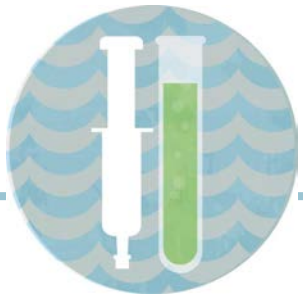
The Dose Makes the Poison



Activity Time: 50 Minutes.

Lesson Plan Summary:

In this lesson, students will determine the appropriate amount of a feed additive to mix in feed to achieve the correct dosage. This activity will provide students with the understanding that concentration increases as moisture decreases and dry matter increases. This lesson complements the study of concentration. Before delivering this lesson, students need to have a basic understanding of the concept of concentration within the context of general chemistry.

STUDENT UNDERSTANDINGS

Big Idea & Enduring Understanding:

- **Concentration:** Concentration is affected by the amounts of solute and solvent.

Essential Question:

- How much additive must be given to ensure that each animal has the correct mg/lb BW concentration?

Learning Objectives:

Students will know…

- All substances can be poisonous if the dose is large enough.
- Dose calculations are important for preventing overdoses and for ensuring that the effective concentration of an additive is achieved when preparing animal feed.

Students will be able to…

- Calculate mg/lb BW concentration.
- Determine the amount of a solute needed to achieve a certain concentration.
- Calculate appropriate dosages given an animal's weight.

Vocabulary:

- Antibiotic
- Aureomycin 4G Crumbles
- Body Weight (BW)
- Chlortetracycline
- Concentration
- Dose
- *Pasteurella multocida* (bacteria, livestock pathogen)
- Poison
- Solute
- Solvent
- Toxicity

Standards Alignment:

This lesson addresses the following Washington State Essential Academic Learning Requirements (EALRs) and/or Grade Level Expectations (GLEs) for grades 9–12:

- **Science EALR (9-12 APPC):** Students know that choosing the best *solution* involves comparing alternatives with respect to *criteria* and *constraints*, then building and testing a *model* or other representation of the final design.
- **Science EALR (9-12 APPD):** Students know that the ability to solve problems is greatly enhanced by use of mathematics and information technologies.

This lesson addresses the following Washington State Career and Technical Education (CTE) model frameworks for Agriculture, Food, and Natural Resources (AFNR):

- **AS.04.02:** Prescribe and administer animal feed additives and growth promotants in animal production.

Common Student Preconceptions:

- The same amounts of medications can be given to any animal.
- Medications have the same concentration of active ingredient.
- Different medications do not have the same active ingredients.

TEACHER PREPARATION

Materials:

Item	Quantity
Classroom computer with projector and internet access	1 per class
1000 mL beaker	4 per class
400 mL beaker	1 per class
100 mL beaker	1 per class
Food coloring	1 bottle per class
Dose Makes the Poison Quiz Student Handout	1 per student
Dose Makes the Poison Quiz Teacher Answer Key	1 per class

Preparation:

- Fill each beaker with water to measured capacity (1000 mL, 400 mL, and 100 mL).
- Review the procedural steps for the class demonstration, as explained in the *Hook* section.
- Photocopy the *Student Handout* including *the* nutritional supplement label.

PROCEDURE

Preconceptions:

1. Write the Essential Question on the board: *How much additive must be given to ensure that each animal has the correct mg/lb BW concentration*?
2. Write the following vocabulary terms on the board:
    - Concentration
    - Solute
    - Solvent
    - Dose
    - Poison
    - Toxicity
3. Ask students for their definitions of these terms. Provide just-in-time instruction as needed to help student develop correct definitions for the terms.
4. Ask students what they think these terms have to do with prescribing and administering animal feed additives in animal production.

Hook:

Demonstration: Same Dose, Different Body Weight

5. Set out three different sized beakers (1000 mL, 400 mL, and 100 mL) on the lab bench or table, filled to measured capacity with water. If possible, place a piece of white paper behind the beakers to make a backdrop.

6. Explain to students that each beaker represents the body of a differently sized cow: a calf, a young heifer, and a grown bull.

7. Explain that the food coloring represents a chemical that is ingested by each cow or injected into the body, such as a feed additive or a medication. Place five drops of food coloring into each beaker as students observe.

8. Provide time for students to conduct a Think-Pair-Share, answering the following questions:

   - What differences did the students observe among the three beakers?
   - What response would each cow have to the same dose of the chemical?
   - In this scenario, what is the solute and what is the solvent?

