Learning and Mastering
PHARMACEUTICAL CALCULATIONS

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Dedication

Thanks to **Susan Ferencz***, my wife and a dedicated math teacher. Your suggestions and support contributed greatly to this book.*

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Introduction

This book can be used by anyone interested in evaluating their skills relevant to the myriad kinds of pharmaceutical calculations done every day by healthcare practitioners. For beginners or more advanced students, the skill set is the same. For ease of communication, the word *student* is used throughout the book to describe the user, since we are all students when learning new skills or refreshing skills that have been dormant for a while.

The hardest part of doing pharmaceutical calculations is developing a strong sense of what comes first—like the examples of the horse and cart or the chicken and the egg. For pharmaceutical calculations, it is important to first have both experience with drug therapy and clinical wisdom, and then using that experience to help analyze a calculation problem. Prior to solving a problem, the facts presented should be laid out in an orderly manner. *Orderly,* of course, is a function of the experience and wisdom of the problem solver. So, how does a student achieve experience, wisdom, and math skills? How does a student get the horse before the cart? By trying, failing, and trying again—just as with most of life's experiences. However, there are several pearls of wisdom, or pieces of advice, that can streamline the process of mastering problem solving.

PEARL #1. Take your time and read a problem several times before writing anything on paper.

Give yourself the luxury of stress-free learning by enjoying the learning process. Remember that using this text is not like taking an exam where the pressure of time rattles even the most well-prepared student. Follow the guidance in this text's next section about how to use this book to the fullest. In testing situations, students get into most trouble when—before reading a problem several times and trying to get in mind the order for the solution steps—they write something down on paper and cannot fit what is written into the scheme of a solution. Something written down in haste often seems much too important to not use in a solution, but often what's written down in haste only confuses a course of action following from a reasoned analysis. So, write only after you have first tried to visualize where you're going.

Realize that solving a word problem is different from answering multiple choice questions. On a multiple choice question it is often said that your first choice is probably your best choice. However, your first selection of an answer is not necessarily your best selection when it comes to math word problems. This book will help you develop your problem-solving *intuition. Intuition* is defined as the ability to know something without any proof or evidence. You just "know it." This intuition is the skill set that most older individuals got by memorizing multiplication tables and by using the "long methods" for multiplying and dividing numbers. However now, the personal computer/calculator has taken over these skills. Until you develop problem-solving intuition new students have to realize that logic is as important to problem solving as the manipulation of numbers and calculators.

Beginning students have one level of experience and wisdom. Obviously, an individual who has worked a long time in healthcare will have a different level of experience and wisdom, but don't assume the more experienced, wise individual always has an easier time solving medical math problems. What matters most is having practiced recently the ordering of a math problem into easily calculated chunks of work. Once a student has mastered the ability to order

a problem and visualize a solution, he or she will have in fact mastered a calculation concept. That student will have begun to apply correctly his or her intuition to problem solving.

PEARL #2. Don't forget to include units of measure in every step of a calculation.

Including units of measure is the backbone of what is called dimensional analysis, which is simply a systematic method to solve word problems. Some students can easily visualize the setup of a dimensional analysis table, but many other students cannot. It's not absolutely necessary to use dimensional analysis in medical math since solutions from a few well-reasoned intuitive steps can reach the correct answer. However, dimensional analysis, done correctly, is a good idea because it serves as a double check of the work even before a numeric answer is actually calculated. If the units of the analysis table cancel leaving only the units required of a correct answer, then the student can be confident that the calculated numeric answer also satisfies the problem. Students having trouble with dimensional analysis may have acquired the bad habit of not including units of measure (dimensions) even in simple arithmetic, such as calculating using ratio and proportions.

It's extremely important to *never* ignore units during calculations—*always* write down the units; don't try to save time by thinking you'll remember the units when crunch time comes at the completion of a calculation. Even when using a series of steps to solve a problem, correct units must still be known and carried from step to step for a correct calculation. Not doing this (especially if a student is over-confident in the logic of the chosen steps because the steps were not carefully reasoned) only contributes to confusion. Many students, when faced with this confusion, simply slap down an answer and hope for the best. Remember that confusion at the end of working a problem typically means confusion existed when planning the approach to solve a problem. Solving a calculation problem is not something done by rote. It is done by planning and reasoning.

