The Controversy Over Generic Equivalency of Drugs

WERNER LOWENTHAL

School of Pharmacy, Medical College of Virginia, Richmond

A drug (single chemical entity) is known by several names. First, the chemical name describes its structure by standard chemical nomenclature. Second, the research code number is assigned to the drug during pharmacodynamic studies in animals, and often during early clinical investigation. Third, it receives a generic name which is often a contraction of the chemical name, but which describes the drug and the class of drugs to which it belongs, e.g., barbital, phenobarbital, pentobarbital, etc. The U.S. Adopted Name Council (USAN), composed of representatives from the American Medical Association, U.S. Pharmacopeia (USP), National Formulary (NF), and Food and Drug Administration (FDA) recommends generic names for all new drugs. Since 1962, the FDA must approve all generic names. Before, 1962, the generic names were often not descriptive of the drug, and were confusing and difficult to use (Wilson, 1960). Fourth, the drug receives a trademarked name (brand name), designated by a superscript ® at the end of the name, signifying that this name has been registered with the U.S. Patent Office. Only the registrant may use the trademarked name for the particular drug; thus his product is distinguished from those of competitors.

Many older drugs that are public domain, or on which the patent has expired, are often best known by the generic name, e.g., phenobarbital. If a prescriber wishes to prescribe the phenobarbital produced by Winthrop Laboratories, he uses the trade name Luminal. Tetracycline HC1 is the generic name for a specific antibiotic, which may be purchased or prescribed by that name. It is also known by certain trade names, e.g., Tetracyn (J. B. Roerig & Co.), Achromycin (Lederle Laboratories), Kesso-Tetra (McKesson Laboratories). Even if a company holds an unexpired patent on a drug, it may be the only manufacturer of that product, so the use of the generic name or the trademarked name becomes immaterial, e.g., Darvon (propoxyphene HC1, Eli Lilly & Co.) and there can be no controversy over equivalency. On the other hand, if many companies manufacture the same drug, in similar dosage form, the question arises as to whether all these products are equivalent with respect to physiological and pharmacological potency.

Equivalency of Generic Products

This is important because in many instances the prescriber has a choice of designating a product by its generic name or by a trademarked name. If the generic name is used, the pharmacist is permitted to dispense that drug manufactured by any company. In this method of prescribing the assumption is that all products of a specific generic name are equivalent. With our present knowledge, however, there is doubt whether products bearing the same generic name are equally efficacious, e.g., sulfisoxazole (F-D-C Reports, Jan. 2, 1967). It may be that the patient

will get less than the desired dose, because the product does not meet labeled claim, or that the drug cannot be absorbed for some reason, e.g., the tablet fails to disintegrate or dissolve. If generic products are not equivalent, then prescribing, either voluntary or by directive, becomes a question of good professional practice. Forcing a prescriber to prescribe any drug in which he does not have confidence or with which he has no experience, is a potentially dangerous practice.

The problem of drug designation is further complicated in that any manufacturer can obtain a trademark for his products, and since all drugs now have generic names, both terms lose their power to differentiate between the quality of drugs. There is a new term coming into use, "branded-generics," which nicely bridges the gap between generic and trademarked drugs. Trademarks are now being obtained for both old and new generic drugs. Comparing statistics between these two groups of drugs becomes a meaningless game of numbers.

In addition, the trademark is on the drug, and not on the final product (dosage form). Yet, the patient is not given micro-packets of powder or liquid to take; he receives a combination of ingredients, including the drug(s), which makes an acceptable physical entity that can be conveniently handled, taken, or administered.

Discrepancies in Drug Costs

The cost of medication is interwoven into this controversy. The products sold under generic names are often less expensive than the trademarked products, e.g., 5 mg dextroamphetamine sulfate tablets may be purchased for as little as $1.25 for a bottle of 1,000 tablets, or purchased as Dexedrine (Smith, Kline & French Laboratories) for $22.60 (Drug Topics Red Book 1967). This phenomenon of price differentials occurs in other fields also.