Demonstration: Different Dose, Same Body Weight

9. Next, place three 1000 mL beakers on the lab bench, filled to measured capacity with water. Explain that the beakers represent three cows, all of which are about the same body size.

10. Place five drops of food coloring in the first beaker, ten drops in the second beaker, and fifteen drops in the third, as students observe.

11. Provide time for students to conduct a Think-Pair-Share, answering the following questions:

    - What differences did the students observe among the three beakers?
    - What response would each cow have to the different doses of the chemical?

Activity Procedure:

12. Write the following quote on the board:

    All substances are poison; there is none which is not a poison. The right dose differentiates a poison from a remedy.
    Paracelsus, 1493-1541

13. Explain that often the quote is simplified to: "The dose makes the poison."

14. Explain that the Food and Drug Administration, a federal agency, publishes a set of regulations known as Title 21—Food and Drugs. Within this set of regulations, Subchapter E focuses on regulations related to Animal Drugs, Feeds, and Related Products. Part 558 in particular includes regulations for New Animal Drugs for Use in Animal Feeds. The term "New Animal Drug" has been used since June 25, 1938. Any drug designated as a "New Animal Drug" in 1938 is still a "New Animal Drug". A new animal drug is defined, in part, as "any drug intended for use in animals other than man, including any drug intended for use in animal feed but not including the animal feed..." (21 U.S.C. § 321)

15. Using the classroom computer and projector, show students the Title 21 CFR 558 website. Scroll down through the list of animal drugs approved for use as feed additives. Explore the website as you have time, specifically focusing on 558.140 Chlortetracycline, an antibiotic.

    Title 21 CFR 558: Regulations for New Drugs For Use in Animal Feeds
    National Archives and Records Administration
    http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&tpl=/ecfrbrowse/Title21/21cfr558_main_02.tpl

16. Explain that in today's learning task, students will be calculating dosage concentrations. In the learning task, they will be focusing on calculating the correct dose of the antibiotic Chlortetracycline using a medicated feed label. These math skills are important in animal care, whether students need to calculate the dose of a drug (like Chlortetracycline) or the correct concentration of any other feed additive (like the essential mineral selenium). It is important for students to understand how to calculate dosage concentrations and do unit conversions, since the dosage guidelines on feed standards, nutritional supplement labels, and medication prescriptions can be stated in different terms.

17. Tell students that for the purposes of today's lesson, the measurement of dose they will be using is mg/lb (pound) of body weight. Let them know alternative ways that we express dose, including:

    - mg/lb of body weight (mg/lb BW) is preferred for today's lesson
    - mg/100 lb body weight (mg/100 lb BW)
    - mg/kg of body weight (mg/kg BW)

18. Pass out copies of the *Dose Makes the Poison Quiz* Handout and explain the learning task.

19. Ask students to work in pairs or small groups to complete the handout.

Wrap-up:

20. After students have completed the handout, ask student volunteers to share their results with the class.

21. Have one or two students share their graphs with the class using a document camera.

Assessment Opportunities:

- Students will share the results of their calculations with the class.
- Using the data, the students will complete the handout and create a dosing graph.

Student Metacognition:

- Students are asked to examine their preconceptions about the vocabulary terms.
- Students will explain their results and receive peer feedback.
- As an Exit Ticket, ask students to document their definitions for the vocabulary terms in their notebooks.

Scoring:

- The *Dose Makes the Poison Quiz* Handout can be scored by checking the accuracy of students' calculations using the *Teacher Answer Key*.

Extension Activities:

- Ask students to calculate the doses from the *Dose Makes the Poison Quiz* Handout in mg/100 lb BW.
- Ask students to calculate the doses from the *Dose Makes the Poison Quiz* Handout in mg/kg BW.

Adaptations:

- Instead of conducting a class demonstration, ask students to complete the dose/response activity themselves at each lab station. Alternatively, a virtual demonstration can be accessed at the **A Small Dose of Toxicology** website, as listed in the *Resources* section. Click on the "Dose" and "Size" buttons to run the demonstration.

- Rather than calculate the pounds of dry matter, alter the *Dose Makes the Poison Quiz* Handout to provide those calculations. Provide the students with completed handouts and discuss as a group that if you feed a constant amount of feed additive, then as feed intake increases the concentration of the feed additive will decease in the total diet consumed.

- Challenge students to portray the data using an Excel spreadsheet or a graphing calculator.

