



LEXSEE 189 FED. 95

**PARKE-DAVIS & CO. v. H. K. MULFORD CO. (two cases)**

Circuit Court, S.D. New York

189 F. 95; 1911 U.S. App. LEXIS 5245

April 28, 1911

**OPINION BY:** [\*\*1] HAND**OPINION**

[\*97] HAND, District Judge. I will first take up the consideration of the mother patent, No. 730,176, and of the issue of infringement, which the complainant alleges to be double: First, the dry powder; and, second, a sodium chloride solution of the boric acid salt of the dry powder. The dry powder Adrin is produced by a somewhat different process from Takamine's "crude product," Adrenalin; but upon the divergence of those processes I do not mean to pass, for it does not seem to me necessary. The crucial step which Takamine discovered was that the base -- it is true with some impurities -- could be directly precipitated by an addition of ammonia, or strictly of caustic alkali and ammonium chloride, which together liberate the ammonia, which in turn effects the precipitation. This being a product patent, it is of no consequence whether the defendant's extraction in the first place by alcohol and trichloroacetic acid is the equivalent of an extraction by water and a subsequent addition of alcohol to precipitate albuminous substances. The purpose of both these steps is the same, and the following and crucial step is certainly the same. It may be possible that the [\*\*2] preliminary steps result in eliminating different substances, and indeed that must be so as appears [\*98] from the difference in the proportion of inorganic contamination in each; but the only question upon infringement is whether Adrin falls within any of the claims here in suit.

It certainly falls within claim 1 if it be free from inert and associated gland-tissue. No one supposes that these words mean that the actual cellular structure of the tissue

remains, for the process involves its destruction, though, were this not so, the words might quite naturally have been so understood. That meaning being eliminated, what is the most natural meaning? I think it can only mean those organic chemical substances, regardless of the structure, out of which the gland-tissue is composed and of the same chemical composition in which they exist and make up the gland-tissues. To these may well be added those substances arising in the normal metabolism of the tissue of other organs or of the glands themselves, which, being carried in the blood, might remain in the glands at death. Such of these substances as have not the physiological activity of the "principle," now known, are the "inert [\*\*3] and associated gland-tissue" mentioned in the claim. Nor can this mean a new chemical disintegration of the "glandtissue" so described of which there is much in Adrenalin and over six times as much in Adrin. This substance, ammonium magnesium phosphate, is a new and inorganic substance arising from the regrouping of atoms which have, it is true, been a part of the gland-tissue, but which have been broken from the molecules which constituted their original form. Since the chemical distinction between "substances" depends, not upon the presence of the same atoms, but upon their definite structural association in known proportion into molecules, it is illegitimate to consider as "gland-tissue" those substances which, while they represent in part the same atoms, have by rearrangement and by addition of new atoms created new molecules. Moreover, the patent itself corroborates this view. The crude product was the patented substance, and it appears (page 2 lines 50-70) that the patentee understood perfectly well that without purification there would be inorganic matter in the crude product. Moreover, the amendment in the Patent Office of the words "inert constituents" to the words "inert [\*\*4]

and associated gland-tissue" clearly indicate the patentee's intention.

The question remains, however, whether Adrin is in fact free from organic tissue, and upon this there is some dispute. Sadtler found that under the biuret test Adrin showed a rose color. This indicated proteids, and for organic sulphur he used the nitro prusside sodium test. These tests in Chandler's opinion are so delicate that they will detect a mere trace, and Sadtler does not dispute that fact. The question may perhaps be best decided by considering first whether Adrin is substantially as free as Adrenalin from organic matter, and then considering whether Adrenalin itself is "practically free" within the meaning of the claims. One test much relied on by both experts is that of physiological activity. Adrin, having a much higher ash than Adrenalin, ought to show a correspondingly lower activity. In fact, it shows a more than correspondingly lower activity, thus indicating the presence of some other substance not inorganic, i.e., organic. It would seem that Adrin had therefore somewhat more organic contamination [\*99] than Adrenalin. However, in view of the very baffling results of the physiological [\*\*5] experiments compared with the other tests, I am not disposed to press this quantitative comparison too far. Indeed, my own belief is that the matter has not been thoroughly cleared up in the testimony at all, and that considering the similarity of the processes, the use of each substance practically, and the approximation of result physiologically, the two are near enough to be an infringement one of the other. Indeed, the contrary is not sharply urged. However, the question remains whether Adrenalin is itself "practically free," and upon that issue the burden is on the defendant, unlike the issue of infringement, because it involves the question whether the claim covers the disclosure.

Sadtler upon this question calls attention to the results of his modifications of Von Furth's process, in which he showed much ingenuity. These so-called Von Furth intermediate products were three: Precipitate 5-A-3, Precipitate 1-B, "Crystalline Base." The first and third were negative in reaction to these biuret and other tests, and the second showed only a slight reaction. This indicated that all were free, or nearly free, from organic impurities; yet the amount of ash in each was very different. [\*\*6] In 5-A-3 it was over 31 per cent., in 1-B it was about 7 per cent., and in "Crystalline Base" about 26 per cent. Now the physiological activity of 5-A-3 equalled that of crude Adrenalin, though the ash was

more than seven times as great, while that of "Crystalline Base" was only one-eighth that of either. Similarly, 1-B had an activity equal to Adrenalin; the ash being also substantially the same. Both experts conceded that the sole physiologically active agent is the principle itself, and the result seems to be that the reason for the discrepancy between the activities must be the presence of organic substances not detected by Sadtler's tests. Against this there is Chandler's opinion that the conditions of crystallinity preclude the presence of organic matter, an opinion shared by Sadtler when dealing with Moore's Dialysate, and we have in the case of "Crystalline Base" purely negative test reactions. Why 5-A-3 shows an activity so disproportionate to the ash, I cannot say; it shows a similar disproportion to the Adrenalin purified, though less absolutely. I think that, to solve this apparent contradiction of evidence, one must have recourse, first, to the fact that the use [\*\*7] of Adrenalin has been now sufficient to show that it is "practically free," and to the presumption from the patent itself that the disclosure answers the claims. Apparently the only difficulty ever arising from the intravenous use of Adrenalin was due to too strong solutions. These did cause destruction of tissue at the point of injection; but even they gave no evidence of contamination. I therefore hold that Adrin infringes claim 1.

