1938
April 25 & 26.

1939
Jan. 31.

BETWEEN:

NOVOCOL CHEMICAL MANUFACTURING COMPANY OF CANADA LIMITED ..... } PLAINTIFF;

AND

W. R. MACFARLANE, ET AL..... DEFENDANTS.

Patent—Chemical patent—Patent for anesthetic composition and process of making the same—Chemical equivalent—Infringement.

The action is for infringement of plaintiff's Canadian Patent No. 355,246. The invention relates to an anesthetic composition and the process of making the same. It is claimed that if a buffer salt is added to the main ingredients of an anesthetic solution, namely, procaine, a vaso-constrictor, a salt and an anti-oxidant, the solution will retain its neutral condition.

Defendants manufacture and distribute an anesthetic solution which they contend does not contain a buffer salt but which is a buffered solution by virtue of the manner in which it is compounded, since procaine is used as a base and converted into a salt by bubbling carbon dioxide through the solution, thereby making an alkaline salt of procaine.

Defendants did not question the validity of plaintiff's patent.

Held: That the solution manufactured and sold by the defendants is the chemical equivalent of the invention claimed by the plaintiff and is not so distinguishable from that of the plaintiff's as to be in fact a different solution, or one made by a process entirely different from that of the plaintiff, and there is infringement of plaintiff's patent.

ACTION by plaintiff to have it declared that Canadian Patent for Invention No. 355,246 is valid and is infringed by defendants.

The action was tried before the Honourable Mr. Justice Maclean, President of the Court, at Ottawa.

R. S. Smart, K.C. and *Christopher Robinson* for plaintiff.

F. B. Fetherstonhaugh, K.C. and *E. H. Charleson* for defendants.

The facts and questions of law raised are stated in the reasons for judgment.

THE PRESIDENT, now (January 31, 1939) delivered the following judgment:

This is an action for infringement of a patent, no. 355,246, granted to the plaintiff in January, 1936, being a re-issue of a patent granted in 1934, on the application of Samuel D. Goldberg, of Brooklyn, U.S.A., the inventor, and by him assigned to the plaintiff company. The in-

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vention relates to an anesthetic composition and the process of making the same. The anesthetic composition is of the kind which dentists use in giving a local anesthetic, a liquid in form, and which is injected hypodermically. The invention of Goldberg is manufactured and distributed in Canada by the plaintiff company, under the name of Novol, I understand.

During the course of the trial no evidence was led on behalf of the defendants in attack upon the plaintiff's patent to show want of invention, or that there was anticipation of Goldberg. The defendants, who all carry on business at Toronto, Ontario, either manufacture or distribute an anesthetic solution called Alkalinic which, it is claimed, infringes the plaintiff's patent. The controversy between the parties is a narrow one. The dispute turns wholly upon whether or not the defendants' solution, Alkalinic, contains a buffer, or a buffer salt, the plaintiff claiming that it does, and the defendants denying it, or, at least contending that their solution is not buffered in accordance with the disclosure made in the plaintiff's patent.

The specification of Goldberg is quite lengthy and it is difficult to make selections therefrom which would afford a connected description of the invention, and the processes therein mentioned for the making of it, without quoting from the specification at an undesirable length. I propose therefore, at whatever risk, to attempt an explanation of the invention and the object which it purports to achieve. I may at once say that the principal object of the invention is to provide a composition for local anesthesia, which would do away with or substantially lessen the pain, swelling and other objectionable symptoms, often resulting from hypodermic injections, at or around the place where the injection was made, while accelerating to some extent the anesthetic effect desired.

