PRODUCT SUBSTITUTION: LEGAL IMPLICATIONS

Activity Overview
This monograph describes the legal responsibilities of pharmacists who engage in product selection through generic substitution and therapeutic interchange. The interaction between federal regulation of product therapeutic equivalence and state regulation of pharmacist professional responsibility is reviewed. Court cases are used to demonstrate how legal principles are applied in the context of pharmacy practice.

TARGET AUDIENCE
The target audience for this activity is pharmacists and pharmacy technicians in hospital, community, and retail pharmacy settings.

LEARNING OBJECTIVES
After completing this activity, the pharmacist will be able to:

• Discuss the balance of cost and quality in product selection.
• List the requirements of an ANDA.
• Describe the process of therapeutic interchange.

After completing this activity, the pharmacy technician will be able to:

• Discuss the principles of generic substitution
• List the responsibilities of the pharmacy for appropriate drug product selection.
• Describe how the FDA approves therapeutically equivalent products.

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## Liability for Expanded Pharmacy Practice

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**Therapeutic Success and Cost Containment**

Pharmaceutical prices are among the most rapidly increasing costs within the health care system. Drugs are available to treat conditions that only a few years ago were untreatable. Some drugs serve as replacement therapy for surgery and other procedures that previously were employed to treat certain conditions. These drugs are not inexpensive. Yet they are often cost-effective, in the sense that they are less costly than the traditional alternatives, or they are more effective than older therapies.

The cost-effectiveness of pharmaceutical products is a persuasive argument in support of high drug prices, as long as there are no equally as good, yet less expensive, products that can be used in place of a drug that has been prescribed for a patient. The goal is not simply to use a cost-effective drug, but to use the most cost-effective drug that is appropriate for a patient’s condition. And in some circumstances, the goal may be to use a product that the patient can afford, or that the patient’s drug plan covers, even if the drug is slightly less effective than an alternative drug that is so pricey it is impossible to acquire. Anything is better than nothing. This is particularly true when a theoretically less effective, yet very affordable, drug turns out to be practically very efficacious for a specific patient.

Generic substitution is one means that health systems have used to reduce costs without sacrificing quality of care. If two products of the same drug are essentially the identical in therapeutic effect, and one product is significantly less expensive than the other, it makes good sense to use the less effective product.

Therapeutic interchange is a step beyond generic substitution, because it involves the use of a different molecular entity in place of the drug that has been prescribed for a patient. Through a formal process, in which pharmacy and medicine participate together, decisions can be made to replace a prescribed drug with an alternate drug within the same class as the prescribed drug.
Pharmacy plays a significant role in both generic substitution and therapeutic interchange

**The Pharmacist’s Role in Product Selection**

Many of the decisions about the dispensing of less expensive alternative products are left to the discretion of the pharmacist. This is a role that pharmacists have now embraced and it was the first decisional opportunity given to pharmacists following the formal creation of an RxOnly class of drugs in 1952, when physicians were given authority over drug choices.

Prior to the development of generic substitution as a pharmacist role, pharmacists were required to dispense exactly the product prescribed by the physician, even if a less expensive, safe and effective alternative was available. Pharmacists followed orders. Generic substitution was the first independent decision delegated to pharmacists. With the advent of managed care, decisions about generic substitution are now largely made centrally and are only implemented by pharmacists. Generic substitution has become an ordinary aspect of pharmacy practice. But it laid the foundation for expanded responsibilities of pharmacists. And that foundation is significant.

**Exemplary Case: Ranbaxy v. First Databank**

This case addresses a controversy between a manufacturer (Ranbaxy) and a database vendor, FDB. Ranbaxy manufactures Absorica, an isotretinoin product that is similar to other products of isotretinoin, with the exception that it is effective even if taken in a fasted state.

The subject of this case is the framework within which the FDA approves generic products, the state laws that allow drug product selection by pharmacists, and computer programs that provide to pharmacists information about the equivalence of generic products.
The claim being made is that the database provided to pharmacists is inaccurate, and that pharmacists are misled by the database to believe that Absorica is equivalent with other isotretinoin products.

All language in italics is quoted directly from the opinion of the United States Court of Appeals for the Eleventh Circuit.