Claim 2 is the same, with the addition of the words that the product is a "whitish" color. It appears that neither crude Adrin nor Adrenalin is, properly speaking, white. Each is a light yellow brownish color. Commercial Adrin is, however, near enough to a white to comply with the claim.

Claim 3 is like claim 1, except that the words "inert constituents" are substituted for "inert and associated gland-tissue." Now it undoubtedly [\*100] appears in the specifications that the patentee did not suppose his crude product was wholly free from inert constituents, because he provided means of purification. However, the changes in the Patent Office clearly show that he must have meant something different by the phrase "gland-tissue" from what he [\*\*8] meant by the phrase "inert constituents," and I do not think that any one can properly construe those words as not including ammonium magnesium phosphate. His own product did not contain a high percentage of ammonium magnesium phosphate -- less than five per cent. -- and it may well be that that is within the terms practically free; but the defendant's Adrenalin contains nearly seven times as much as that. I do not see

how by any stretch of words that can be held to be free from inert constituents.

In claim 4 it is provided that the product shall melt at about 207 degrees centigrade. Now Adrin has not been shown to have melted even at 220 degrees and upwards. The difference proportionately is not great, and the patent is entitled to have a generous construction, yet I cannot think that a product is affirmatively shown to have a melting point of about 207 degrees when there is no proof of when it will melt at that heat, and there is proof that it will not melt at 220 degrees. It is true that Chandler says (Q. 10) that he had subjected the Adrin to all the tests required by the patent, and found that they corresponded; but this general statement cannot stand in the face of the [\*\*9] express testimony of Sadtler upon that particular experiment. If the explanation of the experts be correct, that the high melting point is due to the mineral impurities, this finding is consonant with the finding that Adrin is not free from inert constituents. I therefore hold claim 4 not infringed.

Claim 6 is for a crystalline substance, and that Adrin certainly is. The only question which can arise is as to whether the base is crystalline, or whether it owes its crystalline character to the mineral admixtures. This claim, I think, should be construed as meaning that the substance is crystalline, however large or small the degree of mineral impurities may be. It is of no consequence if the crystals are composed in part of the earthy matter. So far as the substance is purified, the crystals will increasingly become crystals of the active principle.

Claim 7 is eliminated by my decision in regard to the melting point.

The new characteristic of claim 9 is that it shall have an alkali reaction. I do not understand that this is denied, and the same is true of claims 11 and 12.

The defendant's expert concedes that claim 13 covers the substance and claim 14 is involved in the [\*\*10] decision of claim 12.

The defendant's Adrin answers all the characteristics of claim 15; the only question being as to the crystalline substance, which matter I have already passed upon.

Obviously the Adrin cannot infringe claim 16. I therefore find that the dry product infringes claims 1, 2,

6, 9, 11, 12, 13, 14, and 15.

The next question is whether the defendant's solution infringes any of the claims of patent No. 730,176. The solution is of a salt of Adrin [\*101] made with sodium chloride and boric acid, and this salt is dissolved in water and marketed with a preservative to keep it from decomposing. I entirely agree with the complainant that patent No. 730,176 covers solutions in general, and that the criticisms of the claims by the defendant in that respect are trivial. Not only would this be true independently, but the patent itself specifically provides that it shall cover solutions as well as the dried product. If, therefore, the alleged infringing solution was only a water solution of Adrin with a preservative added, I should have no trouble in holding that it infringed all the claims mentioned above. But, in view of patent No. 753,177, it seems to me quite [\*\*11] clear that the earlier patent was not intended to cover any salt of the base itself. This is expressly recognized by the patentee himself on page 2, lines 88-93, where he says:

"Salts of the substance possess the same physiological properties as the substance itself and constitute new substances not claimed herein, but claimed in another application."

Again, claim 7 is for a substance "soluble in acids and forming salts therewith." The second patent was divided out upon the insistence of the examiner, who found that the bases of the salt were substances of separate and distinct chemical composition. Whatever, therefore, may be the proper scope of the claims of the patent, there can be no doubt that the patentee did not intend them to cover any salt, but that he distinguished the salt as a new substance not claimed in his mother patent. It so happens in my judgment that in this respect he was very fortunate, as will later appear.

The question next arises of the validity of all claims infringed by the dry product. This is attacked, first, because they are anticipated in the art; and, second, for a number of technical grounds which I shall take up in turn. The anticipations [\*\*12] I will deal with first, because, in the view which I have taken of the two patents, that is the simpler consideration. The patentee originally attempted to claim the active principle itself. This was in his first application where he claimed process and product; but the examiner would not allow these claims, basing his rejection upon his interpretation of *American Wood Paper Co. v. Fibre Disintegrating Co.*, 23 Wall. 566, 23

L. Ed. 31, that no product is patentable, however it be of the process, which is merely separated by the patentee from its surrounding materials and remains unchanged. After some argument upon this score, the patentee voluntarily divided out the product patents expressing such intention on December 22, 1902. When he came to file his product patent, he proceeded upon the same theory, first claiming the active principle of the glands. The examiner required a division, but raised no objection to the form in which these claims were given. In his amendment of March 13, 1903, which was about two months after his first application, he changed all the claims so that they read substantially as they do at present and were not limited to the active principle. I think [\*\*13] that this effected a substantial change in meaning, and that the defendant is right in insisting that the claims are now broader than a mere claim for the chemically free base, or active principle, and that they cover any substance [\*102] which possesses the physiological characteristics of the glands and is substantially pure. By doing this, Takamine therefore laid himself open to any anticipation which was a substance of that character, even though the substance did not contain the chemically pure base.