It has long been known that there are many natural substances, such as cocaine, which produce anesthesia, or insensitiveness to pain. These natural substances are quite intricate organic compounds usually referred to as alkaloids, and it was discovered that equivalent compounds could be made synthetically. One of the best known of these synthetic compounds was marketed under the name

of Novocaine, which originated in Germany, and later was manufactured in the United States under the name of Procaine. When Procaine was injected as a local anesthetic it had added to it another element, called a vaso-constricting material, designed to restrict the application or extent of the effect of the anesthesia, so that it would be local. The vaso-constricting material most commonly used is epinephrin, popularly known under the name of adrenalin. There was added a third element, sodium chloride, a salt to make the solution compatible with the blood, and the word "isotonic" is used as a general term for a solution which is compatible with the blood. It was explained that an isotonic solution must be one which gives approximately, within reasonable limits, the same osmotic pressure as is given by the blood, in order to avoid too much pressure through the membranes. A fourth element was also added sometimes, an anti-oxidant such as bisulphite, to prevent oxidation of the vaso-constrictor, which was apt to decompose and make the solution brown; the anti-oxidant was usually spoken of as a preservative for the epinephrin. This anti-oxidant is added to the solution in order to preserve the anesthetic in proper condition during what is called by the trade its "shelf life," that is, the length of time the anesthetic normally remains on the shelf of the dealer or dentist, after leaving the manufacturer—usually a period of from six to nine months. So that prior to the invention here in question the anesthetic solution was composed of four ingredients, the procaine, the vaso-constrictor, the salt, and the anti-oxidant.

Procaine is a synthetic alkaloid of a rather complex structure. It is a compound of carbon and hydrogen and nitrogen, which for local anesthesia has largely replaced the use of natural alkaloids, such as cocaine, for example. It is prepared as a procaine base and that base is then later processed into a salt, simply because the base itself has only a relatively minimal solubility in water. A base in the case of an organic compound, means a nitrogen compound having a NH_2 group, or more simply stated, it is a derivative of ammonia, ammonia being NH_3, one of the hydrogens being replaced by an organic radical. That is an organic base in general and that is also a procaine base. All alkaloids are of that general structure. The NH_2 group forms the nitrogen base in procaine. The solu-

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bility of procaine base in water is approximately three-tenths of one per cent, which is a rather minimal solubility. Any base will form a salt with any water-soluble acid. To produce the desired solubility of the procaine base in the vehicle, which in this case is water, it is converted to a salt by its reaction with any water-soluble acid. It would form a water-soluble salt with the common mineral acids, such as hydrochloric, sulphuric and carbonic acids. It would form a water-soluble salt with the common organic acids, such as acetic, tartaric, lactic, and so forth. Carbonic acid is the acid which results when carbon dioxide is dissolved in water.

The use of this anesthetic solution had two main disadvantages. The first was that there was considerable after-pain suffered by the patient, and also there was some delay in its action. This was found to be due to the fact that the solution was an acid solution, and being more acid than the blood it destroyed the tissues and blood cells. This acidity could be avoided if an alkaline substance were added to the solution thereby rendering it neutral and the solution were used immediately. But if the solution were allowed to stand a short time it would again be acid and would again cause after-pain. The invention claimed here is that if instead of an alkali there is added to the main ingredients of an anesthetic solution what is termed a buffer salt, the solution will retain its neutral condition. Buffers are substances which have the quality of keeping a solution either acid or alkaline, according to the nature of the buffer. If, to a solution having a buffer, something is added which would ordinarily make the solution more acid, the action of the buffer prevents the solution from becoming in fact more acid. The original condition of the solution is not affected except so far as the buffer itself may be either alkaline or acid. Here an alkaline buffer is used and the addition of acid has not the effect of making the solution more acid. The buffer first brings the solution to a practically neutral point and then maintains it at that. It is claimed, and it is not denied, that Goldberg discovered that if the anesthetic solution were buffered the solution became nearly neutral and that such condition could be maintained, and that the usual tendency to increased acidity would be counteracted by the buffer agent.