The cost of medication is confounded by the pricing structure of many pharmaceutical manufacturers. They sell their trademarked products to government agencies and hospitals at much lower prices than to the community pharmacist. It was reported that Upjohn Co. sold prednisone tablets (5 mg) to the Government at $4.94 per 1000 (F-D-C Rept., July 29, 1967), whereas the price to community pharmacists was $20.94 (Drug Topics Red Book 1967). It was also reported that Ciba would give a bottle of 1,000 tablets free with the purchase of two bottles of 1,000 tablets of Esidrex (hydrochlorothiazide) and Esidrex K (hydrochlorothiazide and potassium chloride). This offer was made to public and private hospitals, dispensing physicians, but not to pharmacists (Weekly Pharmacy Rept., Jan. 2, 1967). Price cannot be equated to quality. If it is, one may ask if the manufacturers are making products of two different qualities, an expensive one of higher quality and a less expensive one of lower quality. Recently, E. R. Squibb & Sons announced the new price for its Sumycin (tetracycline). The product now will sell for $4.25 per 100 capsules (F-D-C Rept., August 14, 1967). This makes Squibb's prices more competitive with generic products.

Many of the arguments given against the concept of generic equivalency arose before the 1962 Kefauver hearings. These hearings resulted in the Drug Amendments of 1962 to the Federal Food, Drug and Cosmetic Act. These amendments gave new regulatory powers to the FDA, and as a result many of the problems associated with generic drugs due to poor manufacturing practices are being reduced or eliminated. For example, the number of drug recalls have been increasing every year (F-D-C Rept., Dec. 5, 1966), indicating that the poorer quality products are being forced off the market.

There are those who would like to see products prescribed by generic name only, and those who oppose this concept. The former group assumes generic and product equivalency; the latter group does not agree that products are equivalent. Unfortunately, proponents of both sides of the question of generic equivalency have indulged in the luxury of stating half truths.

Let us take a close look at the major arguments presented by the opposing sides in the generic equivalency controversy.

For Generic Equivalency

1. All generic products are equivalent, because they must meet USP or NF standards. If they are equivalent, then one can buy the least expensive product.

Reply: These compendia set standards for purity and identification of drugs and pharmaceutical adjuvants and for the range of drug content in various dosage forms. The compendia do not guarantee therapeutic efficacy or give formulas and directions for manufacture of dosage forms sold. Some of the tests have limited value, e.g., the tablet disintegration test may not be a reliable index of drug availability from the tablet. In some cases, the assay may be misleading, e.g., assay for total iodine in Thyroid USP (Brune et al., 1962; Gatz, Ginsburg, and Salenger, 1962; MacGregor, 1961; Williams, Meister, and Florsheim, 1963). Yet the standards prescribed by these compendia generally reflect present day manufacturing practices, because the committees which establish the standards include industrial scientists.

2. The Defense Personnel Support Center buys only generic products. If these products are used in the Bethesda hospitals and given to our Presidents, generals, and Congressmen, etc., why are they not good enough for everybody?

Reply: The Defense Department buys its drugs under generic names based on competitive bidding. Since all drugs have generic names, and anyone can make generic drug products not covered by unexpired patents, the bidding is open to all. The Defense Department inspects the manufacturing facilities before accepting any bid. After the product is made, representatives from the department again come to the manufacturer to observe all the final tests performed on the product. By this procedure the Defense Department presumably receives a product that meets all its specifications. Not even a large hospital, let alone individual pharmacists, can make these inspections. The manufacturer of trademarked products competes under this system and when successful, sells his trademarked product under its generic name.

As the FDA increases the number of inspectors and is able to enforce its regulations more widely, drug products should be of higher quality, because more manufacturers will be operating under good manufacturing practices and with sufficient quality control.

Against Generic Equivalency

1. The large manufacturers of trademarked products are engaged in research to improve existing drugs and to discover new drugs. The prices of their drug products must be higher to support this research. The small manufacturers of generic products do not engage in research, and have never discovered a new drug.

Reply: The companies who undertake research, do not do it for altruistic reasons. They do it to gain competitive advantages and to make money. This is not to be condemned, but do not ask for public support for it. Many other industries do research and support research, e.g., chemical, electrical, petroleum, etc., but they do not ask for public sympathy. The pharmaceutical industry's research efforts do not justify the large price differentials that often exist many years after the product has been introduced, even if the successful products must pay for the failures.

Companies that discover a new, unique, and useful medicinal can obtain a patent which runs for 17 years after the date of issue (about three years after application). During this time they have a monopoly on this drug, and there is no competition, generic or otherwise. In this manner they can protect their investment and make a profit.

2. The large manufacturers of trademarked products have better quality control and can spend more time and money in the pursuit of excellence. Their products are purer and there is less likelihood of contamination.