For example, if Abel had isolated the base of his monobenzoylated salt, or Von Furth the base of his sulphate, Takamine would have been open to attack by either upon the theory that, even conceding that in neither case the base was that of the active principle alone and not in chemical composition, yet as a substance it corresponded to the claims. This he could have avoided had he limited his claims to the isolation of the active principle itself, and it would then have been of no consequence whether Abel's or Von Furth's compound had practically answered as well as his own. Nevertheless, as I have already said, the claims of patent No. 730,176 do not cover a salt and are [\*\*14] especially designed to exclude a salt. It so happens, moreover, that all of four alleged anticipating products never existed except in the form of a salt. This Sadtler concedes. When I come to consider patent No. 753,177, I shall take up each of these products separately to see whether they anticipate the claims of that patent which covers the salts; but the only necessary question here is: Since they were not actually themselves bases, whether pure or impure, whether it involved invention to produce the base of Takamine. This question does not deserve any extended consideration. The difficulties of the old products were so great as made any substantial advance from them

important. It is enough that Takamine was the first to isolate any base whatever, all other products existing in the form of a salt, because prior investigators were all trying to reduce the principle down as purely as possible. The invention was therefore novel.

The first of the technical objections is because of the vague character of the claims of the patent and their fraudulent reduplication. I can see no basis whatever for this contention. As I have already said, the claims were not for the active principle, [\*\*15] nor for the product of the process. Of course claims for a product not defined as the product of a process must contain in themselves adequate differentia, or they will not be good ( *Cochrane v. Baddische Anilin Fabrik*, 111 U.S. 293, 310, 4 Sup. Ct. 455, 28 L. Ed. 433); but the only valid objection to multiplication of claims is when it appears that the patentee is trying deceitfully to go beyond the fair scope of his invention. I can see no evidence of that here, and the fact that I have sustained the broader claim is a complete answer to such a position. That Takamine in a number of instances should have added other claims more circumscribed in their scope was natural enough, and what every prudent solicitor ought to do. No one can in advance know how far anticipations will go or how little in the end his patent will cover. There is nothing improper, so far as I can see, in first putting your claims as broadly as in good faith you can, and then, ex abundanti cautela, following them successively with narrower claims designed to protect you against possible anticipations of which you are not yet aware. Indeed, the very case upon which the defendant relies ( *Matheson v. Campbell*, [\*\*16] 78 Fed. 910, 917, 24 C.C.A. 384) shows [\*103] the necessity of claims as broad as one can honestly support. If any one of the specified differentia of the claim is missing, the defendant's product does not infringe; if any anticipation includes all the differentia, the claim is bad. To pass between this Scylla and the Charybdis, I think a patentee may fairly be entitled to bend sails upon many yards. The question as to whether or not he is acting colorably is not answerable on general principles. He may, of course, attempt to monopolize more than was fairly his due, but in this case I have already said that I do not think he did so, especially as he was the first person who had ever isolated a nonsalt substance relatively pure.

Nor do any of the claims call for only an "effect." That rule I understand to mean nothing more than that the claims must not be too abstract. I do not think that any of

the claims in the patent are at all abstract, but each forms a concrete enough criterion to test the product intended. There is no claim which selects a single characteristic or function. The very phrase "physiological characteristics and reactions of the suprarenal glands" refers [\*17] to some 15 lines of the specification (page 2, lines 102-116), and this phrase is always coupled with at least two other differentia. That is sufficient to identify the product in my judgment in every case.

Nor is the patent only for a degree of purity, and therefore not for a new "composition of matter." As I have already shown, it does not include a salt, and no one had ever isolated a substance which was not in salt form, and which was anything like Takamine's. Indeed, Sadtler supposes it to exist as a natural salt, and that the base was an original production of Takamine's. That was a distinction not in degree, but in kind. But, even if it were merely an extracted product without change, there is no rule that such products are not patentable. Takamine was the first to make it available for any use by removing it from the other gland-tissue in which it was found, and, while it is of course possible logically to call this a purification of the principle, it became for every practical purpose a new thing commercially and therapeutically. That was a good ground for a patent. *Kuehmsted v. Farbenfabriken*, 179 Fed. 701, 103 C.C.A. 243; *Union Carbide Co. v. American Carbide Co.*, [\*18] 181 Fed. 106, 104 C.C.A. 522. That the change here resulted in ample practical differences is fully proved. Everyone, not already saturated with scholastic distinctions, would recognize that Takamine's crystals were not merely the old dried glands in a purer state, nor would his opinion change if he learned that the crystals were obtained from the glands by a process of eliminating the inactive organic substances. The line between different substances and degrees of the same substance is to be drawn rather from the common usages of men than from nice considerations of dialectic.

A final objection goes to the fact that the patent covers solutions as well as dry products, and that this solution is not stable. I agree with the defendant that the solution mentioned in patent No. 730,176 does not include a solution of the salt, and it is also in evidence that a plain aqueous solution is not stable in any sense of the word. On page 3, line 23 et seq., the patentee uses the following words:

[\*104] "The substance may be kept in the solid

form or in solution, and, where in the claims I have used the terms 'substance,' I desire it to be understood as referring to either the solid [\*19] or the solution form of the substance, except when such signification would be plainly inconsistent with the terms of the particular claim."