TEACHER BACKGROUND & RESOURCES

Career Links:

- Animal drug manufacturer
- Animal feed manufacturer
- Animal nutritionist
- Animal physiologist
- Animal scientist
- Biochemist
- Cattle rancher
- FDA regulation enforcement officer
- Feed ration developer
- State chemist
- Veterinarian
- Veterinary toxicologist

Background Information:

Background information on the Title 21 CFR 558 regulations can be found at the website of the National Archives and Records Administration, as listed in the *Resources* section on the following page.

Resources:

A Small Dose of Toxicology: Dose/Response Demonstration
http://www.toxipedia.org/display/dose/Demonstration+of+the+Principles+of+Dose-Response

Title 21 CFR 558: Regulations for New Drugs For Use in Animal Feeds
National Archives and Records Administration
http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&tpl=/ecfrbrowse/Title21/21cfr558_main_02.tpl

Veterinary Topics: A Necessary Poison (Selenium)
Thoroughbred Times
http://www.thoroughbredtimes.com/horse-health/2003/may/03/veterinary-topics-a-necessary-poison.aspx

Case Study: Elemental Toxicity in Animals
UC Davis, ChemWiki
http://chemwiki.ucdavis.edu/Inorganic_Chemistry/Case_Studies/Case_Study%3a_Elemental_Toxicity_in_Animals

Credit:

Lesson plan written by Nona Clifton of the Washington Global Health Alliance.

Content expertise and Aureomycin 4G Crumbles label provided by Neil Lanning of the WSDA.

Student Handout photograph courtesy of Wikimedia Commons.

Name:_____Date:_____Period:_____

Dose Makes the Poison Quiz

Student Handout

Cows eating silage. **Credit**: Wikimedia Commons.

You have agreed to help out on your aunt's cattle ranch, the DiamondK, while she is out of town for a few weeks. Unfortunately, some of the cattle are sick. Aunt Kay left a note telling you that she suspects a pen of 300 pound calves (25 of them) are coming down with bacterial pneumonia associated with *Pasteurella multocida* and she wants you to feed Aureomycin 4G Crumbles for the maximum time allowed. On her note, she explained that the Aureomycin 4 G Crumbles contain chlortetracycline, an antibiotic. She also said, "Like all antibiotics, if you do not give them enough, it will not be effective, they will not get better, and potentially develop antibiotic resistance. If you feed too much, there could be side effects and make things worse – it could even be a poison!"

She is counting on you to find the feed in the barn read the label, do the math, and figure out how much feed and Aureomycin 4G to give to her cattle.

1. To help care for your Aunt's cattle, look at the Aureomycin 4G Crumbles label on Page 9 and answer the following questions.

   a. What antibiotic is being used?

   b. What concentration of the antibiotic is listed on the label?

   c. Express the concentration listed on the label in grams per ton (there are 2,000 pounds per ton). Show the formula you use to obtain your answer.

   d. Express the concentration listed on the label in milligrams per pound. Show the formula you use to obtain your answer.

   e. Express the concentration listed on the label in milligram per kilogram. Show the formula you use to obtain your answer.

AUREOMYCIN 4G CRUMBLES

(Type C Feed)

MEDICATED

Indication depend on species and level provided. See reverse side for specific feeding directions of this product.

ACTIVE INGREDIENT

Chlortetracycline .....4 g/lb
(8,000 g/ton)

GUARENTEED ANALYSIS

Crude Protein, not less than 11.00%
Crude fat, not less than.....1.00%
Crude fiber, not more than 30.00%
Crude fat, not less than 7.50%
Crude fiber, not more than 8.50%

INGREDIENTS

Processed Grain By-Products, Calcium Carbonate, Mineral Oil and Dried Lignin Sulfonate.

USE DIRECTIONS
See panel to right for specific directions

Manufactured by:
Super Feeds
1200 Parkway
Anytown, WA 98000

Net Weight 50 LB. (22.68 kg)

9AURECR4
LOT# 554711

USE DIRECTIONS

CATTLE

WARNING (for all feeding levels in cattle): A withdrawal period has not been established in pre- ruminating calves. Do not use in calves to be processed for veal.