Reply: This should be true, but they are not immune to mistakes and accidental contamination. This difference is slowly being reduced by increasing FDA inspections, and hopefully, this difference will continue to diminish. Mr. Hansen, program operations director of the Bureau of Regulatory Compliance FDA, stated that there were less than 70 recalls per year before 1962; there were 110 in 1964, 340 in 1965, and 449 in 1966. Of the 449 violations in 1966, 351 (78%) were due to violations of the good manufacturing practice regulations (F-D-C Rept., Dec. 5, 1966).

Purity and control of contamination is a problem that has plagued all manufacturers. Contamination due to diethylstilbesterol (Weber et al., 1963), estrogen (Hertz, 1958), selenium (Keller, 1960), penicillin, *Salmonella,* metal particles in opthalmic ointments, etc., have occured in products of both large and small manufacturers. They are more likely to occur due to poor manufacturing practices. In 1953, a study of vitamin preparations in Canada showed that subpotent products were produced more often under conditions of inadequate quality control than those manufactured under adequate control (Campbell, 1953).

3. The trademark is the identification of the manufacturer, and says he assumes responsibility for the product.

Reply: True! Many manufacturers are concerned about their "good name," and, therefore, may exercise better quality control. All manufacturers are responsible for their products whether they have a trademark or not. A trademark, however, is not synonymous with quality; anyone can obtain trademarks for his products.

4. Physicians, dentists, etc., prescribe by trademark because they are familiar with the company and its products and know the therapeutic results to expect from these products.

Reply: True! But, do they really know the company? How much of the prescriber's information comes from the company representative, and how complete is that information? Ciba was accused of not reporting toxicity data on Elipten (amine-glutethimide) (FDA Rept., 1966). Frosst made an inadvertent mistake in its reformulation of Dicumerol (bishydroxycoumarin) (Lozinski, 1960). Cannot the physician just as well become acquainted with certain companies that manufacture nonproprietary pharmaceuticals?

5. Some formula ingredients in a dosage form make generic prescribing hazardous for patients with certain diseases that require restricted caloric or sodium intake. When the physician prescribes by trademark, he knows what the patient will be getting.

Reply: How does the physician know what the ingredients other than the drug are? This information is not always readily available to the prescriber. The manufacturers do not list tablet formula ingredients and their amounts. One gram of sugar produces about four calories and no tablet would contain this much sugar as a diluent.

The prescriber must write to the company to ascertain the ingredients.

It is possible that a large manufacturer may be more concerned as to the ultimate user of his product, and therefore make adjustments in his formulation, e.g., omit calorie producing materials or sources of sodium ion. He would state this in the package inserts, etc.

6. When a generic product is prescribed, the same product is not always dispensed. This can lead to varying therapeutic results. A trademark or designation of the manufacturer insures that the same product is always dispensed.

Reply: The same product should always be dispensed unless it is no longer available. The source of the generic product should be noted on the prescription order by the pharmacist, to insure that the same product is dispensed when the prescription order is refilled.

When a patient is on long term drug therapy, e.g., insulin, penicillin, anticoagulants, thyroid, etc., a constant drug blood level in the therapeutic range is necessary to prevent relapse. A reliable product which will give the same absorption pattern is necessary. Changing brands may result in different levels of the drug in the blood. The second brand may be satisfactory for a patient just starting on the therapy regimen, but may not be satisfactory for refilling of a prescription order. Dosage adjustment is easiest when the patient is just starting therapy. The prescriber learns what to expect from each product regardless of the name.

7. The pharmacist has greater liability when filling prescriptions for products prescribed generically.

Reply: True, but what does this have to do with the proper treatment of patients?

If a trademarked product is prescribed, or the manufacturer of the product is stated on the prescription order, then the pharmacist has no choice as to what to dispense, and he is only liable under the implied warranty doctrine. If a generic product is requested and the manufacturer not designated, then the pharmacist has a choice. If he uses care and exercises his knowledge and experience to choose a reliable product from a source in which he has confidence, then he cannot be considered negligent, but the implied warranty doctrine still applies. Since the product is sold in interstate commerce, a new drug application has been approved by the FDA, so that the pharmacist does not have to guarantee efficacy. When products are prescribed by generic name, the pharmacist has more responsibility and hence more liability, but he should be willing to accept this.

8. Products sold under non-proprietary names do not maintain their potency as well as proprietary products.

Reply: This is one of the quickest tests that can be performed on a product by the FDA or a state agency. Judging from the results reported in the *Medical Letter* (Aug. 19, 1960), potency is rarely outside the set limits. On the other hand, taking the data collected by the analyst of the city of Birmingham, England, it appears that the potency of many English products does not meet official requirements (Bagnall and Stock, 1955). There is not sufficient published data available at this time to determine if this statement is true.

