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Hope for Mass Vaccine Production Spreads Across the Province

December 10th, 2020

COVID-19 Global Pandemic

COVID-19 is a disease caused by the human pathogen SARS-CoV-2. The disease is associated with fever, severe respiratory illness, and pneumonia.[1] Recent efforts by Pfizer and BioNTech have met success as Health Canada has approved administration of this vaccine under an interim order for emergency use. The mRNA vaccine elicits immunity by providing the instructions for ribosomes to produce a segment of the COVID spike protein.[2] RNA is composed of repeating monomer units that contain a ribose sugar, a nitrogenous base, and a phosphate group. The COVID spike protein is responsible for allowing the virus to attach itself to human cells, after which it can infect those cells and begin self-replication. The spike protein segment produced from the mRNA vaccine causes the immune system to produce antibodies to bind and block those spike proteins.

The very low temperature (-70 °C) required for storage of the Pfizer-BioNTech vaccine poses logistical complications. Improper storage conditions are believed to accelerate vaccine degradation due to the hydrolysis of the phosphodiester bonds in RNA.

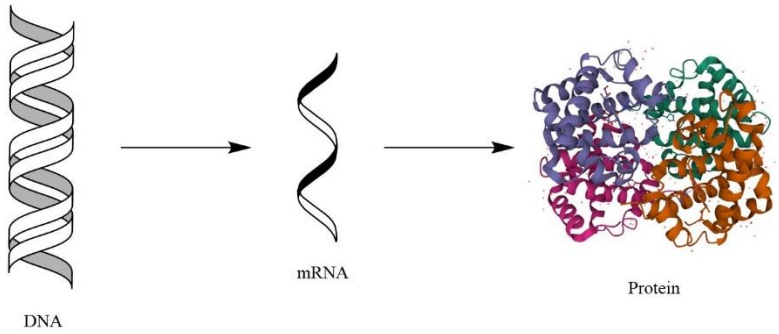


Figure 1. *The central process of protein production. mRNA is produced from DNA via transcription, followed by translation which uses the direction from mRNA to synthesize proteins.*

HELP WANTED!

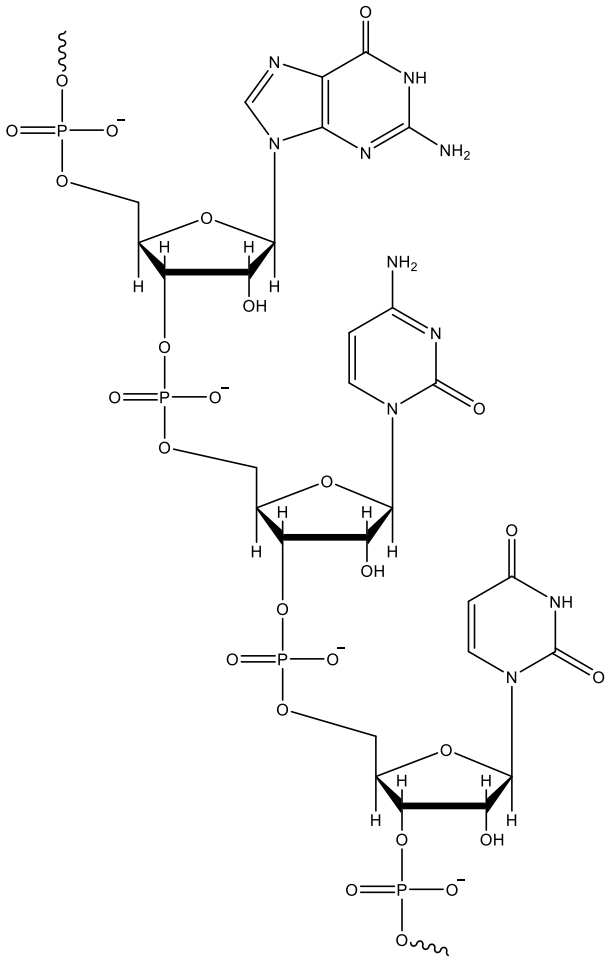
The need to vaccinate the population against COVID-19 has become apparent as the global pandemic continues to intensify. Health Canada is hiring for vaccine administration and distribution logistics positions to assist in a mass-immunization program. To ensure that qualified individuals are selected, an application vetting program has been initiated and interested applicants should visit Health Canada's website for more information.