Level	Claim	4G Crumbles
10 mg/lb body weight daily	For the treatment of bacterial enteritis caused by *E. coli* and bacterial pneumonia caused by *Pasteurella multocida* organisms susceptible to chlortetracycline in calves, beef and nonlactating dairy cattle. Feed for not more than 5 days.	One pound will medicate 400 lbs of body weight daily.
350 mg/head daily	For the control of active infection of anaplasmosis caused by *Anaplasma marginale* susceptible to chlortetracycline in beef cattle over 700 pounds.	One pound per 11.4 head daily.
0.5 mg/lb body weight daily	For the control of active infection on anaplasmosis caused by *Anaplasma marginale* susceptible to chlortetracycline in beef cattle over 700 pounds.	One pound will medicate 8,000 lbs of body weight daily.
350 mg/head daily	For the control of bacterial pneumonia associated with shipping fever complex caused by *Pasteurella spp.* susceptible to chlortetracycline in beef cattle.	One pound per 11.4 head daily.
70 mg/head daily	For an increased rate of weight gain, improved feed efficiency, and reduction of liver condemnations due to liver abscesses in growing	One pound will medicate 57 cattle daily.
25-70 mg/head daily	For an increased rate of weight gain and improved feed efficiency in calves between 250 and 400 pounds.	One pound will medicate 57-160 calves daily.
0.1 mg/lb body weight daily	For an increased rate of weight gain and improved feed efficiency in calves under 250 pounds.	One pound will medicate 40,000 lbs of body weight daily.

SHEEP

Level	Claim	4G Crumbles
80 mg/head daily	For reducing the incidence of (vibrionic) abortion caused by *Campylobacter fetus* infection susceptible to chlortetracycline in breeding sheep.	One pound will medicate 50 head daily.
20-50 grams	Increased rate of weight gain and improved feed efficiency in grow-	Five (5) to 12.5 pounds per

SWINE

Level	Claim	4G Crumbles
10-50 grams per ton	Increased rate of weight gain and improved feed efficiency in growing swine.	2.5 to 12.5 pounds per ton of feed.
50-100 grams per ton	Reducing the incidence of cervical lymphadenitis (jowl abscesses) caused by group E streptococci susceptible to chlortetracycline in swine.	12.5 to 25 pounds per ton of feed.
400 grams per ton	Control of leptospirosis (reducing the incidence of abortion and shedding of leptospirae) caused by *Leptospira pomona* suseptible to chlortetracycline in breeding swine. Feed Continuously for not more than 14 days.	100 pounds per ton of feed.
10 mg/lb body weight daily	For the treatment of bacterial enteritis caused by *E. coli* and *Salmonella choleraesuis* and bacterial pneumonia caused by *P. multocida* organisms susceptible to chlortetracycline in swine. Feed continuously for not more than14 days.	One pound will medicate 400 lbs of body weight daily.

Figure 1: Aureomycin 4G Crumbles feed label.

2. What is the amount of drug required to treat bacterial pneumonia associated with *Pasteurella multocida* in cattle as stated on the label?

3. How many milligrams of chlortetracycline are required to treat one 300 pound calf? Show the formula you use to obtain your answer.

4. How many pounds of this medicated feed will it take to properly treat all 25 calves for one day? Show the formula you use to obtain your answer.

5. Each cow is a unique individual, with different eating habits and dietary needs. Most animals eat between 2-3% of their body weight in dry matter per day and really high producing animals might eat as much as 4% of their body weight. Moreover, all animals will eat more total pounds of feed when the diet gets wetter (saturated with heavy water).

   Calculate the total pounds of feed that the calves will eat as the moisture level increases in the feed and fill in ***Table 1***.

Table 1: Diamond K Feed Calculation Tables — Feed Intake

Body weight lb	Feed Intake in DM as % of BW	Pounds of Feed Expected to be Consumed at Different Dry Matters				
		100% Dry Matter Basis	90% Dry Matter Basis	80% Dry Matter Basis	70% Dry Matter Basis	60% Dry Matter Basis
300	2	6	6.67			
	2.5					
	3					