There is indeed no way to avoid the conclusion, therefore, that the patentee has wrongfully specified his aqueous solution as stable, unless such an adjective would be plainly inconsistent with the terms of the particular claims. Now the infringed claims in which this word appears are Nos. 1 and 2. In these it is used in conjunction with the word "concentrated," and it appears beyond a doubt that the solution is not a concentrated substance, but, on the contrary, a highly dilute one. Thus, page 2, lines 104-107, the specifications mention solutions of 1 to 1,000 and 1 to 10,000. Moreover, the art knew that the only solutions of the suprarenal gland therapeutically possible were very dilute, though not to the extent indicated in the specification. I think that, considering this knowledge both from the patent itself and from the existing art, it is apparent that the two claims are "plainly inconsistent" with a solution, though the complainant appears to be content otherwise. And therefore I think that a solution is not comprehended by the [\*20] adjective "concentrated." Indeed, without more knowledge than that it was a solution of the base, I should have no trouble in holding that it was not "concentrated." If so, the objection disappears to the instability of the solution, and the claims are valid, for no one asserts that the crystals are instable.

I therefore hold that dry Adrin infringes claims 1, 2, 6, 9, 11, 12, 13, 14, and 15.

The next question is of patent No. 753,177, and the first matter there to be decided is of infringement. The defendant's solution is concededly a sodium chloride solution of the borate of the Adrin base with some preservative added. In the first place, one can easily dismiss the suggestion that only claim 2 is for a solution. It is trivial to urge that the substances mentioned in the other claims are solids and so do not cover themselves when in a water solution. What then are the claims? They are in three groups of two each. The first is for the "principle" which can only be Takamine's base -- and any other stabilizing substance. The second is any substance having the properties of the base, and still stable. The third is for a stable salt of the "herein-described product,"

or the [\*\*21] base. It is to be observed that the first and third groups are therefore explicitly for the base itself, and it is only the second which is answered by any substance defined only by its qualities. While this is not of consequence so far as infringement goes, it becomes so when the question arises of anticipation.

The only serious question which does arise upon the issue of infringement is whether the defendant's solution is "stable" or "inert" to the action of the air; these words being defined as used only in "a practical or commercial sense." The complainant attempts to help out this word by insisting that at least in claims 1 and 2 the addition of the preservative such as chloretone or chloroform can be considered as [\*105] within the nonsuprarenal substances which insure stability. It is conceded that the defendant's solution, and, for that matter, the complainant's also, is commercially stable, when to the salt solution is added some such preservative. I do not think, however, that the complainant can insist upon the use of the preservative as a part of the patent. Such use is stated on page 2, lines 39-41, to be optional, and it is well settled that what is optional [\*\*22] in a patent cannot be taken as part of the patent itself. *Sewall v. Jones*, 91 U.S. 171, 185, 23 L. Ed. 275. Therefore the patent must be regarded as only including a substance which is stable without the addition of a preservative. Moreover, in claims 1 and 2 the nonsuprarenal substance is asserted to be in chemical combination with the active principle, and it does not appear that the preservative is in chemical composition. That phrase, of course, includes the molecular combination of the acid with the base, even though the molecules of each retain their own integrity atomically; but it cannot include the addition of a preservative, which so far as appears is only in physical admixture with the salt so created. It is quite clear that the words "chemical combination" in claims 1 and 2 are intended to refer to the same kind of combination which claims 5 and 6 intend when claim 6 speaks of the salt as being itself a "stable compound" even when in a water solution. This conclusion is further confirmed by the fact that on page 1, line 38, the patent states that the solution of the salts of the base and water is commercially stable; and further (page 1, lines 49-53) that the water [\*\*23] solution refrains from absorbing the oxygen of the air to such an extent as to be practically stable for ordinary commercial handling use and sale. The same statement is also substantially repeated on page 1, lines 85-90.

The question therefore arises: What is commercial

stability? There is no question that the boric acid adds to the stability of the base itself in solution, though even in a stopper bottle the defendant's Adrin without the preservative elements will not last for a long time. There is no evidence of just how long it takes for the solution without a preservative to become unfit for use. A slight discoloration owing to oxidation from contact with the air is not sufficient to be injurious, for it is only when after exposure it becomes a dark color that its therapeutic use ceases. Making allowance for the character of the patent itself which is in my judgment a pioneer, I am not disposed to construe the words "commercially stable" as not extending to the defendant's solution. That Takamine could not have meant more than the stability which in fact exists is indicated by the fact that it was known when the patent was applied for just what was the actual degree of [\*\*24] stability of the solution without a preservative, and it can hardly be supposed that he was deliberately intending to misinform the public upon a matter as to which he could have no possible reason for so doing; at least, I can see nothing which he could gain by overstating in his patent the stability of the solution. Rather I prefer to interpret the words as controlled by his actual knowledge and as meaning only such stability as he himself then knew to exist. This is especially so since the alternative seems to be to hold the patent void as not containing an adequate disclosure to support the claims. I do [\*106] not feel disposed to take from the patentee the results of his ingenuity because he did not say that it would prove in practice desirable to use some one of the well-known preservatives. I therefore hold that the solution violates all six claims of the patent.

The question next arises of validity, and upon this the defendant urges two objections: First, the novelty of the patent; and, second, its forfeiture, because it has been publicly used in this country for more than two years prior to the filing of the application.

At the taking of testimony, the defendant [\*\*25] introduced a great number of allegedly prior compositions; but in its brief it has omitted consideration of any but four, which are respectively Moore's Dialysate, Abel's Monobenzoylate Salt, Von Furth's Sulphate, and Von Furth's Iron Compound. The defendant's failure to deal with the other substances mentioned in the testimony indicates that it does not rely upon those. It will be necessary therefore to consider only the four above mentioned.

It is now supposed that the active principle which Takamine first isolated exists in the gland itself in the form of a salt; that is to say, in combination with an acid. For some time after the discovery in 1894 by Oliver and Schafer of the physiological action of the suprarenal glands, it had become customary to make therapeutic use of the substance by drying and powdering the glands and selling them in the form of a liquid solution preserved with chloretone. This the complainant itself had done, and the substance in that form attained a large and important use in therapy. Indeed, it was on occasion even used in intravenous injection; but, as the principle itself in this form was in physical admixture with many organic substances so as [\*\*26] to form an apt nidus for bacteriological culture, the result was an extremely dangerous substance for injection into the body. The complainant, it is true, speaks of the demonstrated asepsis of the substance in this form; but that, I think, was too strong a statement, not in fact justified by the facts, and, indeed, as soon as Takamine Adrenalin became known, the use of the dry gland solution with a preservative practically disappeared altogether, so that the disadvantages of the original substance have the clearest proof in subsequent history. The too extravagant claims, even, of the complainant, for the aseptic character of the powdered dried glands, must therefore, in the light of subsequent facts, be disregarded.

