Agriscience – Cell Respiration & DNP *by C. Kohn, Waterford WI*

Name: Hour Date:

Date Assignment is due: Why late? Score: + ✓ -  
 Day of Week Date If your project was late, describe why

## **Directions – read and follow carefully!**

Use the reading below to answer the accompanying questions. You can and should work in groups to complete this assignment but you are responsible for completing your own sheet.

ARTICLE (*adapted* *from Wikipedia*): 2,4-Dinitrophenol (DNP), C6H4N2O5, is an inhibitor of efficient energy (ATP) production in cells with mitochondria. It uncouples oxidative phosphorylation by carrying hydrogen protons across the mitochondrial membrane, leading to a rapid consumption of energy without generation of ATP.

Pharmacological action In living cells, DNP acts as an agent that can shuttle protons (hydrogen) across biological membranes. It defeats the hydrogen-proton gradient across mitochondria, collapsing the proton motive force that the cell uses to produce most of its ATP chemical energy. Instead of producing ATP, the energy of the proton gradient is lost as heat.

Dieting aid DNP was used extensively in diet pills from 1933 to 1938 after Cutting and Tainter at Stanford University made their first report on the drug's ability to greatly increase metabolic rate. After only its first year on the market Tainter estimated that probably at least 100,000 persons had been treated with DNP in the United States, in addition to many others abroad.

DNP acts as a *protonophore*, allowing protons to leak across the inner mitochondrial membrane and thus bypass ATP synthase. This makes ATP energy production less efficient. In effect, part of the energy that is normally produced from cellular respiration is wasted as heat.

The inefficiency is proportional to the dose of DNP that is taken. As the dose increases and energy production is made more inefficient, metabolic rate increases (and more fat is burned) in order to compensate for the inefficiency and meet energy demands.

DNP is probably the best known agent for uncoupling oxidative phosphorylation. The production or "phosphorylation" of ATP by ATP synthase gets disconnected or "uncoupled" from oxidation. Interestingly, the factor that limits ever-increasing doses of DNP is not a lack of ATP energy production, but rather an excessive rise in body temperature due to the heat produced during uncoupling. Accordingly, DNP overdose will cause fatal hyperthermia (bodily overheating). In light of this, it's advised that the dose be slowly titrated according to personal tolerance, which varies greatly and makes this drug dangerous when used in an unregulated fashion.

1. Explain in your own words how DNP works.   
   *NOTE: Use ALL of the following terms: mitochondria, hydrogen, ATP Synthase, ATP, inner membrane, intermembrane space*.
2. Explain whether or not you think this would work to help people lose weight AND how it would help.
3. What negative side effects could you see occurring as a result of this drug? Think of a side effect and explain how it could occur *and* what damage it could do.
4. As a group, design a drug that would do the opposite of DNP for cattle. In other words, use what you know about how DNP works to design a drug for cattle to help them gain weight faster. Describe how that drug would work in regards to ATP production in the space below:

1. On a scale of 1 (no knowledge) to 5 (expert in this), how would you rank yourself?
2. What is something you still do not fully understand? -OR- Summarize what you think is the most confusing part of this unit.