mg = milligram lb = pound
DM = Dry Matter BW = body weight

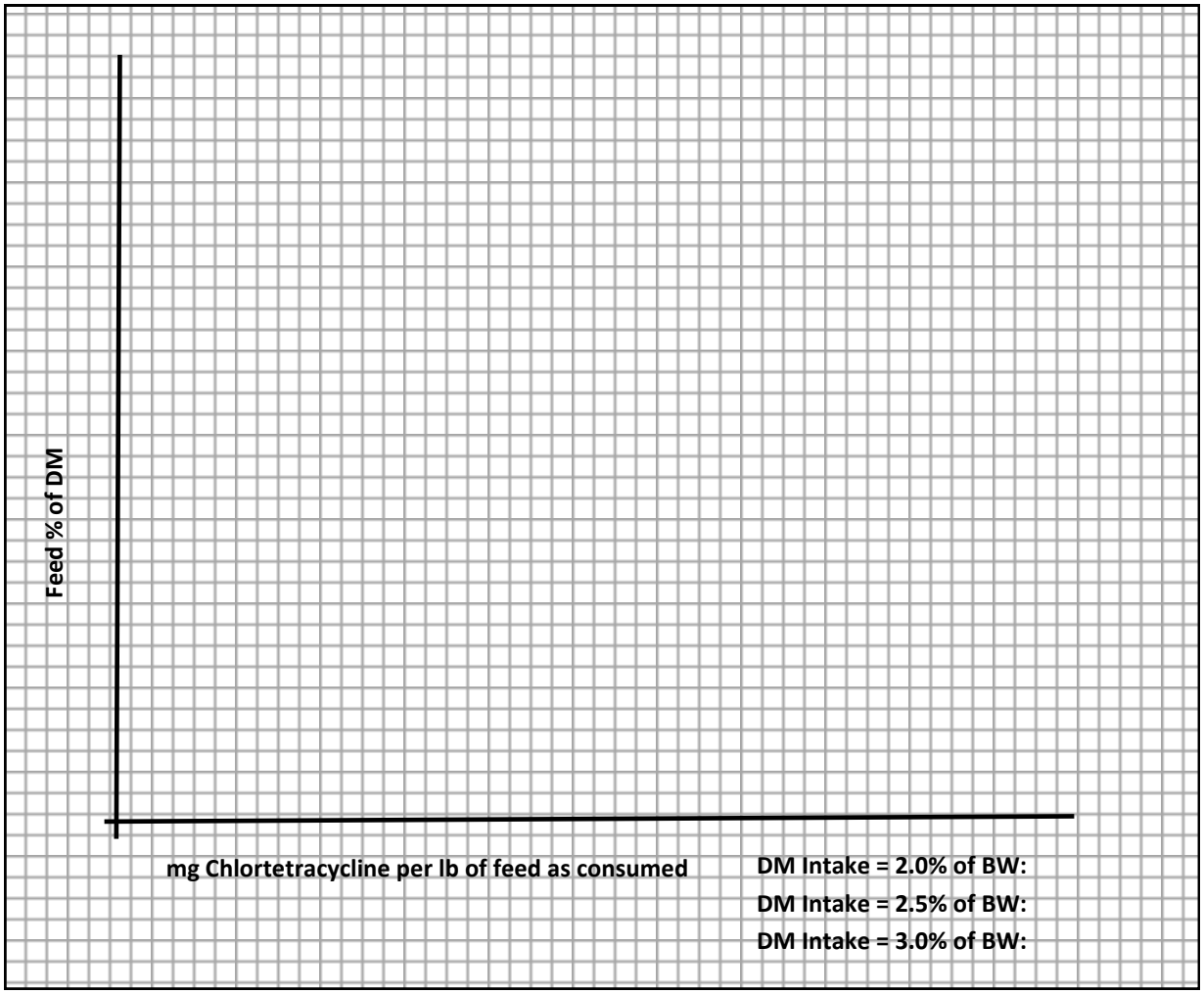
Next, determine the concentration in mg/lb of chlortetracycline in the feed and fill in ***Table 2*** using information determined in ***Table 1*** as well as the mass (in mg) of chlortetracycline required to treat a 300 lb calf (an amount that you determined previously for *Question 3*).

Table 2: Diamond K Feed Calculation Tables — Drug Concentration

Body weight lb	Feed Intake in DM as % of BW	Chlortetracycline Drug Concentration in Total Diet (mg / lb of feed)				
		100% Dry Matter Basis	90% Dry Matter Basis	80% Dry Matter Basis	70% Dry Matter Basis	60% Dry Matter Basis
300	2.0	500	450			
	2.5					
	3.0					

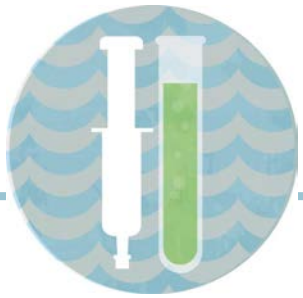
mg = milligram lb = pound
DM = Dry Matter BW = body weight

6. Create a graph of the data points collected in ***Table 1*** and ***2***. You may use either Excel or graph paper to plot your points. Once the graph is completed , extend the three lines created to interpolate Chlortetracycline concentrations in the feed when the dry matter in the feed changes at varying dry matter intakes (as expressed as a percentage of body weight). Full points will be awarded for graphs that include a legend and all three data curves (DM Intake at 2.0% of BW, DM Intake at 2.5% of BW, and DM Intake at 3.0 % of BW).