**Regulatory Background**

*The FDA issues a publication called the “Orange Book,” which is used by pharmacists in many states to help identify which drugs are interchangeable with other drugs. The Orange Book provides a wide range of information about drugs approved by the FDA, but only two metrics are relevant here: Pharmaceutical equivalence and therapeutic equivalence. Two drugs are pharmaceutical equivalents if “they contain the same active ingredients, are of the same dosage form, route of administration and are identical in strength or concentration.” The Orange Book designates Absorica as pharmaceutically equivalent to several other isotretinoin-based acne medications. By contrast, two drugs are therapeutic equivalents only if “they are pharmaceutical equivalents and if they can be expected to have the same clinical effect and safety provide when administered to patients under the conditions specified in the labeling.” Because of Absorica’s unique effectiveness when taken in a fasted state, the Orange Book has given Absorica a “BX” rating, which indicates that no drugs are therapeutically equivalent to Absorica.*

*The Orange Book is used in many states as the authoritative source for determining whether a pharmacist may substitute a prescribed drug with a cheaper generic version. In “Orange Book states,” pharmacists may only substitute a drug for another if the two drugs are designated by the Orange Book as being therapeutic equivalents. However, in “non-Orange Book states,” pharmacists are not required to consult the Orange Book (though
they may choose to do so), and instead make substitution decisions by relying on their own professional judgment and the information provided by their companies’ software programs.

The Database

FDB publishes the MedKnowledge database, which is a collection of information about various drugs for use by pharmacies when they fill prescriptions. MedKnowledge is a raw data file—it is not organized in a way that is meaningful or useful to pharmacists at local drug stores. Instead, FDB sells subscriptions to the MedKnowledge database to consumers who then develop software that sorts and organizes the raw data into a display format usable by pharmacists. MedKnowledge provides thousands of fields for each drug, with each field populated with a coded piece of information. For example, in one field that relates to the Orange Book’s therapeutic equivalent designation, Absorica is marked as “BX,” indicating it has no therapeutic equivalent. FDB’s customers choose which data to display to pharmacists and how to display it. FDB has no control over how the information is displayed to the pharmacists issuing prescriptions.

The Plaintiff’s Claims

Ranbaxy’s complaint concerns two pieces of data published in the MedKnowledge database. First, each drug is assigned a 5-digit Clinical Formulation ID. Several drugs may be assigned the same Clinical Formulation ID if they have the same active ingredients, route, dosage form, and strength (the same factors considered in determining pharmaceutical equivalence).

Ranbaxy protests that the assignment of a non-unique Clinical Formulation ID to Absorica falsely represents that Absorica does not have a clinically unique dosage form,
thereby misleading pharmacists in to believing that Absorica is substitutable with other acne medications.

The second piece of data challenged by Ranbaxy is Absorica’s designation as a multi-source drug. Ranbaxy admits that, in Orange Book states, there is no risk of confusion because pharmacists there are required to consult the Orange Book code before offering a substitute for a drug and Absorica’s BX rating, accurately notated in the MedKnowledge database, indicates that it has no therapeutic equivalent. Ranbaxy contends, however, that in non-Orange Book states, a pharmacist might not consult the Orange Book code for Absorica, and instead will see its non-unique Clinical Formulation ID or its multi-source designation and wrongly conclude that other generic acne drugs may be safely substituted for Absorica.

The Court’s Analysis
Ranbaxy first argues that because the MedKnowledge documentation indicates that unique Clinical Formulation IDs may be assigned when a drug’s dosage form is “clinically unique,” Absorica should have its own Clinical Formulation ID. But there is no evidence that FDB has ever assigned a unique Clinical Formulation ID merely because a drug may be taken in a fasted state. And despite an extensive list of dosage forms, nothing in the MedKnowledge documentation suggests that such a metric is relevant to FDB’s determination of clinical uniqueness.

Ranbaxy protests that the MedKnowledge documentation is so lengthy and cumbersome that no representative from FDB could even say they read the entire manual, and there is no evidence that any customers have ever done so. Ranbaxy’s insistent reference to the size of the documentation is of no help. The user documentation is not a novel to be read cover-to-cover; it is a reference manual designed to be consulted and searched as needed.
The very passage cited by the parties in this litigation can be found simply by referencing the Table of Contents, Index, or other search function.