Acidity in this connection is measured in very small degrees. Goldberg, in his specification, refers to the measure of acidity and alkalinity by the term pH, one well known to, and much used by, chemists. The plaintiff's expert witness, Dr. Snell, explained it by saying that acidity in dilute solutions such as there is commonly expressed by the pH scale, a convenient chemical shorthand which is used almost universally. Pure water has what is called neutrality, that is, it has the same degree of acidity as alkalinity. When chemists speak of pH 7, they mean that water has a pH of 7. This pH may be measured in fractional units. We may have a pH 7, or pH 6, or pH 8, and so on. Those fruits which have just a little acid have a low pH, that is a higher acidity about 4 to 4·5; vinegar has a pH of about 3 to 3·5; sodium bicarbonate in aqueous solution is about pH 3·5. The acidity of pH 6 is ten times that of pH 7, and so on. The normal pH of the blood is 7·4. The critical acid value of the blood is about 5·7. If any material is injected into the blood which produces an acidity lower than that, there is a decomposition of red blood corpuscles, actual destruction of the essential materials of the blood, and similarly there is actual destruction of the tissue. If any material is to be injected into the blood or tissues it is desirable that it be in the range between the critical acid value of the blood, about 5·7, up to the normal pH value of the blood, approximately neutral, that is 7·4. It was explained how chemists determine whether a solution is acid or alkaline. Hydrogen ions are the things which determine whether a solution is acid. If it contains a preponderance of hydrogen ions it is acid; if there is a preponderance of hydroxyl ions over hydrogen ions it is alkaline.

The specification states that the term "buffer," as employed in the claims, refers to a salt like di-sodium phosphate, preferred by Goldberg, which upon being put into water solution dissociates and produces a small amount of weak acid and alkali, and it refers to a definition of buffer salts given by Horace G. Deming, in a named publication. In the specification, in a preferred formula, is to be found an example of the use of phosphate buffer in an anesthetic solution. But the specification also plainly states that instead of the phosphates mentioned in this

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formula as a buffer, acetates, tartrates, carbonates and citrates may be employed, and one of these, it is claimed, is the buffering agent employed in the preparation of Alkalinic.

The following of the claims of Goldberg, which are typical, might be mentioned:

1. An anesthetic solution for hypodermic injection containing a solvent, an acid containing anesthetic material for local anesthesia, a vaso-constricting material and a buffer including a weak acid to dissolve and maintain said vaso-constricting material in solution and to modify the pH of the solution, said solution being substantially stable and having a pH value in a range from approximately 5·7 up to approximately neutral.

4. An anesthetic solution ranging from slightly acid to nearly neutral containing an anesthetic acid salt for local anesthesia, a buffer, a vaso-constricting material, a weak acid to dissolve the vaso-constricting material and an anti-oxidant.

9. A base composition for making a substantially stable anesthetic solution for hypodermic injection, including acid-containing anesthetic material for local anesthesia and a buffer material containing a salt for altering the pH of the base when in solution, a vaso-constricting material and an anti-oxidant material, said base when placed in water being adapted to produce an anesthetic solution having a pH value within a range from approximately that of the critical acid value of blood up to that of the blood itself.

The defendants assert that they do not employ a buffer salt in making Alkalinic, but it is conceded that Alkalinic includes the epinephrin, the vaso-constricting material, the anti-oxidant, and the salts designed to make the solution isotonic with the blood. They contend that the buffering agent is inherent in the manner in which they compound the ingredients of Alkalinic, and that they do not designedly buffer it in the sense of Goldberg. Mr. Norris, chemical expert for the defendant Unity Chemical Company, denied that any buffer was used in the manufacture of Alkalinic. He stated, however, that procaine was used as a base and to get it into solution it had to be converted into a salt, by adding a weak acid, carbon dioxide, in the form of a gas. The gas, carbon dioxide, was bubbled through the solution, the last step in the preparation of Alkalinic, which had the effect of making an alkaline salt of procaine. Professor Rogers, an expert witness called by the defendants, admitted that the solution of the defendants which he tested was buffered, but no buffer salt was added, nor any of the buffer agents named or suggested in the specification of Goldberg; that is to say, that the ingredients of the defendants' Alkalinic did not contain a buffer

