer vaccines include nasal mists (e.g. influenza) and oral drops (e.g. polio).

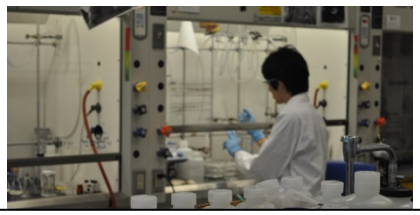
3- Vaccines and pharmaceutical drugs are two methods used to ensure the health of a population. However, their objectives and mechanisms of action differ. Summarize the main differences between pharmaceutical drugs and vaccines by completing the following table.

Characteristics of Drugs and Vaccines

	Drugs	Vaccine
Main role	Cure or treat an established infection or disease	Prevent the development of an infection or disease
Time of administration	After the infection or disease is established	Before the infection or disease is contracted
Period of effectiveness	As long as it is administered	Several years, depending on the type
Distribution	Small scale and individualized	Large scale and in specific cases (travellers)

4- In your own words, what do doctors and scientists have to say about the ability of vaccines to control against epidemics and diseases in the general population?
Vaccination is the most effective way of fighting epidemics in a population, as it allows a very large number of people to be protected against an infection. The risk of a disease spreading uncontrollably is thereby greatly reduced. For this reason, the vast majority of scientists and medical professionals believe vaccination to be a very effective means of preventing disease.

You are now ready to help the team at Laval to complete their antifungal vaccine with a stabilizer and adjuvant!



One of Dr. Giguère's students working on sugar molecules: the basis of the antifungal vaccine.

Activity 2: Choosing a stabilizer for the antifungal vaccine

In order for a vaccine to be widely used, it must be storable for a sufficient period of time. Therefore, a stabilizer is added to all vaccines to extend the shelf life. Stabilizers should not influence the action of the vaccine and therefore, must have the right level of acidity.

Thus, you will have to determine which substance will be the most appropriate stabilizer for your vaccine against fungal infections. You will have two options, and your choice should meet the requirements listed below.

Stabilizer required properties:

- *It must allow the vaccine to be stored for up to one year.*
- *It must react with cobalt dichloride paper.*
- *It must be between 10 and 100 times more alkaline than water.*

In order to make the most informed choice possible, first answer these questions.

1- The stabilizer in a vaccine increases its shelf life. Why do you think this is important? Give at least two reasons.
First, vaccines must be storable for long periods of time because large-scale vaccination campaigns can take weeks or months. As well, the majority of vaccines are manufactured in Western countries, and it may take a long time before they can be delivered, distributed, and administered to a large population in a developing country. The stabilizer helps ensure that doses of the vaccine remain effective for as long as possible.

2- What does a reaction with cobalt dichloride indicate?
The presence of a certain amount of water.

3- How is cobalt dichloride paper used to observe this property?
The water reacts chemically with the cobalt complex, changing the color of the paper from blue to red.

4- What is a synonym for the word “alkaline?” Basic

5- What pH range must your stabilizer be within?
It must be between pH 8 and 9 (10 to 100 times more basic than water).

6- pH indicators are regularly used to measure the acidity or basicity of a substance. However, it is sometimes possible to obtain greater accuracy by mixing indicators. Complete the following table to determine the colors obtained mixtures of indicators.

Indicator 1	Indicator 2	Mixture Color
Blue	Transparent	Blue
Blue	Red	Violet
Red	Yellow	Orange
Blue	Green	Blue-green
Yellow	Blue	Green

7- Some characteristics of the first stabilizer are given below. After considering the required criteria, would you recommend Abax-3 for use in your vaccine? Why or why not?

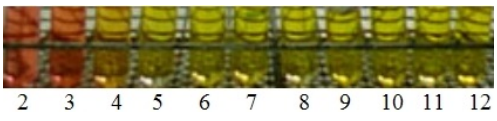
Characteristics of Stabilizer Abax-3	
Color in presence of phenol red	**Yellow**
Color in presence of methyl orange	**Yellow**
Color in presence of phenolphthalein	**Transparent**
Storage life	**9 000 hours**
Solvent	**Water**

Indicator Color Ranges (for reference)

Phenolphthalein

Phenol Red

Methyl Orange



a- Based on the color of **phenolphthalein** in Abax-3 solution, what pH might this stabilizer possess? Between pH 1 and pH 8

b- Based on the color of **phenol red** in Abax-3 solution, what pH might this stabilizer possess? Between pH 1 and pH 5

c- Based on the color of **methyl orange** in Abax-3 solution, what pH might this stabilizer possess? Between pH 5 to pH 12

d- Therefore, what is the pH of the Abax-3 stabilizer? pH 5

e- Could this stabilizer be used in your vaccine? Why or why not? No, because the stabilizer must have a pH between 8 and 9; the pH of Abax-3 is 5, which is below the given threshold.

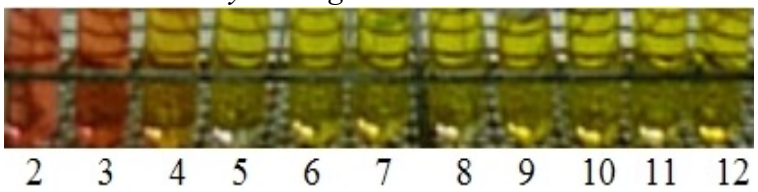
8- Some notes about stabilizer **Baxat-4** gathered by your team of researchers are presented below.