We are not persuaded that the sheer volume of the documentation undermines FDB’s reliance on it. Because FDB provides ample explanation of the information and terms in its database, no reasonable reader would conclude that Absorica was therapeutically equivalent to, or substitutable for, other drugs.

The Take-Home Message

The Court of Appeals affirmed dismissal of the manufacturer’s lawsuit. The bottom line message from this case is that pharmacists make independent decisions based on their own expertise as applied to a large volume of information they have available to them. Computerized databases used by pharmacists at their clinical practice sites provide useful information for pharmacists, but they don’t make decisions for pharmacists. The decisions pharmacists make are likely to be based, at least in part, on the materials provided by decision-assistance software, but they are not dictated by that software.

Decisions made by pharmacists when they engage in generic substitution are not entirely based on computerized information, or any other information derived from sources that report the results of drug use with a population of patients.

Pharmacists who engage in generic substitution can interact with patients and with prescribers prior to a first substitution and when refill requests are made. A factor such as therapeutic equivalence data in a fasting or non-fasting state may be relevant to a population of drug users, yet of no particular concern to an individual patient for whom medication has been prescribed. Pharmacists can take into consideration patient individuality when they substitute products.
Requirements Of An ANDA

A generic product can be approved by the FDA pursuant to an ANDA submission. An ANDA is much shorter than an NDA. The information required to be included in the ANDA is summarized in the FDCA Section 505(j):

(i) information to show that the conditions of use prescribed, recommended, or suggested in the labeling proposed for the new drug have been previously approved for a “listed drug”;

(ii)(I) if the listed drug referred to in clause (i) has only one active ingredient, information to show that the active ingredient of the new drug is the same as that of the listed drug;

(II) if the listed drug referred to in clause (i) has more than one active ingredient, information to show that the active ingredients of the new drug are the same as those of the listed drug.

(iii) information to show that the route of administration, the dosage form, and the strength of the new drug are the same as those of the listed drug referred to in clause (i) or, if the route of administration, the dosage form, or the strength of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), such information respecting the route of administration, dosage form, or strength with respect to which the petition was filed as the Secretary may require;

(iv) information to show that the new drug is bioequivalent to the listed drug referred to in clause (i);

(v) information to show that the labeling proposed for the new drug is the same as the labeling approved for the listed drug.
Interpreting ANDA Requirements

Note that the ANDA section of the FDCA refers to a “listed drug” as the reference standard against which an ANDA approval is being measured. Through the ANDA process, a sponsor is limited to approval consistent with the labeling of the listed drug. Generic equivalence is possible only when two products have the same molecular entity, the same route of administration, in the same strength, and in the same dosage form. There is a petition process that allows ANDA approval when two products do not have this characteristic of sameness.

The standards for bioequivalence are specified elsewhere within the FDCA, and are applied by the FDA in approving an ANDA.

Note the requirement that the labeling of the generic product be the same as the labeling of the listed drug. This is a requirement that has come under criticism recently, as the sponsor of the listed drug may have no incentive to change the labeling of a drug that is sold almost exclusively in its generic form by another company.

A Note On Terminology

Often the comparison between a product approved through an NDA and one approved through an ANDA is referred to using the words “brand” and “generic.” While this is a useful shorthand that is understood by most pharmacists, it is not necessarily a universal way to refer to these two products. The terms “brand” and “generic” are sometimes confusing.

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The original NDA’d product is often also referred to as the “pioneer” or the “innovator” product. Because many products approved through an ANDA use brand names (sometimes called “branded generics”), the reference to a “brand” product does not necessarily identify the pioneer or innovator.
Out of abundance of caution, and to assure clarity of communication, it is sometimes considered advisable to distinguish between products “approved though an NDA” and those “approved though an ANDA.” This is a way to effectively make the brand vs. generic distinction and avoid confusion.

