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Law Notes

Albert Rolland S.A. v. SmithKline Beckman Corp. United States District Court for the Eastern District of Pennsylvania; judgement of May 23rd 1990.

On May 23rd 1990, the U.S. District Court for the Eastern District of Pennsylvania found that Plaintiff Albert Rolland S.A., a French corporation, had failed to prove by a preponderance of the evidence that defendant SmithKline Beckman Corporation's failure to report accurately and in a timely manner to the FDA material accruing to it on adverse hepatic reactions to the drug Selacryn was the proximate cause for the FDA to direct that Selacryn be removed from the United States market, or that Rolland lost any royalty payments to which it might otherwise have been entitled because of any breach of duty owed by SmithKline with respect to the licensing and marketing of the drug.

The case is an important one in that when two pharmaceutical companies are opposing parties in civil litigation relating to adverse effects of drugs the proceedings can throw an important light on current concepts of a manufacturer's duty in this regard. Such cases are often settled out of court or in arbitration behind closed doors; this is one of the very few to be published. The facts, distilled largely from the judgement but in part from publicly available material, were as follows:

On September 4th 1973 Rolland granted Smith, Kline and French Laboratories (SKF), a subsidiary of SmithKline Beckman Corporation, a license to "develop, investigate and promote as if it were its own product" the new diuretic agent tienilic acid. The drug was intended as primary therapy for physicians treating hypertensive patients. Unlike most other hypertensive agents then on the market, tienilic acid had the ability to lower serum uric acid; this was conceived as an important marketing advantage and very large sales were foreseen.

Tienilic acid had been patented in the United States by CERPHA, Rolland's predecessor in interest, but had not yet been approved for sale. It had already been registered for marketing in France. The license agreement provided for royalties to Rolland on the basis of SmithKline's sales. SmithKline was given exclusive rights in the United States and a number of other countries, though renaming the drug "ticrynafen" and selling it under the trade name "Selacryn". Rolland named its drug "Diflurex" and began aggressively marketing it in 1976. Tienilic acid was licensed separately to a Swiss company for sale in Switzerland only.

The license agreement having been signed, SmithKline proceeded to prepare for obtaining the necessary FDA approval. In order to manufacture and market a drug in the United States, the FDA requires the filing of an Investigational New Drug Application (IND), followed by a New Drug Application (NDA). SKF undertook a series of studies in the U.S. in order to obtain proof of efficacy and

safety and submitted reports on these and on the evidence available from abroad. On May 2nd 1979, the FDA granted SmithKline permission to manufacture and sell Selacryn as a prescription drug. However, nine months later, on January 15th 1980, the FDA ordered the drug removed from the market because of a series of adverse hepatic (liver) reactions which had been reported to the agency. Dr J. Richard Crout, Head of the Bureau of Drugs of the FDA, himself took the unusual step of informing regulatory agencies in other major countries by telephone of the FDA's action. Shortly thereafter, and following adverse publicity in the mass media in various countries, the SKF took the decision to withdraw the drug from all markets for which it had a license. In France, Rolland continued to sell the product but the regulatory agency required that physicians be warned of the hepatic effects. From then on sales fell, ultimately to negligible levels. In Switzerland the licensees, who had received reports of several instances of adverse liver effects, took the drug off the market on their own initiative.

SmithKline admitted to concealing some of the adverse hepatic reactions from the FDA. In fact, prior to official approval of the drug in 1979 SmithKline had received reports of twenty two cases of abnormal liver function tests; there were also two positive rechallenges, i.e. cases in which the effect had reappeared when the drug was administered again. SmithKline had also been in the possession of information on studies in Japan in which similar adverse liver reactions had been reported. Despite this, SmithKline had reported only eight cases of possible hepatic reactions to the FDA prior to drug approval, seeking to attribute even these to an outbreak of viral hepatitis in San Francisco. For that reason, the approved labelling in the U.S.A. had noted merely that "Abnormal liver function tests and jaundice have been reported in a few patients treated with Selacryn; however, no causal relationship has been established."

For such reasons, following withdrawal of approval of the drug, the FDA in 1980 successfully brought criminal proceedings (cited on pp. 64–65 of the present judgement) against SmithKline and certain of its executives. Each entered a plea of guilty or *nolo contendere* to some or all of the charges.

The present civil case was brought much later. Claiming very substantial damages, Rolland in essence claimed:

a. that if SmithKline had behaved in an open manner with the FDA from the start and properly reported the known or suspected adverse liver reactions during clinical testing, the company would have received a less acute response from the FDA when the problems with the marketed drug became known, e.g. the FDA would have required a warning to physicians, performance of monitoring tests during treatment or some narrowing of the indications but would not have removed the drug from the market. Such a reaction would not have led, directly or indirectly, to the virtual collapse of the drug worldwide.
b. that, in consequence, SmithKline's failure to report adverse reactions was the cause of severe loss and damage to Rolland.

There were a number of subsidiary claims, e.g. one as regards a supposedly deviant synthesis of the drug in the U.S.A., but this was not proceeded with.

Essentially, Rolland appears to have maintained to the end that minor liver reactions were only likely to occur in 1:10,000 patients using its product, and that it was therefore entirely defensible to sell it. There was also a remarkable claim, dismissed by the civil court, that SmithKline could have foreseen the sensational reporting of the drug's injurious nature in the mass media, and thus must be held responsible for the consequences thereof.

The case raises interesting questions as to how the incidence of adverse reactions is calculated by pharmaceutical companies. Rolland's calculation was almost certainly based upon a comparison between the adverse hepatic reactions reported through its salesmen or other channels (and regarded as credible by its medical staff) and the total volume of sales, thus failing to take into account the very considerable degree of under-reporting. The civil court in Philadelphia, having taken into account the nature and extent of the evidence of liver damage with the drug, quite simply concluded that they were such as to render it unfit for its intended use. That conclusion was reached after a careful review by the court of various other drugs which have remained on the market despite hepatic reactions, since their benefit or uniqueness outweighs the risk, a situation which did not pertain with tienilic acid. To quote the impressive judgement by Vanartsdalen S.J.: "... if SmithKline had properly reported the results of the clinical tests to the FDA, the New Drug Application for Selacryn would never have been approved by the FDA.... Plaintiff did not prove by a preponderance of the evidence that the wrongdoing of SmithKline, i.e. the failure to properly report to the FDA the known adverse hepatic reactions, was a proximate cause of the decline of sales of Diflurex rather than the inherent dangers of the product itself".

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