Much had been ascertained about the substance itself prior to Takamine without which his invention would certainly have been impossible; but no one, as I have already said, had succeeded in chemically isolating the principle as now chemists suppose has been done. Indeed, it was not originally known whether the principle existed as a definite chemical compound in the gland itself, or whether it might not be a condition resulting from the coexistence of definite substances [\*\*27] in the gland which might altogether disappear upon their dissociation. It is too much to say that the last statement remained uncertain after the disclosures of Abel and Von Furth; but the defendant itself does not assert that they ever succeeded in definitely isolating the principle out of combination.

[\*107] The chemical reactions of what now is ascertained to have been, and what was supposed to be, the active principle, had undoubtedly all been known just as they are set forth in the patent No. 730,176; and it was by these reactions that Takamine in part assured himself that the substance which he had obtained was in fact the

active principle, though the final test must rest, and did rest, upon its physiological activity. In this case, however, as I have construed the first patent, these prior compounds are not there of consequence; but in view of the prior discovery of allied substances as a salt, and also in view of the fact that patent No. 753,177 refers to and so incorporates into itself the disclosure of No. 730,176, it becomes essential to consider whether any of the former salts of the active principle anticipate the claims of No. 753,177.

The first of the four [\*\*28] products is Moore's Dialysate. This discovery is set forth in an article in the *Journal of Physiology* by B. Moore, April, 1895. The successful experiment was described as follows: The dried glands were first extracted with ether. Then they were placed in absolute alcohol for three weeks. Both these steps were to remove the other substances from the glands. An extract was then made with a small quantity of distilled water, and the filtrate thus arising was allowed to dialyze into distilled water through parchment. The defendant has put in evidence three products of this process, the first of which showed an activity of about one-third that of Adrenalin; the second was the process carried down by evaporation to a crystalline salt; and the third was the precipitation of the active base from this salt by ammonia. The third is obviously the creation of Takamine's subsequent invention, and is not claimed to be an anticipation. There is considerable dispute as to the importance of the changes in the process which Sadtler adopted, particularly because he protected the extract with water during digestion by a film of paraffine so as to prevent any oxidation from contact with the atmosphere. [\*\*29] Sadtler, on the other hand, insists that all the devices which he used were so common for chemists that it must be presupposed as an incident to Moore's process. However that may be, the resulting activity of the product is only one-third that of Adrenalin, and such a deficiency can hardly be accounted for except by the hypothesis that the substance is not as free as Adrenalin from inert substances. The Dialysate, it is true, shows no reaction to the biuret test which discovers proteid matter, and yet there is no reason to suppose that all inert substances can be of a mineral character, since there is in the process nothing chemically to change the organic substances extracted from the glands. Unless mineral substances existed as such in the gland and were carried out into the extract along with the salt, it is hard to see how the presence of so large a quantity of inert substances as is indicated by the small activity of the resultant Dialysate

can be accounted for except upon the theory that they are organic substances from the gland itself. I do not forget that Sadtler says that such substances are colloidal, and so could not enter a Dialysate; but yet it is conceded that the [\*\*30] natural salt itself is a crystalline organic product, a conclusion which seems at variance with the universality of the statement that all these organic [\*108] compounds are amorphous and will not dialyze. At best it seems to me doubtful whether the Dialysate is a salt of the principle free from any but inorganic substances, and that doubt must of course be resolved against the defendant. As I shall show later, at least claims 5 and 6 require substantial freedom from organic impurities.

However this may all be, it is clear that Moore's experiment will not in any event serve as an anticipation. The description is so vague that at least two distinguished and ingenuous chemists cannot agree upon just what the process was. It was certainly not intended to be a set of directions for producing a commercially useful drug, even by skilled chemists, and it did not result in being so used, though the demand was great. While it did of course form a part of the science in the sense that it added to the store of knowledge about the active principle, the best proof that experts did not regard it as a satisfactory solution of what all were seeking is that Abel and Von Furth, who were [\*\*31] both generous investigators, never treated it as of any consequence. Nor may this be laid down to their ignorance of Moore's work, because it was published in a well-known technical magazine, and was almost certainly known to such skillful and persistent scientists. It was at most only a laboratory experiment without practical and commercial fruit, for there is not the slightest evidence that any one has ever used it in a single instance. Such disclosures do not enrich the art in the sense required for an anticipation. The test is whether the disclosure would have answered itself for the claims of a patent, and that it obviously would not do. Sadtler had now, it is true, thrown down the active principle by Takamine's process; but it is an awkward process, which no one would think of substituting for the directer method first disclosed by the mother patent here in suit. I do not therefore regard Moore's Dialysate as an anticipation of any of the claims.