HEALTH CANADA

Thank you for your interest in a vaccine distribution logistics position at Health Canada. Found below are a set of comprehension problems relating to the chemistry behind the COVID-19 immunization program. By solving these problems, you will demonstrate that you possess a fundamental understanding of chemistry that we deem necessary for success in this position. Please email your solutions, along with your resume to canada@health.ca. Only short-listed candidates will be contacted for an interview.

(1.a.) The primary mechanism of mRNA degradation is via hydrolysis. Describe the process of hydrolysis in general terms, including a balanced equation for a hydrolysis reaction.

(b.) Why would hydrolysis affect mRNA? Which part of the mRNA would be affected? (*Hint:* Circle the effected component on the truncated mRNA structure to the right).



(2.a.) The hydrolysis of mRNA is an exothermic reaction. Draw and label a free-energy diagram for the hydrolysis of a phosphodiester bond.

(b.) Would the activation energy of the reaction change if it were to take place at a higher temperature?

(3.a.) Compare what would happen to the rate of a hydrolysis reaction if the temperature was:

i.) Increased

ii.) Decreased

Elaborate on how temperature influences the rate of a chemical reaction.

(b.) Describe factors other than temperature that could influence the rate of reaction.

(4.) Why should the Pfizer-BioNTech vaccines be stored at low temperatures?

HEALTH CANADA

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HEALTH CANADA

Dear John Doe,

As the spread of COVID-19 accelerates dramatically, there is an increased urgency to vaccinate all Canadians in order to promote herd immunity. There has been a logistics error at a government storage facility and 10,000 doses of the Pfizer-BioNTech mRNA vaccine were accidentally stored in a standard 4 °C refrigerator rather than the -70 °C ultra-low temperature freezer. To reduce the reoccurrence of similar storage errors, we would like to determine if the vaccine can be safely administered when it is stored at a temperature of -35 °C, which can be achieved by a standard commercial freezer. Laboratory technicians have calculated the first order reaction rate constants at different storage temperatures for the hydrolysis of phosphodiester bonds in mRNA (Table 1).

Table 1: First order rate constants for the hydrolysis of a phosphodiester bond. *Disclaimer:* The data is hypothetical and does not accurately reflect the degradation of the Pfizer and BioNTech vaccine.

Rate Constant (k) (s^{-1})	Temperature (K)
$\mathbf{9.61 \times 10^{-5}}$	298
$\mathbf{4.11 \times 10^{-5}}$	277
$\mathbf{8.29 \times 10^{-6}}$	263
$\mathbf{6.81 \times 10^{-7}}$	223
$\mathbf{4.58 \times 10^{-8}}$	203

We anticipate that using standard cold-storage equipment will reduce the intricacy of vaccine distribution. For a vaccine to be safely stored and retain its efficacy, its half-life cannot be less than 2 months. Using the data provided in Table 1, construct an Arrhenius plot using spreadsheet software to determine the first order rate constant (k) at -35 °C. The calculated value of k can then be used to predict the vaccine half-life ($t_{½}$) at the given temperature using the following relation.

$$t_{½} = \frac{ln(2)}{k}$$

Using your predicted half-life, summarize your conclusions on the potential for -35 °C storage of vaccines, appropriate for a public announcement (be sure to define half-life in your statement).

Dr. Amtelias

Health Canada

References

(1) Yang, D.; Leibowitz, J. L. The Structure and Functions of Coronavirus Genomic 3′ and 5′ Ends. *Virus Res*. **2015**, *206*, 120–133. https://doi.org/10.1016/j.virusres.2015.02.025.

(2) mRNA Science and Function: What Does mRNA Do? – Moderna. https://www.modernatx.com/mrna-technology/science-and-fundamentals-mrna-technology (accessed Jan 8, 2021).