agent within the description of such as found in the specification of Goldberg. He stated that the procaine base was put into solution with carbon dioxide, the latter being bubbled through the solution until the procaine base was dissolved and while the solution was buffered nothing was contributed to it in the nature of a buffer. Procaine, he said, was a weak alkaline base, and if a carbonate were formed there it was a weak acid, carbonates being weak acids; and he stated that a procaine carbonate was a weak base with a weak acid, which was a material that could buffer an acid solution. It was obvious that it did so, he said, because the result of the two was an alkaline solution, and he said the procaine solution was the buffer. He stated also, that when one uses procaine hydrochloride the solution is acid, but Alkalinic employs a procaine solution which is alkaline, which needs no buffer. Professor Bain, testifying also on behalf of the defendants, stated that he had prepared an Alkalinic solution but no buffer salt was added to it. He stated however, agreeing with Professor Rogers, that if procaine is dissolved by passing through the solution carbon dioxide, the carbon dioxide unites with the procaine, forming either a procaine carbonate or a procaine bicarbonate, and that substance is capable of buffering the solution, because a weak acid was formed.

While the invention of Goldberg is not attacked upon any ground it is perhaps desirable to refer briefly to its early history, and its reception by that section of the public who would be concerned with an anesthetic composition. That has some legal significance. Mr. Nevin, president of the Canadian plaintiff company, and I think the United States parent company, and a dentist, stated that he was the first in America to use Novocaine, the German product. After the United States entered the war the Government of the United States took over certain German patents including that relating to Novocaine. Nevin, under some authority, began the manufacture of Novocaine under the name of Procaine. On account of the numerous complaints of after-pain incident to the use of Procaine, he employed Goldberg, a chemist, to seek a solution of the problem of after-pain, who in the end discovered and produced the plaintiff's anesthetic solution, for which discovery Goldberg applied for a patent, which was subsequently granted to his assignee, the plaintiff.

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Nevin, or a company of which he was the head, commenced marketing this anesthetic solution in 1930 with the result, he stated, that complaints about after-pain are a rarity to-day. He said that in clinical experiments he would inject one of the anesthetics then generally in use on one side of the patient's mouth, and on the other side Goldberg's buffered solution, and after twenty-four or forty-eight hours he would observe that the side of the mouth where the former solution was injected was considerably inflamed, whereas on the other side normal healing had proceeded. There was also he found, an improvement in the rapidity of induction of the anesthesia, and the toxic effect was eliminated to a considerable extent. He stated that generally dentists now use a buffered solution in preference to an unbuffered one. It is not denied that the buffered anesthetic solution has met with favour from the dental profession. In Canada the sales have progressively increased. In 1931, when manufacture was begun in Canada, the plaintiff company sold 300,000 tubes of Novol, and that had increased to 1,500,000 in some one year before the trial, at least that is my inference from the evidence, but probably that includes sales throughout the British Empire. The plaintiff's anesthetic solution is sold and distributed in many other countries, and in fact it is being produced in Brazil and Argentina.

I come now to the question as to whether or not infringement has been established, which is a difficult one for me because of the chemistry involved in that issue. It is clearly established, and in fact admitted, that Alkalinic is a buffered solution. Professor Bain, one of the defendants' expert witnesses, stated that it was the procaine carbonate or bicarbonate in the Alkalinic solution, a weak acid, formed in the manner already pointed out, that had the buffering action, that was the buffering agent, and which was capable of buffering the solution. And Professor Rogers agreed that it was obvious that a procaine carbonate, an alkaline material, which is a weak base with a weak acid, was a material which could buffer an acid solution, and give an alkaline solution. Professor Bain and Professor Rogers were referring to an Alkalinic solution which was prepared by them, or under their supervision, in 1938. It therefore would appear to be beyond controversy that the carbonate or bicarbonate in

the Alkalinic solution is a buffer agent, and that the solution is buffered. Whether this should be called a buffered solution, or a buffer solution, does not impress me as a distinction of importance. The Alkalinic solution is a buffered solution. It contains material which has the properties of a buffer. I think there is no real distinction between a buffer solution, and a buffered solution, at least for our purposes here.