Also, relying on a formula to solve a problem is sometimes misguided, especially if a student has given little thought to why a particular formula may, in fact, solve a problem. Unlike dimensional analysis, some formulas may not be simply a contracted form of a dimensional analysis table or series of simple, logical calculations. For example, some formulas in common use are regression equations showing the best fit of several independent variables as they define the function of a dependent variable (creatinine clearance, for example, discussed in Chapter 11). These formulas are determined by studying the amount of variance in the numeric values of independent variables rather than by simple arithmetic cancellation of the units associated with the independent variables. These formulas are accepted for the purpose intended, but they may not be intuitive for many students.

The bottom line for solving problems where specific formulas don't apply is this: knowing how to cancel units of measure in a calculation—either through use of a formal dimensional analysis table or by applying a series of simple, logical (intuitive) steps—is what gets to the correct answer.

PEARL #3. Have a plan to double check your answer.

Using a process for quick-and-dirty estimation of the approximate correct answer is one good method. For example, relying on your calculator to get it right is a really bad idea. Miss-keyed digits entered into a calculator is a typical problem, so be ready to check your answer.

Repeating the same steps in the original solution is good, but trying to get the correct answer by a different route is better. Rounding the numbers used in the calculation and applying the appropriate steps in your head is very often good enough to help a student get a ballpark estimate and stop an incorrect answer from being reported, whether on an exam or during the preparation of an intravenous dose of a potentially toxic drug. For example, doing a calculation requiring multiplication of 5 mg of drug given per kilogram of body weight for a patient weighing 198 lb yielding a calculated answer of 890 mg should be seen on its face as a wrong answer. Five times approximately 200 is 1,000 mg—not 890 mg; and, obviously, 198 lb is not what is asked for in the calculation. 198 lb is less than 100 kg, so the answer should be less than 500 mg—not 5 mg × 198 lb (entered erroneously as 178 into a calculator) = 890 mg. See how it works? *It is most important to understand that all answers should be double checked, and that an intuitive estimate is effective as a check.*

PEARL #4. *Correct* analysis means feeling confident that an end result is truly answering the question.

Correct analysis also means the arithmetic used is reliable to achieve the correct numeric answer. However, it's important to know also that there are usually different routes one can take to reach the correct answer. This notion causes some difficulty trying to help students learn medical math calculations. Many students want to know the "correct answer" to problems. This implies the one, sure-fire way to the right answer. Yes, in some cases problems can be well-categorized so that a single set of steps, usually known as a "rule," can be employed in getting the correct answer. This approach can be taken, but confusion occurs quickly when so many exceptions to the rule exist that the rule itself becomes nonsensical. If a problem does indeed have enough information to reach a correct answer, there is a single correct numeric answer to it. Experience and wisdom can shorten the route for you by reducing the number of logical steps employed. Don't be embarrassed if you use more steps than others. The important point is that you, yourself, understand the steps you used to reach the correct numeric answer.

Solving a problem actually becomes the easy part of the work, if the analysis of the problem is done effectively. The hardest part of solving any word math problem, whether or not the problem involves medical calculations, is applying analytical skills based on experience. Of course, frustration can overwhelm the beginner because experience and wisdom are minimal, and the student struggles with definitions of the individual words in a problem rather than the math concepts involved. The best advice for the beginner is to stay calm, start simply and move on to the more complex tasks after understanding the fundamentals. This is the approach taken by this book—assess simplest skills before moving on to the more complex. Also, understand that any new learning can be frustrating. Stay with the work. Don't try to master a skill more complicated than your current skill level, and *do the homework*. Yes, homework is assigned as part of several chapters. Please don't think you can cram for the final exam. Students will confront some difficult concepts in this book (such as measurement using aliquots, milliequivalent calculations and isotonicity determination). Perform the work as described, do the homework assigned and be diligent in understanding the fundamentals before moving on to more difficult concepts, and you should do well. To this end, the next section, "How to Use the Learning Guide" explains how this book is structured.