**FDA Bioequivalence Standards**

Section 505 (j)(8)(B) of the Public Health Act describes one set of conditions under which a test and reference listed drug will be considered bioequivalent—the rate and extent of absorption of the test drug does not show a significant difference from the rate and extent of absorption of the reference drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses; or the extent of absorption of the test drug does not show a significant difference from the extent of absorption of the reference drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses and the difference from the reference drug in the rate of absorption of the drug is intentional, is reflected in its proposed labeling, is not essential to the attainment of effective body drug concentrations on chronic use, and is considered medically insignificant for the drug. Where these methods are not applicable (e.g., for drug products that are not intended to be absorbed into the bloodstream), other in vivo or in vitro test methods to demonstrate bioequivalence may be appropriate.

Bioequivalence may sometimes be demonstrated using an in vitro bioequivalence standard, especially when such an in vitro test has been correlated with human in vivo bioavailability data. In other situations, bioequivalence may sometimes be demonstrated through comparative clinical trials or pharmacodynamic studies.
The Orange Book

The FDA publishes (now available exclusively online) a book titled Approved Drug Products with Therapeutic Equivalence Evaluations (referred to as the Orange Book because in print form its cover was the color orange). This is the place to go for a list of all listed products and all generic products approved under an ANDA. If two products have been approved through an NDA, they may not be listed as bioequivalent. The definitions with the Orange Book are critical.

Pharmaceutical Equivalents. Drug products are considered pharmaceutical equivalents if they contain the same active ingredients, are of the same dosage form, route of administration and are identical in strength or concentration.

Pharmaceutical Alternatives. Drug products are considered pharmaceutical alternatives if they contain the same therapeutic moiety, but are different salts, esters, or complexes of that moiety, or are different dosage forms or strengths.

Therapeutic Equivalents. Drug products are considered to be therapeutic equivalents only if they are pharmaceutical equivalents and if they can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling.

The Two-Letter Codes

A listing in the Orange Book indicating the lack of equivalence does not mean one or the other product is a bad product, it simply means that the two products are not considered to be bioequivalent under the FDA criteria.

The two basic categories into which multisource drugs have been placed are identified using a code with the first letter being either “A” or “B” and a second letter that explains the reason for the A or B rating.

“A” drug products are considered by the FDA to be therapeutically equivalent to other pharmaceutically equivalent products, i.e., drug products for which: (1) there are no known or suspected bioequivalence problems. These are designated AA, AN, AO, AP,

“The definitions within the Orange Book are critical.”
or AT, depending on the dosage form; or (2) actual or potential bioequivalence problems have been resolved with adequate in vivo and/or in vitro evidence supporting bioequivalence. These are designated AB.

“B” drug products are, at this time, considered by the FDA not to be therapeutically equivalent to other pharmaceutically equivalent products, i.e., drug products for which actual or potential bioequivalence problems have not been resolved by adequate evidence of bioequivalence. Often the problem is with specific dosage forms rather than with the active ingredients. These are designated BC, BD, BE, BN, BP, BR, BS, BT, BX, or B* (referred to as B star).

**Therapeutic Interchange**

Unlike generic substitution, therapeutic interchange (TI) occurs when a pharmacist dispenses a product that may be a different molecule, different route of administration, different dosage form, or different strength from the product that was prescribed. A TI may be either pre-approved by the prescriber or it may be approved contemporaneously with each dispensing. Most states permit pre-approved TIs in the institutional practice setting, some permit TIs in a managed care setting, and a relatively few states permit TIs in a community setting.

There is never a legal issue with a pharmacist contacting a prescriber about a specific prescription and requesting a change in the prescription based on the pharmacist’s professional judgment that an alternative therapy is safe, effective, and less expensive than the prescribed therapy. That becomes a new verbal order for the new therapy if adopted.

In the institutional setting, rules of the institution, with which prescribers have agreed, may permit pharmacists though a TI to dispense a drug that has been judged to be preferable to the drug prescribed without contemporaneous permission of the prescriber. Most institutional systems provide a mechanism for prescribers to justify the patient’s need for the prescribed drug as opposed to the drug that would be dispensed under a TI. These objections must be science based with support in the literature.
The Formulary Process

A drug formulary is a list of drug products that are available within an institution or a system, and it may serve as the informational basis of therapeutic system. A drug formulary is not a static document; it is constantly revised as information is learned from experience using the drug within an institution or a health system.