Dose Makes the Poison Quiz

Teacher Answer Key



1. To help care for your Aunt's cattle, look at the Aureomycin 4G Crumbles label on Page 9 and answer the following questions.

   a. What antibiotic is being used?

      Chlortetracycline

   b. What concentration of the antibiotic is listed on the label?

      4g/lb

   c. Express the concentration listed on the label in grams per ton. Show the formula you use to obtain your answer.

      4 g/lb x 2,000 lb/ton =4,000 g/ton

   d. Express the concentration listed on the label in milligrams per pound. Show the formula you use to obtain your answer.

      4 g/lb / 1000 mg/g =4,000 mg/lb

   e. Express the concentration listed on the label in milligram per kilogram. Show the formula you use to obtain your answer.

      4000 mg/lb x 2.203 lb/kg = 8,812 mg/kg

      -or-

      4g/lb / 454g/lb x 1000,000 mg/kg = 8,810 mg/ kg

2. What is the amount of drug required to treat bacterial pneumonia associated with *Pasteurella multocida* in cattle as stated on the label?

   10 mg/lb of body weight per day

3. How many milligrams of chlortetracycline are required to treat one 300 pound calf? Show the formula you use to obtain your answer.

   10 mg/lb BW/day x 300 lb BW = 3,000 mg/day

4. How many pounds of this medicated feed will it take to properly treat all 25 calves? Show the formula you use to obtain your answer.

   25 calves x 3000 mg/day = 75,000 mg / day

   75,000 mg / 1000 mg/ g = 75 g

   75g / 4 g /lb = 18.75 lbs of medicated feed required to dose 25 - 300 lb calves

5. Calculate the total pounds of feed that the calves will eat as the moisture level increases in the feed and fill in ***Table 1***.

300 lb BW x 2% of BW = 6 lbs of DM
6 lbs DM / 90% DM = 6.67 lb at 90% DM

Table 1: DiamondK Feed Calculation Tables – Feed Intake

Body weight lb	Feed Intake in DM as % of BW	Pounds of Feed Expected to be Consumed at Different Dry Matters				
		100% Dry Matter Basis	90% Dry Matter Basis	80% Dry Matter Basis	70% Dry Matter Basis	60% Dry Matter Basis
300	2	6	6.67	7.5	8.57	10
	2.5	7.5	8.33	9.38	10.71	12.5
	3	9	10	11.25	12.86	15