The next supposed anticipation is Abel's Monobenzoylated Salts. This is the salt of a base constituted in part by the atoms which together make up the active principle in question -- Adrenalin -- and for the remainder by a benzoyl [\*\*32] radical; that is, a group of

other atoms having their own proper integrity within the molecule. Now, the present science of chemistry presupposes that substances retain their identity so long as the atomic structure of their molecules remains the same, not only in the number and kind of atoms which go to compose them, but in their relative arrangement to one another, about which, as I understand it, final knowledge is not yet ascertainable. When two molecules come into permanent association, one being an acid and the other a base, a salt results; but chemists do not suppose that such association is of the same kind as that within the molecules themselves. Thus, as has been shown, the association may be broken, and the two substances dissociated, while each resumes its proper characteristics; the molecules retaining throughout their identity. Abel never succeeded in procuring a substance which contained the molecule of the active principle as such. His monobenzoylated compound had all the atoms of the base, but in atomic association within [\*109] a single molecule with the benzoyl radical. When he tried to dissociate the atoms of that radical, which were associated with the [\*\*33] other atoms that together do form the base, he either affected their arrangement, or added to or subtracted from their numbers, so that the result was not physiologically active. Thus he did not, properly speaking, destroy the base in so doing, for it had never existed in a chemical sense at all, since that presupposes the existence of a molecule containing only such atoms in the proper arrangement, whatever that may be. It is true that the monobenzoylated salt which he did obtain seems to have been physiologically active, comparably with Adrenalin, though I can find no figure given to express its power. On this account the defendant insists that the question is immaterial of its exact chemical composition, since the claims do not speak of the free base and are not concerned with its molecular integrity.

Claims 1 and 2 are, however, specifically limited to "the blood pressure raising principle" of the glands in chemical combination with another substance. The "principle," so mentioned, is the organic substance first isolated by Takamine and does not include any other substance, whatever its properties may be. There is no room for ambiguity, because the word is used to cover [\*\*34] only that product which all had been trying to get; that is, the "free base." Had Abel ever succeeded in isolating his monobenzoylated base, a serious question might have arisen as to whether that was a valid anticipation of the claims of patent No. 730,176, which,



as has been seen, do not refer to the "principle"; but the claims of the present patent are drawn more nicely and speak in obviously chemical terms. The "principle" is the isolated principle which is described in the disclosure, but not the claims, of patent No. 730,176. Nor will it answer to say that the "principle" is chemically combined with the benzoyl radical as mentioned in these claims. In the first place, there is no evidence that the benzoyl elements add to the stability of the compound, and the "nonsuprarenal substance" of the claims must have that effect. But the difficulty goes deeper than that. The principle does not exist at all, as I have said, till it is broken away from the benzoyl radical. It cannot be said to be in combination with the radical, because the very word "principle" presupposes its molecular integrity, not varied by the atomic union of any other group. The purpose of the claims is quite [\*\*35] clear, and they speak in technical terms, with a corresponding limitation of scope. It will need no argument to show that it was invention to produce the "principle," notwithstanding the prior discovery of the monobenzoylated salt.

Similarly of claims 5 and 6, which speak of "the herein-described product of the suprarenal glands." Whatever the scope of the claims in No. 730,176, the product there described -- which is the same as that described in No. 753,177 -- is the "crude product," and that, as I have already shown, is not the same chemical substance as Abel's base. Indeed, these claims are even more limited than claims 1 and 2, since they are limited practically to salts of the free base, with some inorganic impurities admixed. The patentee could, of course, if he liked, make his claim in narrow language and cover specifically only [\*110] the actual product of his process. That he has substantially done, with the result that he need not fear anticipations which are not covered by such claims.

However, I cannot interpret claim 3 as so limited. Here the patented product is not defined by the process or the chemical active principle, but by the properties of the product [\*\*36] itself. That is in quite a different category and is anticipated by any product, whether chemically identical or not, which possesses the stated qualities. These qualities are those of the "salt," free from other constituents of the gland. It is anticipated by any substance which will have the physiological activity of the salt, and will be as stable and as pure. I omit reference to the chemical reactions because nothing turns upon these. Does Abel's salt conform to these

requirements? It is certainly physiologically active, indeed apparently as active as Adrenalin. It is likewise as stable as that product. There remains therefore only the question of its purity; that is, of its freedom from the other organic constituents of the gland. Sadtler testifies that it is so free, and Chandler cannot definitely say to the contrary except as he so infers from its gross appearance (XQ. 159, 160). I must conclude, therefore, that it does answer the requirements of claim 3.

The only remaining question is whether as a publication it is a valid anticipation. It does not appear to have been ever used in practice; but that is not necessarily conclusive, for it was not merely a tentative [\*\*37] experiment without adequate disclosure. On the contrary, it was fully described and published in well-known medical journals, and the disclosure would have answered the claims of a patent. While it was in a sense a laboratory experiment, it was published as a direction for all who wanted to use it, unlike Moore's vague disclosures, which were meant rather for investigators. In view of such publications, Takamine cannot claim to have been the first to discover a stable and pure salt having the physiological activity of the suprarenal gland.

As to the fourth claim, the question depends wholly upon what meaning is given to "compound" and what to "constituent." Chandler, especially when dealing with Von Furth's zinc sulphate, lays especial stress upon the word "compound" as indicating atomic association in a single molecule, an interpretation which would here result in making Abel's salts an anticipation. It is so used in the eleventh edition of the Encyclopedia Britannica, sub tit. Chemistry, and I think it must be so understood in the claim. The word "constituent" would then include those elements of the gland from which it is separated, and from those Abel's salts have been separated. [\*\*38] The benzoyl radical is not from the gland, but is introduced by the process itself. Such a construction leads to the invalidity of claim 4.

The next alleged anticipating product is Von Furth's Sulphate. This product was patented to Von Furth in Germany on May 16, 1899, and was offered upon the market in Germany. There is therefore no ground for objecting to it as an anticipation provided that it falls within claims 1, 2, 5, and 6.