The formulary system is a process of discovery and discussion, through which the health care professionals at a hospital or in a health care system decide which drug products are safe, effective, and cost-effective. The goal of the formulary system is to determine what drugs are most appropriate for use within the hospital or system in which patients are being cared for. Formulary system policies may reflect the patient conditions being treated, the latest science on drug therapy, prescriber experience and preferences, and insurance payment.

Many states recognize the utility of formularies in their pharmacy acts. Usually, this recognition is limited to institutional pharmacy practice.

The Pharmacy & Therapeutics Committee

The Pharmacy and Therapeutics (P&T) Committee is usually constituted as a medical committee with a majority of members being prescribers, and significant membership also coming from pharmacy and other health professions. The P&T Committee oversees the administration of the formulary system, including therapeutic interchange.

One key responsibility of the P&T Committee is Medication Use Evaluation (MUE), a process through which data are collected concerning the safe and effective use of medications within the hospital or health system. These data can be used to influence decisions about policies and procedures within the health system.

The P&T Committee is a standards setting group. The decisions it makes to support an approach to therapy set the standard for that therapy. A health professional who practices
consistent with P&T Committee policies has necessarily met the standard of care. This can be a strong defense argument if adverse events occur.

**Biosimilars**

The Biologics Price Competition and Innovation Act of 2009 (BPCI Act) was passed as part of the Affordable Care Act on March 23, 2010. The BPCI Act creates an abbreviated licensure pathway for biological products shown to be biosimilar to, or interchangeable with, an FDA-licensed biological reference product. The objectives of the BPCI Act are conceptually similar to those of the Hatch-Waxman Act, which in 1984 established the ANDA pathway for the approval of generic drug products. The implementation of an abbreviated licensure pathway for biological products can present greater challenges given the scientific and technical complexities that may be associated with the larger and typically more complex structure of biological products, as well as the processes by which such products are manufactured. Most biological products are produced in a living system such as a microorganism, or plant or animal cells, whereas small molecule drugs are typically manufactured through chemical synthesis. The BPCI is controversial and the FDA is currently working toward its implementation. No products have yet been approved under the authority of the BPCI. Even when they are approved, states will have to enact legislation that allows pharmacists to substitute biosimilars. Just as is the case with generic products, the substitution of biosimilars will have to be done in a way that protects patient health.
The 351(k) Application

Section 351(k) of the Public Health Service Act was added by the BPCI Act. It sets forth the requirements for an application for a proposed biosimilar product and an application or a supplement for a proposed interchangeable product. Section 351(i) defines biosimilarity to mean “that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components” and that “there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product.” A 351(k) application must contain, among other things, information demonstrating that the biological product is biosimilar to a reference product based upon data derived from analytical studies, animal studies, and a clinical study or studies, unless FDA determines, in its discretion, that certain studies are unnecessary. To meet the higher standard of “interchangeability,” an applicant must provide sufficient information to demonstrate biosimilarity, and also to demonstrate that the biological product can be expected to produce the same clinical result as the reference product in any given patient and, if the biological product is administered more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between the use of the biological product and the reference product is not greater than the risk of using the reference product without such alternation or switch.

Process for Biosimilar Approval

The process for biosimilar approval will necessarily differ from that of generic product approval. The FDA intends to consider the totality of the evidence submitted in a 351(k) application and is recommending that sponsors use a stepwise approach in their development of biosimilar products. In draft guidance, the agency discusses important scientific considerations in demonstrating biosimilarity, including:
• A stepwise approach to demonstrating biosimilarity, which can include a comparison of the proposed therapeutic protein product and the reference product with respect to structure, function, animal toxicity, human pharmacokinetics and pharmacodynamics, clinical immunogenicity, and clinical safety and effectiveness;

• The totality-of-the-evidence approach that FDA will use to review applications for biosimilar products; and

• General scientific principles in conducting comparative structural and pharmacodynamics studies, clinical immunogenicity assessment, and clinical safety and effectiveness studies (including clinical study design issues).

**Court Case: Turetsky v. American Drug Stores**

Liability by one party to another requires that there be some type of damages caused to the other party. What could have happened is not relevant. Courts deal in actualities, and not in hypotheticals. Imagine how crowded the courts would be if they entertained hypothetical cases.