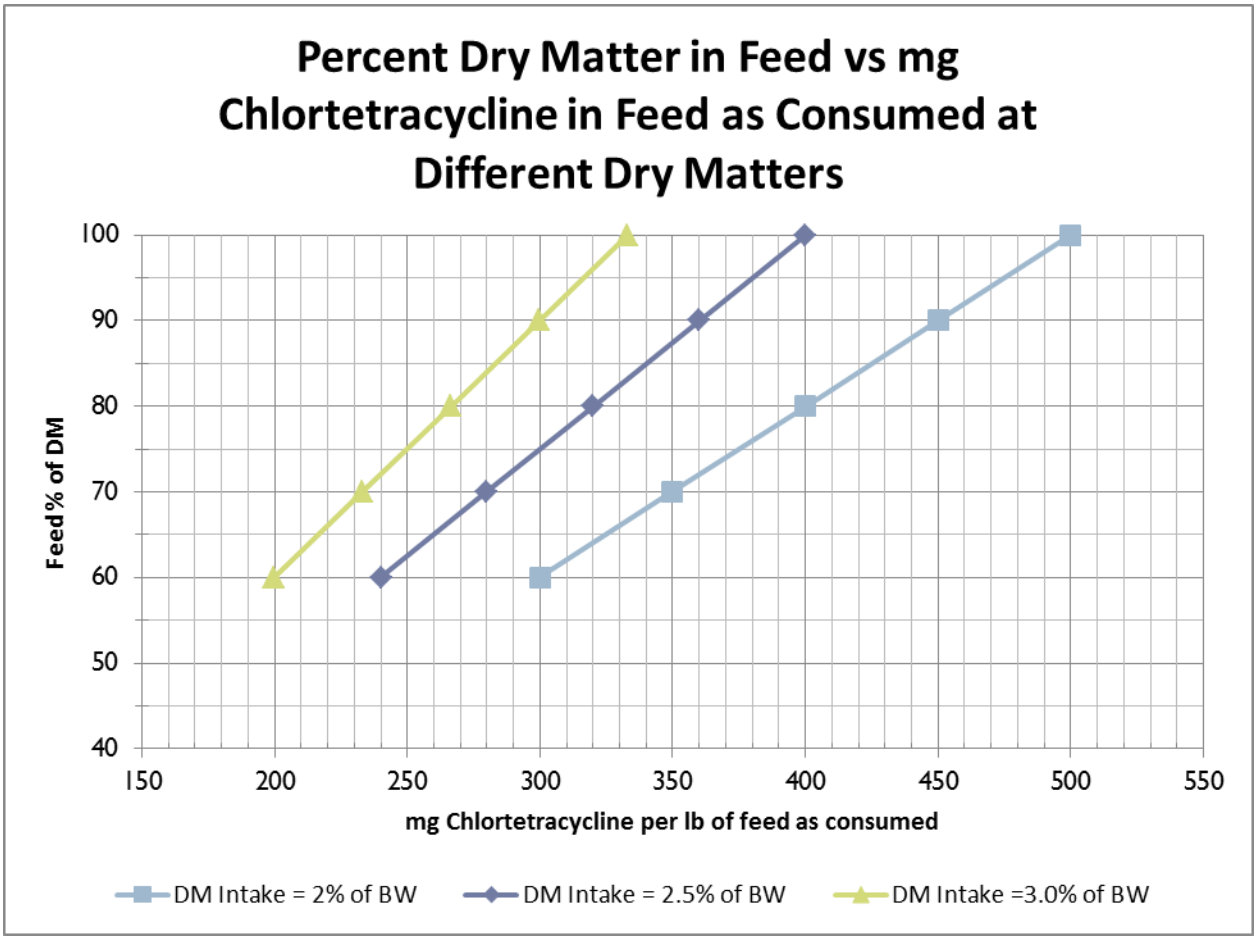
Next, determine the concentration in mg/lb of chlortetracycline in the feed and fill in ***Table 2*** using information determined in ***Table 1*** as well as the mass (in mg) of chlortetracycline required to treat a 300 lb calf (an amount that you determined previously for *Question 3*).

300 lb BW x 10 mg/ lb chlortetracycline per day = 3000 mg chlortetracycline intake per day
3000 mg chlortetracycline intake per day/ lbs in chart 1 = Drug concentration for ***Table 2***

Table 2: DiamondK Feed Calculation Tables – Drug Concentration

Body weight lb	Feed Intake in DM as % of BW	Drug Concentration in Total Diet (mg / lb of feed)				
		100% Dry Matter Basis	90% Dry Matter Basis	80% Dry Matter Basis	70% Dry Matter Basis	60% Dry Matter Basis
300	2	500	450	400	350	300
	2.5	400	360	320	280	240
	3	333	299.7	266.4	233.1	199.8

6. Create a graph of the data points collected in ***Table 1*** and ***2***. You may use either Excel or graph paper to plot your points. Once the graph is completed , extend the three lines created to interpolate Chlortetracycline concentrations in the feed when the dry matter in the feed changes at varying dry matter intakes (as expressed as a percentage of body weight). Full points will be awarded for graphs that include a legend and all three data curves (DM Intake at 2.0% of BW, DM Intake at 2.5% of BW, and DM Intake at 3.0 % of BW).



Fails to Meet Expectations	Approaching Expectations	Meets Expectations	Exceeds Expectations
Does not label x-axis and y -axis AND does not include appropriate scale. -AND- Incorrectly plots data points.	Does not label x-axis and y -axis OR does not include appropriate scale. -AND- Correctly plots some data points and connects them with a line.	Correctly labels x-axis and y-axis AND includes appro-priate scale. -AND- Correctly plots most data points and connects them with a line.	Correctly labels x-axis and y-axis AND includes appro-priate scale. -AND- Correctly plots all data points and connects them with a line. -AND- Provides correct legend showing maximum and minimum dose.