Nicholas Ferencz

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How to Use the Learning Guide

This section serves as a learning guide for users of the book. It describes how chapters are structured, pathways for a student to take, and the idea of phasing a problem's solution. Because solutions to problems often become easier when seen as discrete chunks of work, phasing a problem helps with the analysis of complicated calculations. A *phase* is simply a group of solution steps that, when combined with additional phases, yields the numeric answer to a calculations problem. Phasing is illustrated throughout the later chapters.

Selection of a pathway will, most likely, depend on experience level. This book can be used by anyone wishing to study medical math and apply it in practice. It should be comfortable for a beginning or advanced student or those wishing to validate their skills prior to a certification exam or at any time.

Chapters 1 through 6 describe the fundamental concepts and skills needed to perform calculations and interpret the language of prescriptions. These chapters also help students develop skills needed for prescription compounding and describe aspects of the physical chemistry (pharmaceutics) underlying medical math. Chapter 7 serves primarily as a review of the material covered in Chapters 1 through 6 and has an extensive list of objectives, many flowing from the objectives of the preceding chapters. Chapter 7 also restates and refines a number of calculations developed in the first chapters to unite the various systems of weights and measures and calculation methods (e.g., proportions) that, studied individually, often distract students. Chapters 8 through 12 cover more advanced concepts needed for drug product compounding and clinical practice.

Following one of the pathways through the book described in this section should make a student's time spent with the book as efficient as possible.

Chapter Structure

Chapters are organized following this plan:

- Statement of overall goal, learning objectives, and keywords for the chapter
- Discussion of the clinical relevance or other significance of chapter topics
- Presentation of the material in outline format containing problem examples
- Imbedded explanations/comments within the outline
- Summary statement of the chapter's learning experience
- Additional practice problems offered as homework

The chapters are designed using basic teaching tactics: tell the student what is about to be told and practiced; tell the student and allow practice; and, then, tell the student what has been told, allowing further practice. Note the Progress Test included in this section. Take the progress test and see how well you do. You may be able to bypass the first several chapters of the book if you're comfortable with the results. This should help to use the book efficiently. Calculation examples shown in the chapters are vital for developing a concept, and these have answers displayed with the problems. Additional review problems may also appear as homework in the chapters, and the answers for these problems are listed in Part II: Answers to Problems and

Selected Problem Solutions. Extended explanations within the outline may also have problems and answers—and possibly other information—shown in the Answers section as well.

Key Concept: Don't look at the answers until you've worked the problems.

Homework simply means a pause to reflect and set up the steps and phases in the solution of a problem. In some cases, this pause may be short, but in other cases a student may need to reflect and come back to a problem the next day. The point to consider is this: you can easily look in the back of the book for an answer, but do you really understand the calculation? Please remember this book is not an exam, and give yourself the luxury of time to truly grasp the solutions. Time spent doing this should solidify your own personal calculation style. Remember, again, what counts most is your ability to sort and analyze before arriving at the correct answer. It's not really important how many steps or phases you use in the solution, as long as you're confident of your logic and numeric answer. With practice, many of the routine elements of calculations will become intuitive—meaning you'll be doing the most important work in your head.

A brief discussion is needed at this point about phasing a problem's solution and this book's practice problems. Although not categorized by level of difficulty, in parts of the book covering particularly difficult concepts, a student will see problems defined by two difficulty levels: basic and advanced. These labels do not necessarily imply difficulty of the mathematics. These levels mean that the number of steps in the calculation becomes more cumbersome because the problem is more complicated. *Phasing* means that as difficulty level increases the student will probably find it easiest to group the facts given in a problem into discrete phases (bundles) to reach the final answer. Each phase comprises a number of steps in the individual phase's solution, but additional phases are needed to satisfy a particular problem's ultimate question.