9. The large manufacturer has more staff, facilities, information, and manufacturing "know how" than the small company. Therefore the large manufacturer is better able to produce a more stable, uniform, and efficacious product.

Reply: The large manufacturers do not have a monopoly on information and the small manufacturer can hire knowledgeable and experienced personnel. The good manufacturing practice regulations and their interpretation are available to all. A great deal of stability data and incompatibility information has been published. Unfortunately, however, the availability of this information does not guarantee its application. The FDA has this knowledge too, and uses it in judging new drug applications, and in their plant inspections.

The argument does not end here. It has been demonstrated many times that there are numerous factors in the formulation and manufacture of dosage forms that may affect the efficacy of the product. Levy and Nelson (1961) and Delgado and Cosgrove (1963) review this problem in detail. These authors discuss the effect of variables such as drug particle size, sterility of ophthalmic preparations, rubber and polymer closures on multidose vials, ingredients of ointment and suppository bases, salts and esters of the parent drug molecules, and the ingredients added to the drug to permit manufacture of the dosage form such as solvent, sufactant, and fillers.

A commonly used filler for tablets and capsules, dicalcium phosphate, was found to depress blood concentration of tetracycline (Boger, 1959). Drug particle size may affect absorption of both oral and parenteral product (Levy, 1963a), e.g., sulfa drugs, griseofulvin, and insulin. Increasing the solubility of the tablet base increased the absorption of spironolactone (Levy, 1962). "Soft" tablets of phenylindanedione produced drug blood levels similar to that produced by loose powder in capsules, whereas "hard" tablets gave delayed and poor absorption (Schulert and Weiner, 1954). The salt form of PAS and the presence or absence of an enteric coating influenced the PAS blood level (Frostad, 1961). The salt form, molecular modification, and the formulation of aspirin tablets affected the salicylate blood level (Leonards, 1963; Levy and Gagliardi, 1963; Levy and Sahli, 1962). An in vitro test to determine the dissolution rate of a drug has explained why certain drug products, such as predni-

sone (Campagna et al., 1963) and tolbutamide (Levy, 1963b), were reportedly poorly absorbed. In an investigation of 18 commerically available tolbutamide tablets, it was found that the amount of drug dissolved at the end of one hour varied from 30% to 86% (Brudney, Stewart, and Eustace, 1963). In vitro studies (Levy et al., 1963; Levy and Gumtow, 1963) have shown several factors that influence the rate of tablet dissolution. Studies have shown that in commerically available sustained release products, drug absorption may vary from complete absorption immediately (no sustained effect) to almost no absorption (Shenoy, Chapman, and Campbell, 1959).

Stability of a product is important not only because the potency of the product must be maintained, but also because the decomposition products may produce untoward reactions, e.g., tetracycline (Frimpter et al., 1963; Editorial, *J. Am. Med. Assoc.*, 1963).

Isolated clinical cases have been reported in which a generic product gave poorer results than a trademarked product, e.g., prednisone (Keller, 1960), cortisone (Rosenheim and Ross, 1958, Boch, 1959; Bayliss, 1959), tolbutamide (Carter, 1963; Caminetsky, 1963), and phenylbutazone (Searl and Pernarowski, 1967). Even if ineffectiveness has not been shown, it may still be there.

We have learned much about the formulation and manufacture of dosage forms, often only after the product has been marketed. Oversights, even by large manufacturers, have come to light in this manner. The large manufacturer has the personnel and the facilities that would seem to make him more able to do thorough investigations before marketing a product, but he has not always done so.

The large companies also have produced drugs for a very limited market as a public service, because the drug is needed. This is not an argument against generic equivalency.

Conclusion

The truth about generic equivalency has not yet been determined. The arguments in the generic equivalency controversy are confounded by names, proprietary (trademark, brand name) as opposed to nonproprietary (generic, branded-generic), yet quality of the products is not necessarily related to any name. The efficacy and not the name of the product is important. The crucial question to ask is whether the product is clinically or therapeutically effective, giving reliable and uniform results.

Drugs called by their generic names are here to stay and more than likely their use will increase, especially as state and federal governments pay more of the medication bills. Kentucky and Louisiana already have issued lists of generic equivalents to trademarked products.