In the case excerpted here, a patient’s father claims, perhaps correctly, that a pharmacist at the defendant pharmacy substituted a generic product contrary to the state generic substitution law. The court dismisses the case, because no damages are alleged. When a patent says something like “in theory I might have been hurt by that error,” pharmacy risk managers often say something like “in theory we might give you some money.” The state board of pharmacy could punish the pharmacist in this case, but that would not provide any money to the plaintiff, and it is not what this case is about.
Summary of the Court’s Opinion

Defendants allegedly operate pharmacies. Plaintiff Alex Turetsky contends that in order to protect patients’ health, pharmacists are required to follow physicians’ orders in filling the physicians’ prescriptions for patients. Turetsky further contends that while a pharmacist can substitute certain drugs for prescribed drugs, a pharmacist cannot substitute a drug that is not a therapeutically equivalent drug. Turetsky brings this action on behalf of his minor son J.T. Turetsky contends that J.T.’s physician wrote J.T. a prescription for Concerta to treat J.T. for attention deficit hyperactivity disorder. Turetsky asserts that when he sought to have the prescription filled at one of defendants’ pharmacies, the pharmacist improperly substituted a generic drug that was not a therapeutically equivalent drug for Concerta. Although Turetsky does not allege that J.T. actually received any less therapeutic value with the generic, Turetsky asserts that technically defendants did not abide by the guidelines for pharmacists when filling prescriptions.

Although Turetsky contents that the generic was not a therapeutically equivalent product, defendants are correct that Turetsky has not alleged or suggested that the generic failed to act in the same manner as Concerta or failed to provide J.T. with safe and effective treatment for his ADHD. So in the end, even with the substitution, J.T. got what his physician and father desired, namely effective treatment for his ADHD.

Although Turetsky contends that he received the “wrong pills,” he does not allege facts that show any concrete physical or financial harm to himself or to J.T. as a result. Therefore, the motion to dismiss is granted.
What This Case Teaches

The most obvious lesson from this case is that generic substitution will result in pharmacy liability only if harm can be proven. And proving harm from a generic substitution will be very difficult. The plaintiff, who bears the burden of proof, must show that harm occurred (the plaintiff in this case could not show even that), and also that the harm would not have occurred had the prescribed product been dispensed by the pharmacist without a substitution. It is a significant requirement to meet; perhaps impossible.

Perhaps less obvious in this legal opinion is the court’s conclusion that what a patient is purchasing from a pharmacy is not a drug product but effective treatment.

Under this approach to reasoning, if a patient’s drug therapy is safe and effective, it does not matter what product the patient received. The product could be what the prescriber ordered, or it could be a different product. It is outcomes that matter and not structures or processes. Wellness is the desired outcome.

Court Case: Michigan v. CVS Caremark

This case involves the interpretation of a section of the Michigan generic substitution law, in which pharmacists are permitted to substitute generics, and must pass on the savings in cost that result from that substitution. The section of Michigan law that is the subject of the case is section 17755. The plaintiffs' case was initially dismissed, but the Michigan Court of Appeals reinstated the case. The language quoted below is from the Supreme Court of Michigan’s legal opinion, in which that court reverses reinstatement of the case and affirms dismissal of the case. For reasons explained in the language below, the Supreme Court held that the plaintiffs had not sufficiently alleged legal violations of 17755 by the defendants. The case alleges fraud in overcharging for generic products.
Summary of the Court’s Opinion

Plaintiffs argue that defendants systematically violated 17755 by charging prices for generic drugs that produced a higher profit margin than had been achieved by selling the equivalent brand-name drugs.

Before enactment of 1755, a pharmacist was required to dispense a prescription as written and was prohibited from substituting a less expensive generically equivalent drug. After enactment, pharmacies are generally permitted to substitute generic drugs for their brand-name equivalents. Section 17755 states in part: (2) If a pharmacist dispenses a generically equivalent drug product, the pharmacist shall pass on the savings in cost to the purchaser or to the third party payment source if the prescription purchase is covered by a third party pay contract.

The parties disagree whether Subsection (2) applies to all transactions in which a generic is dispensed or only in situations in which a generic drug is substituted for its brand-name equivalent. The parties disagree about what it means to “pass on the savings in cost.”