For example, dopamine is an intravenous drug used to treat shock, where a patient's blood pressure is falling precipitously. Dopamine is administered using body weight expressed in kilograms starting at 1 to 5 mcg per kilogram of body weight per minute (mcg/kg/min) and increasing to higher doses depending on the response of a patient. This drug has a range of doses because it is titrated to its effect of restoring blood pressure—meaning the dosing begins at 1 and can increase up to 5 mcg/kg/min as needed. Calculating the dose actually given each minute would be the first phase in the needed calculation. This is 1 mcg and 5 mcg multiplied by the patient's body weight in kilograms. If a problem, however, asks you to calculate not only this initial dose range but also prepare an intravenous solution of this drug and also set an intravenous infusion pump to deliver the needed dose, you must add additional phases to your calculation. This approach will be demonstrated in the upcoming chapters.

The simple math of proportions can be used 60% to 70% of the time to solve medical math problems with just a few steps. This is why so much time is spent in the first chapters developing students' facility with ratio and proportion. Complicated problems, however, might require proportions to be applied several times in different phases of your solution to get the correct numeric answer. This book is not designed to provide example problems for every patient case that will be encountered in clinical practice or in compounding a drug product for dispensing. It is designed to give students the confidence of knowing how—by using a series of calculation steps linked, when necessary, by the needed number of calculation phases—to reach the correct numeric answer. This allows formation of good calculations habits. Forming these habits should allow you to tackle most problems encountered in practice. Try not to memorize the problems in this book. Try to memorize the logic you used for solving them.

Examples of make-believe drugs as well as real drugs will be used to help you learn good calculation habits. *It's extremely important that students know how to find details for dosing drugs in authoritative sources such as drug package inserts, references reporting the contents of the package inserts, and other references.* Drug dosing information changes. Drugs have uses and doses other than those found in the package insert ("off-label" uses and doses). Healthcare practitioners must know how to *use authoritative sources* of drug information. This calculations book must not be considered an authoritative source for drug dosing information. This book is an authoritative source for understanding medical math calculations.

Pathway Options:

Fundamental Pathway: Chapters 1–3 → Chapters 4–6 → Chapter 7 → Chapters 8–12

Advanced Pathway: Progress Test → Chapter 7 → Chapters 8–12

Pathways. There's nothing wrong with jumping into this book anywhere. Using the chapter structure, a student should be able to start anywhere depending upon the student's current understanding of medical math concepts and existing calculation skills. A brief reading of a chapter's objectives and keywords and working a few of the chapter's problems may be enough to assess your skill/experience level. Working in Chapter 7 should allow a quick self-appraisal of the necessary basic math skills related to the various systems and terminology of weights and measures used in healthcare. Usually, the single most difficult obstacle to overcome in learning medical math is the mingling of these systems and terminology in a single problem. This is where intuition becomes most important.

Fundamental Pathway. This pathway should be selected by those who have limited experience with medical math. It doesn't matter in which of the healthcare professions you work. Your personal feelings about your math skill set should be your guide when choosing a pathway. Don't assume that training and certification in any one particular profession automatically equips you to do well with medical math. It's not your credential, it's the skills you actually have that count.

Start with Chapter 1, and continue working through the first six chapters. And, no, don't pass lightly over Chapter 1! A major way this book's material becomes intuitive is through nudging students to perform "long methods" for applying arithmetic. Focus intently on making sure you can readily convert common fractions to decimal fractions to percentages. Practice doing multiplication and division the long way by setting up a multiplication table or using a long-division bracket before checking your work using a calculator. A major stumbling block for students is loss, over time, of the skills associated with place holding when doing arithmetic. Being able to intuit whether a calculated number has the required digits in the correct places (units, tens, hundreds, tenths, hundredths, etc.) is vital to gaining confidence in your performance. Be sure to know how to move a decimal point in a calculation (e.g., 0.25% does not equal 0.25; it equals 0.0025). This ability provides one way to double check final answers.