Indicators	**Color**
Bromothymol blue + methyl orange	Green
Bromocresol purple + thymol blue	Green
Storage life	**9600 hours**

Indicator Color Ranges (for reference)

Bromocresol purple

Methyl Orange



Thymol Blue

Bromothymol Blue

a- According to the result of the **bromothymol blue + methyl orange test**, what pH range must Baxat-4 be within? Between pH 8 and pH 12

b- According to the result of the **bromocresol purple + thymol blue test**, what pH range must Baxat-4 be within? Between pH 7 and pH 8

c- Therefore, what is the pH of the Baxat-4 stabliizer? pH 8

d- Could this stabilizer be used in your vaccine? Why or why not? Yes, Baxat-4 meets the criteria and is sufficiently basic to be used in your vaccine. With a pH of 8, it is 10 times more basic than water.

Activity 3: Choosing an adjuvant for the antifungal vaccine

In most vaccines, an adjuvant is added in order to improve the immune response and increase the number of antibodies. As a result, a vaccinated person will be able to fight off an infection more easily.

Like the stabilizer, the adjuvant must not interfere in the vaccine's mechanism of action, and it must also be present in a sufficient concentration. In this activity, you will compare two adjuvants used in the biopharmaceutical industry and then use a set of criteria to choose the best one for your antifungal vaccine.

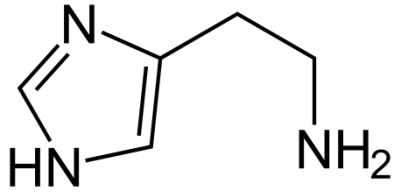
Did you know?
Aluminum salts are the most commonly used adjuvants in the pharmaceutical industry

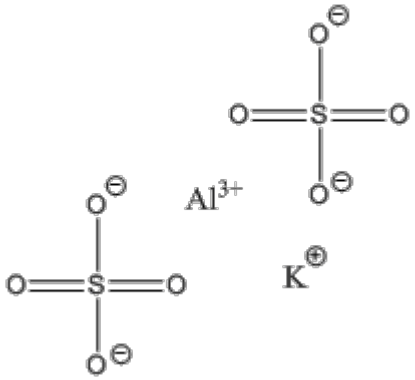
Adjuvant required properties:

- *It must have a maximum concentration of 0.005 mol/L.*
- *It must have a minimum concentration of 0.0002 mol/L.*

In order to make the most informed choice possible, first answer these questions.

1- Two potential adjuvants are presented in the following table. Fill in the missing information.

Adjuvant Name	Molecular Formula	Molecule Structure
Histamine	$C_5N_3H_9$	

Aluminum potassium sulfate	$KAl(SO_4)_2$	 * It should be noted that this compound is ionic and will form a crystalline structure.

2- Determine the molar mass of these two adjuvants. Show your calculations in the space below.

Adjuvant	Molar mass
Histamine	C : 5 x 12.01 g/mol = 60.05 g N : 3 x 14 g/mol = 42 g H : 9 X 1.01 g/mol = 9.09 g M $_{C5N3H9}$ = 111.14 g/mol
Aluminum potassium sulfate	K : 1 x 39.09 g/mol = 39.09 g/mol Al : 1 x 26.98 g/mol = 26.98 g/mol S : 2 x 32.07 g/mol = 64.14 g/mol O : 8 x 16.01 g/mol =128.08 g/mol M $_{KAl(SO4)2}$ = 258.29 g/mol

3- Based on the masses given, calculate the concentration of each adjuvant in 0.05 mL of vaccine solution. Show your work.

Adjuvant	Mass (mg)	Adjuvant Concentration (mol/L)
Histamine	0.017 mg	n=m/M n=? m= 0.017 mg = 0.000017g M= 111.4 g/mol n=0.000017g/111.4g/mol =1.52 x 10^{-7} mol C=n/V n= 1.52 x 10^{-7} mol V=0.05 ml = 0.00005 L C= 1.52 x 10^{-7} mol/0.00005L = C= 0,003 mol/L

Aluminum potassium sulfate	0.08 mg	n=m/M n=? m= 0.08 mg = 0.00008g M= 258.29 g/mol n=0.00008g/258.29 g/mol =3.1 x 10^{-7} mol C=n/V n= 3.1 x 10^{-7} mol V=0.05 ml = 0.00005 L C= 3.1 x 10^{-7} mol/0.00005L = C= 0,0061 mol/L

4- Which of these two adjuvants is available in the proper concentration for your antifungal vaccine? The histamine adjuvant can be used, as its concentration (0.003 mol/L) is within the desired concentration range.

5- Although these two adjuvants have proved their worth in the past, current studies are trying to develop other molecules that may be even more effective and less costly to produce. Although the World Health Organization has recently demonstrated that aluminum salts do not pose any serious health risks, some people are still afraid to use them.

In 2015, the Giguère group attempted to develop a type of adjuvant based upon sugar molecules, which would be very compatible with the human immune system. Moreover, this type of adjuvant would be very stable in the human body, which possesses a great tolerance to these types of molecules since they are already found in a number of tissues.

Using the Internet, determine what motivates researchers to find alternatives to aluminum-based adjuvants. You may want to start with this article from the U.S. FDA or this article from vaccines.gov.

(Answers will vary) Aluminum is a metal that does not have any known biological role. Thus, unlike iron, zinc or potassium, it is not needed for the proper functioning of the body. In rare cases, some people experience side effects after receiving a vaccination, including muscle pain and acute fatigue. Recent studies have examined these cases, and they hypothesize that these individuals may have a genetic predisposition that makes them more sensitive to aluminum adjuvants. Although the World Health Organization and other public health authorities around the world claim aluminum adjuvants are safe, some doubt remains in the population because of these isolated cases.

The field of glycomics holds promise for improving the effectiveness of current adjuvants while avoiding the controversy surrounding the use of aluminum salts. Compounds based on sugars may be equally effective and possibly more compatible with the human body, and could provide an effective alternative adjuvant for people who may be sensitive to a vaccine containing aluminum.