Meanwhile, the prescriber and the pharmacist still must ponder the question of therapeutic equivalency of drug products. What product is to be requested on a prescription order and what product is to be dispensed if the drug is prescribed by its generic name. More information is needed to answer this question. Clinical trials testing the hypothesis of generic equivalency are required. A national clearing house for information on the efficacy of drug products may be necessary. A national organization such as the American Pharmaceutical Association, American Medical Association, or the FDA, or an organization composed of representatives of interested groups could collect and disseminate the information to physicians, dentists, pharmacists, etc.

The U.S. Pharmacopeia and National Formulary monographs should include formulas and manufacturing directions for the various drug products. The specifications should be based on clinically demonstrated efficacy. The monographs could also include information on known factors that may impair the effectiveness of the product. Formula and process variations would be permitted only if the same therapeutic results can be demonstrated clinically.

The knowledge that the Defense Department has concerning its drug purchases and the use of these products in its facilities could be made available. Manufacturers, both large and small, could make available clinical and physiochemical data on their products, such as assay, drug content variation per unit dose, tablet dissolution rates, drug levels in blood or urine, and stability. It is important that the FDA or the proper state agency be informed of any suspected drug products so that substandard products may be removed from the market as rapidly as possible.

Finally, it is necessary that more people become aware of the true magnitude of the problem of generic equivalency. Because of the present lack of knowledge of which drug products are therapeutically equivalent, the prescriber and pharmacist must rely on their experience as to which products and companies are reliable. They *must* also continually search their journals for information on the therapeutic equivalency of products. Perhaps the pharmacist should compile information on generic and therapeutically equivalent drug products, which companies consistently make poor products, using sources as *Weekly Pharmacy Reports* (The Green Sheet), *F-D-C Reports* (The Pink Sheet), *FDA Papers* (U.S. Government Printing Office), and *The Medical Letter on Drugs and Therapeutics*. These compilations would then be available for the prescriber.

Acknowledgements

Discussions with and critical comments of Dean Warren E. Weaver and Dr. Albert J. Wasserman are gratefully acknowledged.

References

*BAGNALL, H. H., AND F. G. STOCK. Tablets of glyceryl trinitrate. *Pharm J.* 174: 437, 1955.

BAYLISS, R. I. S: Letter to the editor. *Lancet* 1: 98, 1959.

BACH, F. Dangers of "cheap" cortisone tablets. *Lancet* 1: 50, 1959.

BOGER, W. P., AND J. J. GAVIN. An evaluation of tetracycline preparations. *New Eng. J. Med.* 261: 827–832, 1959.

BRUDNEY, N., D. J. STEWART, AND B. T. EUSTACE. Rates of dissolution of tolbutamide tablets. *Canad. Med. Assoc. J.* 90: 90–981, 1963.

BRUNE, D. F., C. VAN GASTEL, P. J. DER KINDEREN, AND F. SCHWARZ. Myxoedematous coma with extreme hypothermia in a patient treated with a thyroid preparation of a very low biological activity. *Acta Endocrinol.* 41: 154–160, 1962.

CAMPAGNA, F. A., G. CURETON, R. A. MIRIGIAN, AND E. NELSON. Inactive prednisone tablets U.S.P. XVI. *J. Pharm. Sci.* 52: 605–606, 1963.

CAMPBELL, J. A. The potency of vitamin products. *Canad. Med. Assoc. J.* 68: 103–107, 1953.

CAMINETSKY, S. Substitution for brand-name drugs. *Canad. Med. Assoc. J.* 88: 950, 1963.

CARTER, A. K. Substitution for brand-named drugs. *Canad. Med. Assoc. J.* 88: 98, 1963.

CATZ, B., E. GINSBURG, AND S. SALENGER. Clinically inactive thyroid U.S.P. A preliminary report. *New Eng. J. Med.* 266: 136–137, 1962.

DELGADO, J. N., AND F. P. COSGROVE. Fallacies of generic equivalence thesis. I. Some physiologic factors influencing gastrointestinal absorption. *Texas State J. Med.* 59: 1008–1012, 1963.

DELGADO, J. N., AND F. P. COSGROVE. Fallacies of generic equivalence thesis. II. Physico-chemical and pharmaceutical factros affecting gastrointestinal absorption. *Texas State J. Med.* 59: 1106–1112, 1963.

Drug Topics Red Book 1967. New York: Topics Publishing Co., 1966.

EDITORIAL: Effects of tetracycline and degradation products. *J. Am. Med. Assoc.* 184: 143–144, 1963.

FDA Report on Enforcement and Compliance, pp. 19–20, Feb., 1966.

F-D-C Reports. 28(49), Dec. 5, 1966.

F-D-C Reports. 29(1), Jan. 2, 1967.