If Subsection (2) applies to all transactions in which generic drugs are dispensed, including transactions in which no brand-name drug was prescribed, then the term “equivalent” is ineffectively written out of the statute because there is no referent to which the generic drug product is equivalent. Similarly, the definition of “savings in cost” in Subsection (2) refers to the difference between “the 2 drug products.” Without a prescribed brand-name drug that is equivalent to the generic, there is only a single drug product.

The amount that a pharmacist must pass on to a purchaser or third-party payer is the difference between the wholesale cost of the two drugs. In other words, “savings in cost” equals the brand-name wholesale cost minus the generic wholesale cost.

Plaintiffs’ approach of identifying all transactions in which a generic drug was dispensed fails to highlight the only relevant transactions—those in which a generic drug was substituted for a brand-name drug.

What This Case Teaches

It seems pretty simple, but it took years of legal wrangling, including multiple appeals, to reach the result in this case. Generic substitution laws apply only to generic substitutions. When a prescription is written using a drug’s generic name, with no mention made of a trade name, then there can be no substitution and the generic substitution laws do not apply. If your friend asks you for a “soft drink” and you provide a Coca-Cola, then you have not substituted anything because nothing in particular was specified by your friend. You have simply selected which soft drink to provide. On the other hand, if your friend asks you for a Pepsi and you provide a Coca-Cola, then you
have substituted one thing for another. They are both cola drinks, so they are very similar, but they are not the same. For some people this difference matters, while for others it does not.

The plaintiffs in the case excerpted above, and their lawyers, attempted to argue that cost savings should be passed one even when a prescription has been issued using a generic name. But the court figured out that nothing had been substituted for anything else when nothing in particular had been specified to begin with. The interpretation of “savings in cost” is interesting, but irrelevant, because it is a provision of the generic substitution law. When no substitution has occurred, no provisions of the generic substitution law apply to the activity. This is pharmacist selection and not substitution.
Exam Questions

1. What was the first independent decision delegated to pharmacists after the RxOnly class of drugs was created in 1952?
   a. Immunization.
   b. Patient education.
   c. Generic substitution.
   d. Packaging.

2. According to the case of Ranbaxy v. First Databank, how was Absorica rated in the Orange Book?
   a. C-II.
   b. OTC.
   c. AB.
   d. BX.

3. Through what approval mechanism are generic products approved under Section 505(j) of the FDCA?
   a. IND.
   b. ANDA.
   c. NDA.
   d. AMA.

4. According to the Orange Book, there is a category of products that contain the same active ingredients, are of the same dosage form, route of administration, and are identical in strength or concentration. What are these products called?
   a. Pharmaceutical equivalents.
   b. Pharmaceutical alternatives.
   c. Therapeutic equivalents.
   d. Biosimilars.

5. According to the Orange Book, there is a category of products that can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling. What are these products called?
   a. Pharmaceutical equivalents.
   b. Pharmaceutical alternatives.
   c. Therapeutic equivalents.
   d. Biosimilars.
6. Which of the following two-letter codes could be used by the Orange Book for a product that has actual or potential bioequivalence problems that have not been resolved?
   a. BN.
   b. AA.
   c. AN.
   d. AT.

7. Which of the following terms refers to a process of discovery and discussion through which health care professionals at a hospital or in a health care system decide which drug products are safe, effective, and cost-effective?
   b. ANDA.
   c. FDA.
   d. APhA.

8. A section of the Affordable Care Act creates a licensure pathway for products of large molecules that are highly similar to the reference product notwithstanding minor differences in clinically inactive components. What are these products called?
   a. Pharmaceutical equivalents.
   b. Pharmaceutical alternatives.
   c. Therapeutic equivalents.
   d. Biosimilars.

9. In the case of Turetsky v. American Drug Stores, what damages did the plaintiff allege had been caused by an illegal substitution by a pharmacist at the defendant pharmacy?
   a. Death.
   b. Blindness.
   c. Coma.
   d. None.

10. According to the court in the Michigan v. CVS Caremark case, what does the term “savings in cost” mean?
    a. Brand name wholesale cost minus generic name wholesale cost.
    b. Generic name wholesale cost minus brand name wholesale cost.
    c. Brand name retail price minus generic name retail price.
    d. Generic name retail price minus brand name retail price.

    Please submit your final responses on freeCE.com. Thank you.