The first question is whether Von Furth succeeded in isolating a salt of the free base, for concededly he did not produce it as a base [\*111] but as a sulphate, and by a

later patent as an iron salt. Sadtler presented a product made by a variation of Von Furth's process which he judged to be the pure base in physical admixture with zinc hydroxide. This is not put forward as in itself an anticipation because Von Furth never recognized it as the base, and carried on the process beyond the point at which Sadtler stopped it. A precipitate was formed by Von Furth through the introduction of ammonia into a zinc sulphate solution which precipitate Sadtler washed and dried and then examined microscopically. His conclusion was that the base was free, [\*\*39] and from that conclusion he also believed that the "end product" of Von Furth was a sulphate of the free base. Indeed, though he agrees that Von Furth never explicitly claimed the precipitate to be the base (XQ. 178), he still insists (R.D.Q. 305) that inferentially that conclusion did appear from Von Furth's patent. I do not think that this at all satisfactorily appears. Von Furth called the precipitate a "zinc compound" (Verbindung), and speaks of it as decomposed (zersetzt) by the addition of sulphuric acid. Both words more properly designate a chemical combination, and indeed it would have been hardly possible that Von Furth could have recognized the base in mere physical admixture with the zinc hydroxide, and still have carried on the process as he did by decomposition and the subsequent zinc dust treatment. Moreover, Sadtler himself was originally unwilling to assert that the precipitate contained the free base (XQ. 84, 85, 92), or that Von Furth had ever isolated it, and that doubt he only abandoned after he had produced his three intermediate products and examined them. It by no means follows from the high activity of these products that they contain the base out of chemical [\*\*40] combination, because, as appears in the case of Abel's Monobenzoylated Salt, there are chemical compounds of the base which are themselves equal in physiological activity to the base itself. Moreover, it is perfectly clear that both Abel and Von Furth thought that no ammonia precipitate did isolate the base, for they at once conceded to Takamine, as soon as they learned his process, that he had by so doing made a new step in the investigation of the substance. Chandler, who is himself a scientist of high reputation, insists that the precipitate is what Von Furth calls it, a zinc compound, and that the sulphuric acid added to the alcohol solution decomposes it, just as Von Furth says it does. In view of this conflict of authority, I cannot think that the defendant has proved that the precipitate was an admixture of zinc hydroxide with the free base, as Sadtler finally supposed. The most that one can say is that the matter must yet be regarded as

doubtful.

Now all this is in itself not material, because the defendant does not put forward the intermediate products of Von Furth as in themselves anticipations, but it has an importance due to its bearing upon the character of the "end [\*\*41] product" of Von Furth which is so put forward. Sadtler has no doubt whatever that this "end product" is a sulphate of the free base; but his conclusion in that respect depends, I assume, upon his earlier conclusion that the precipitate held the free base in mere admixture. It nowhere appears that he would say that the remainder of the process, beginning with the suspension of the precipitate [\*112] in 95 per cent. alcohol, would itself have decomposed out a zinc compound of the base into a sulphate of the free base, which would be necessary, if he is wrong in his conclusion about the character of the precipitate itself. It is true that Chandler will not commit himself (XQ. 202), as to the effect which the remainder of the process has upon the precipitate, and it must be taken therefore as possible that the "end product" may be a sulphate of the free base, even if the precipitate be a zinc compound. In that regard he is at one with "Sadtler's original guarded conclusion (XQ. 84, 85) that the result "may have been" a pure product, and his statement (XQ. 92) that he had never produced the free base by Von Furth's process. At that time, before he had reached his intermediate products, [\*\*42] he appears to have thought that the precipitate was a zinc compound. The doubt about this question prevents the defendant from showing clearly enough that the sulphate is a salt of the base.

But, even if Von Furth's product be the sulphate of the active principle, it would not anticipate claims 5 and 6, however it might be with claims 1 and 2, because those claims call for a salt of the "hereindescribed product," and that product is "my crude product," of patent No. 730,176. It is not enough in order to sustain the patent, therefore, that a supposed anticipation should contain a salt of the free base chemically true; but it must also, like the "crude product," be practically free from inert and associated gland-tissue. That requirement Von Furth's sulphate does not fulfill, as indeed sufficiently enough appears by the fact that Takamine's invention has now substantially the whole field therapeutically. The chief reason for the impurity of the product arises from the process which produces it, for it is made by the precipitation of a zinc sulphate solution and precipitates the zinc along with the active principle. Now zinc has an

affinity for many organic impurities containing [\*\*43] amino acids or xanthin bases. Moreover, because of the same affinity, those portions of the base which may have become oxidized during the period of digestion and extraction will be carried down with the zinc, nor can it be eliminated by the subsequent boiling in zinc dust. In this respect the process is just the opposite of Takamine's, which frees the precipitate from organic impurities, leaving them suspended in the filtrate. It is true that Sadtler found the smallest trace of proteids with the use of the usual test reagents; but that, as I have shown, does not by any means exclude the presence of organic compounds. The presence of organic substances in large quantity would seem to be indicated by the low activity of the salt itself, which, beginning at about 25 per cent. of Adrenalin, finally disappeared in the course of time. While, as I have shown, this form of reasoning cannot be pressed too far under the testimony here, I think, in view of the small activity of this substance, only one-quarter that of Adrenalin, that it is fair to assume that it is not "practically free"; there being no mineral matter. Sadtler, XQ. 62. Moreover, Abel's opinion was that Von Furth's iron [\*\*44] compound was the only one even approximately pure that he had ever got, and yet Von Furth speaks of this iron compound as being more or [\*113] less dark because of the "decomposition" products which it contained. If both are right, there must have been a substantial quantity of such products in the sulphate itself. That there is no adequate admixture of mineral or inorganic substances to account for such a diminution of activity does not seem to be denied, and, while this reasoning is not wholly satisfactory, as I have shown, it must count in the scale, for both sides concede that the hemostatic activity is due wholly to the free base and in proportion to its presence in the substance actually used.

Nor does the actual use, as indicated in contemporaneous documents, of Von Furth's sulphate, indicate that it is free from organic matters. It was perhaps as useful an extract from the glands, as had appeared up to the time of Takamine's disclosure and had value on that account. It is quite understandable that even intravenous injection might be indicated in extreme cases, though the sulphate was contaminated and dangerous. A disease of the heart might well call for such heroic [\*\*45] measures as would in less desperate conditions be wholly out of the question. Therefore claims 5 and 6 are not anticipated even if the sulphate be that of the free base itself.