Chapters 3 and 6 will be the most challenging for many students following this pathway. Chapter 3 begins discussion of measurement by aliquots. Application of the aliquot method requires very solid understanding of the arithmetic for ratio and proportions. Chapter 6 introduces concepts of physical chemistry that can be confusing for a student who is still unsure of the meaning and use of the systems of weights and measures employed in doing medical math. As already discussed, Chapter 7 can be used to test what was learned in the earlier chapters. However, the last sections of Chapter 7 relate this early material to some of the finer points of concentration expressions used in labeling drug products and in clinical practice. Focus on the

initial sections of Chapter 7 to confirm your understanding of Chapters 1–6, and then move on to the sections of Chapter 7 representing objectives 14 through 19. Chapter 8 will confirm your understanding of these objectives from Chapter 7 and move you on to more complex problems of diluting and concentrating drugs.

The remaining chapters (Chapters 9, 10, 11, and 12) are somewhat freestanding in that there is no need to cover them in order. Depending on your interest, you can work on them in any order. However, do be sure to work on all of them. These chapters, though quite specialized in terms of technical skills, have great use in clinical practice.

A Few Examples

- Understanding the tonicity and electrolyte content of a drug in aqueous solution for injection helps you understand the therapeutic outcome following dosing of that product.
- Understanding the well-recognized formulas shown in Chapter 11 for dosing drugs having serious side effects helps you recognize possible toxic outcomes.
- Understanding how the formulation of a commercial drug product can be altered helps you begin therapy as quickly as possible, or allows you to deliver a product that is much easier for a patient to use.

Advanced Pathway. Little direction on how to use this book should be needed by advanced practitioners—those for whom intuition is already playing a major role in performing calculations. Using Chapter 7 for a quick review first, skimming the objectives of the book imbedded in the chapters as needed is the way to start for those who have medical math well in hand. These students should be able to work many medical math problems intuitively and should be comfortable searching the early chapters of the book only if needed for brief refreshers. The practice problems and tests in the book can be used to double check skills. Chapters 9, 10, 11, and 12 should be used as described in the last paragraph for the Fundamental Pathway. These chapters have enough clinical examples to allow adequate practice using multiple phases in reaching a solution. For advanced users, spend time creating your own problems relevant to your particular practice using the problems in the book as models. Often, constructing a model using a make-believe drug ("drug X," perhaps in a mixture with "drug Y," etc.) reinforces problem-solving skills. It also could become a formula that the advanced practitioner can use in the workplace. It's very common for pharmacies to use formulas for compounded products. Used in this sense, the formula for a compounded product serves the same purpose as the formulas (equations) shown in Chapter 11. They make reaching an endpoint, whether a finished compounded product or a therapeutic outcome, as efficient a process as possible.

Topics Not Included in This Book

While pharmacogenomics are mentioned briefly in Chapter 11, this book does not address details of the evolving mathematics of pharmacogenomics. For that matter, this book does not address math of the newly-developing field of Quantitative Systems Pharmacology. Both involve complex multivariate analyses and probably math processes as yet to be fully developed. Although pursuing the theoretical math of this new science is exciting, the practical application is, more or less, the creation and use of nomograms. An example for the drug warfarin is used in this book to illustrate these advances in therapeutics.

Additionally, the math of pH and pH buffer systems is not included because the emphasis of this book is mostly on clinical applications. Discussions of pH are, typically, most suitable for pharmaceutics books dealing with formulation of drug products. Creating new products must always consider pH, since maintenance of drug stability in its delivery vehicle is a major concern.

Summary

You'll find, while working through the book's features, uses of a word or phrase in various different contexts. For example, the word "solution" describes the calculations for a problem and also a drug dissolved in a vehicle (solvent). As you encounter new information and methods it's best to clarify immediately the meanings of words or phrases with which you're not yet familiar. A glossary is provided in the book to help you do this. Not only the individual meanings of these words is important for you, the context in which the word or phrase appears is very important as well. It's only arithmetic, some students say, but it's the context of words and phrases that makes all the difference in understanding how to move forward with a calculation. Many students of medical math are frustrated not by the math but by failure to understand the words describing the problem to be answered. To get the most out of this book, first determine as best you can what your existing skill level is, then select a pathway you think is best for you, and then plunge in.