F-D-C Reports. 29(31), July 31, 1967.

F-D-C Reports. 29(33), Aug. 14, 1967.

FRIMPTER, G. W., A. E. TIMPANELLI, W. J. EISENMENGER, H. S. STEIN, AND L. D. EHRLICH. Reversible "Fanconi syndrome" caused by degraded tetracycline. *J. Am. Med. Assoc.* 184: 111–113, 444, 1963.

FROSTAD, S. Continued studies in concentrations of para-amino-salicylic acid (PAS) in the blood. *Acta Tuberc. Scand.* 41: 68–82, 1961.

HERTZ, R. Accidental ingestion of estrogens by children. *Pediatrics* 21: 203–206, 1958.

KELLER, W. Short communication concerning the difference in effectiveness of prednisone tablets [in German]. *Die Pharmazie* 15: 56, 1960.

LEONARDS, J. R. The influence of solubility on the rate of gastrointestinal absorption of aspirin. *Clin. Pharmacol. Therap.* 4: 476–479, 1963.

LEVY, G. Availability of spironolactone given by mouth. *Lancet* 2: 723–724, 1962.

LEVY, G. Effect of particle size on dissolution and gastrointestinal absorption rates of pharmaceuticals. *Am. J. Pharm.* 135: 78–92, 1963a.

LEVY, G. Effect of dosage form properties on therapeutic efficacy of tolbutamide tablets. *Canad. Med. Assoc. J.* 90: 978–979, 1963b.

LEVY, G., J. M. ANTKOWIAK, J. A. PROCKNAL, AND D. C. WHITE. Effect of certain table formulation factors on dissolution rate of the active ingredient. II. Granule size, starch concentration, and compression pressure. *J. Pharm. Sci.* 52: 1047–1051, 1963.

LEVY, G., AND B. A. GAGLIARDI. Gastrointestinal absorption of aspirin anhydride. *J. Pharm. Sci.* 52: 730–732, 1963.

LEVY, G., AND R. H. GUMTOW. Effect of certain tablet formulation factors on dissolution rate of the active ingredient. III. Tablet lubricants. *J. Pharm. Sci.* 52: 1139–1144, 1963.

LEVY, G., AND E. NELSON. Pharmaceutical formulation and therapeutic efficacy. *J. Am. Med. Assoc.* 177: 689–692, 1961.

LEVY, G., AND B. A. SAHLI. Comparison of the gastrointestinal absorption of aluminum acetylsalicylate and acetylsalicylic acid in man. *J. Pharm. Sci.* 51: 58–62, 1962.

LOZINSKI, E. Physiological Availability of dicumarol. *Canad. Med. Assoc. J.* 83: 177–178, 1960.

MACGREGOR, A. G. Why does anyone use thyroid B. P. *Lancet* 1: 329–332, 1961.

**Medical Letter on Drugs and Therapeutics.* 2(17), 65, Aug. 19, 1960.

ROSENHEIM, M. L., and E. J. ROSS. Dangers of "cheap" cortisone tablets. *Lancet* 2: 1371, 1958.

SCHULERT, A. R., AND M. WEINER. The physiologic disposition of phenylindanedione in man. *J. Pharmacol. Exp. Therap.* 110: 451–457, 1954.

SEARL, R. D., AND M. PERNAROWSKI. The biopharmaceutical properties of solid dosage forms. *Canad. Med. Assoc. J.* 96: 1513–1515, 1967.

SHENOY, K. G., D. G. CHAPMAN, AND J. A. CAMPBELL. Sustained release in pelleted preparations as judged by urinary excretion and in vitro methods. *Drug. Standards* 27: 77–84, 1959.

WEBER, W. W., M. GROSSMAN, J. V. THOM, J. SAX, J. J. CHAN, AND M. P. DUFFY. Drug contamination with diethylstilbesterol. Outbreak of precocious puberty due to contaminated isonicotinic acid hydrazide (INH). *New Eng. J. Med.* 268: 411–415, 1963.

Weekly Pharmacy Reports 16(1), Jan. 2, 1967.

WILLIAMS, A. D., L. MEISTER, AND W. H. FLORSHEIM. Chemical identification of defective thyroid preparations. *J. Pharm. Sci.* 52: 833–839, 1963.

WILSON, C. O. Statement to Subcommittee on Anti-Trust and Monopoly of the Senate Committee on the Judiciary, May 10, 1960.

* Refers to only the first of a series of articles reporting results of assays on various commonly prescribed drugs.