The last alleged anticipation is Von Furth's iron compound. There is no dispute that this was a chemical "compound"; that is, that the iron atoms were in intramolecular association with the base, and, under my treatment of Abel's salts, they cannot be anticipations of claims 1, 2, 5, and 6. It is true that Sadtler refuses to commit himself as to whether the iron is or is not in chemical combination with the atoms composing the base, and to that extent the experts cannot be said to be in affirmative agreement, for Chandler is satisfied that iron will not enter into association of molecules with the amide group, of which the base is apparently one. This, however, raises no dispute, as I have said, and fails to raise a valid anticipation under the construction that I have given to the claims of No. 753,177.

Finally the defendant urges that it involved no invention to create the salt after the base was once discovered. It is quite true that Abel had already found that his monobenzoylated derivative of the [\*\*46] base existed as salt, and that as such it had greater stability than the base; but then this was only an inference, for he never succeeded in isolating the monobenzoylate base itself. Holme also inferred that the active principle had the properties of a weak base, and Moore observed that it resisted destruction better in combination with acids than with alkalis. So also Von Furth's "iron compound" patent refers to the greater stability of the salt. One claim of his "sulphate" was based especially upon the stabilizing of the product by "reduction," though just what he means is not apparent. However, no one had yet produced the free base, and no one knew what the effect of an acid would be upon it, when it was found. At best the former experimenters had only wise surmises, excellent lanterns of approach by which science alone can advance, but quite different from the full light of discovery. Even if any one had actually discovered the free base and knew it as such, it would be doubtful whether Takamine's discovery of a salt would not be invention, in spite of its apparently obvious character; but it [\*114] is not necessary to speculate about that, because no one did discover [\*\*47] such a base. The new product, a salt of the principle, was therefore quite unanticipated and was entitled to a patent, nor is it of any consequence whether the patent for the base alone might not have covered the salt, if it had been so intended. Having, as I have shown, claimed the two products as separate and been compelled to divide one from the other, the patentee will be prevented from protecting the salt altogether if the second patent is held invalid. There is no

warrant in law for such a holding; the salt which he produced being a wholly new product in the art.

Next arises the separate defense that the salt had been used for more than two years before the application was filed, a defense which rests upon the assumption that the original application out of which No. 753,177 was divided did not adequately describe the salts, so as to form the basis of a patent for them. As the patentee was required to divide, this defense ought not to prevail unless the patenting of the salt was quite clearly an afterthought. The original application, No. 35,546, included both process and product, and the product was subdivided into the "active principle" and the "salt." This application [\*\*48] was filed in November, 1900, and the applicant after some struggles with the Patent Office decided voluntarily to divide out the product claims, which he afterwards did; the divisional application resulting upon compulsory division in Nos. 730,176 and 753,177. Now the only difficulty alleged to exist either in specification or claim with the original application is that the salt was then said to be crystallizable. Takamine apparently then supposed that he had crystallized, or could crystallize, his salts, and he so disclosed his discovery. Subsequent experiment satisfied him that he could not, and his application was erroneous in that particular. Suppose the whole original application had remained single for the process and the two products; would an amendment have been outside of the applicant's rights? That is, I think, the proper test upon this division. *Victor Talking Machine Co. v. Amer. Graphophone Co.*, 145 Fed. 350, 76 C.C.A. 180. If his result is a new invention, then of course it could not be introduced by amendment, but otherwise the amendment is unobjectionable. Indeed, in the case cited the second application was not even a division from the first, but an independent [\*\*49] application. Now it scarcely needs argument to show that the salt remains the same invention whether Takamine was right or not in thinking it crystallizable. Moreover, apparently he was right when he thought so, or at least Sadtler appears now to agree with his original statement, for he presented in evidence crystallized salts of Adrenalin (R.D.Q. 297). I think that, regardless of this question of fact, the original applicant completely enough covered the invention in question, and that the point is not well taken.

Therefore I conclude that claims 1, 2, 5, and 6 are valid and infringed.

Whatever confusion the intricacy of the subject-matter causes, one fact stands out, which no one

ought fairly to forget. Before Takamine's discovery the best experts were trying to get a practicable form [\*115] of the active principle. The uses of the gland were so great that it became a part of the usual therapy in the best form which was accessible. As soon as Takamine put out his discovery, other uses practically disappeared; by that I do not mean absolutely, but that the enormous proportion of use now is of Takamine's products. There has been no successful dispute as to that; hardly [\*\*50] indeed any dispute at all. What use remains is, so far as the evidence shows, of the old dried glands, which every one concedes to have been dangerous, at least for intravenous use. All this ought to count greatly for the validity of the patent, and Takamine has a great start, so to speak, from such facts. It is true that he overstates the degree of stability of his acid solution without any preservative. Strictly it is not in that form fit for sale about in drug stores where it may be kept for long even in a stoppered bottle; but commercial or practical stability is a somewhat elastic term, and this is a case where he should be entitled to a lenient construction, for he has been author of a valuable invention and has succeeded where the most expert have failed.

I cannot stop without calling attention to the extraordinary condition of the law which makes it possible for a man without any knowledge of even the rudiments of chemistry to pass upon such questions as these. The inordinate expense of time is the least of the resulting evils, for only a trained chemist is really capable of passing upon such facts, e.g., in this case the chemical character of Von Furth's so-called "zinc [\*\*51] compound," or the presence of inactive organic substances. In Germany, where the national spirit eagerly seeks for all the assistance it can get from the whole range of human knowledge, they do quite differently. The court summons technical judges to whom technical questions are submitted and who can intelligently pass upon the issues without blindly groping among testimony upon matters wholly out of their ken. How long we shall continue to blunder along without the aid of unpartisan and authoritative scientific assistance in the administration of justice, no one knows; but all fair persons not conventionalized by provincial legal habits of mind ought, I should think, unite to effect some such advance.

Let a decree pass upon the claims as above indicated; no costs.