In 1937 an Alkalinic solution was produced on discovery by the defendants and this was examined by Dr. Snell, the plaintiff's expert witness. He testified that he found that this solution contained sodium bicarbonate which is a buffer, and a weak acid in the form of carbonic acid, which would fall apparently within claim 4 of the plaintiff's patent, and he stated that the buffer was present as a bicarbonate-carbonic acid mixture, and was therefore a solution of a strong base and a weak acid, being a mixture of sodium bicarbonate and carbonic acid. He was of the opinion that the result could be produced by the action of carbon dioxide, and this seems to explain the reason for the defendants' buffered solution, and in fact that seems to be their contention. Without the carbonate or bicarbonate element the solution would be acid. This 1937 solution was not examined by the defendants' expert witness and therefore Dr. Snell's evidence cannot well be repelled as to this production on discovery, and he was of the opinion that the solution which he analysed in 1937 was not the same as that analysed by Professors Bain and Rogers. If I correctly comprehend the facts I do not think there is much conflict between the plaintiff's expert witness and those of the defendants. Alkalinic is a buffered solution, or it is a solution which has been buffered. And I take it that the defendants, when they advertise as they do, that there is "no after soreness" attributable to Alkalinic injections, they have in mind that this is due to the fact that their solution has been buffered, otherwise there would be no reason for referring to "after soreness" at all. In 1934 the defendants, or some of them, produced an anesthetic solution which the plaintiff apparently complained of as infringing Goldberg. This solution, I understand, was abandoned, presumably because it appeared that it might be held to be an infringement of Goldberg. I cannot avoid the conviction that

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the defendants designedly buffer their anesthetic solution, but in a way which it was hoped might afford a defence in an infringement action. It appears to me as if the manufacturers of Alkalinic have taken an important leaf out of the book of Goldberg, and are attempting to re-write a few words of it, without changing the substance of it. My opinion therefore is that infringement has been established, unless there is some legal impediment in the way of the plaintiff, or, that the Alkalinic solution is something entirely different from that of the plaintiff.

I do not think that Alkalinic is an anesthetic solution so distinguishable from that of the plaintiff's as to justify one in holding that it is a different solution, or that it is made by a process entirely different from that of the plaintiff. The only real distinction between them, or the compounds or materials entering into them, relate to the agency which produces the effect of buffering. Goldberg was a trained chemist, and when he was requested to find out some means of avoiding after-pain from the effects of procaine injections he discovered, it seems to me, the cause, and he claims to have found a solution. As a chemist he would have some knowledge of chemical equivalents and alternatives. I wish to avoid any lengthy recital from the specification and its claims, and therefore I merely point out that, while expressing a preference for a phosphate buffer, Goldberg states, that instead of such a buffer, acetates, tartrates, carbonates and citrates might be employed. It is to the carbonates that the defendants attribute the buffering in the Alkalinic solution. In the claims of Goldberg there is reference to a "buffer including a weak acid," "a buffer containing an alkaline buffer," "a buffer," "a buffer including a buffer salt." This impresses me with the fact that Goldberg having once discovered the reason for after-pain incident to the use of procaine,—an excess of acidity—and then having discovered that if the solution were buffered it would become nearly neutral, and that the usual tendency to increased acidity, through the operation of the anti-oxidant or otherwise, would be counteracted by a buffer agent, he did not tie himself down to one formula, or one buffering agent, because he would at once know that chemistry could supply equivalents or alternatives to his preferred formula, and he numbers several of them. Into

one or more of them the defendants' solution and process fall, in my opinion.

As I have already stated, the defendants do not attack the validity of Goldberg and they therefore must be taken to admit that no one had before disclosed what Goldberg disclosed in his specification. The plaintiff asserts that Goldberg made an invention of more than usual importance; in fact it is claimed he made a very important discovery, and I am bound to concede this upon the facts as revealed, and this the defendants did not attempt to dispute. And apparently Goldberg's invention has had a very considerable commercial success, which means that his invention found favour with members of the dental profession at least, whom, I assume, are the principal users of Goldberg's anesthetic solution. If Goldberg made a great step in advance in the art, which seems to be admitted, then it would not be fair to look upon him as one who had made merely a slight improvement in any known anesthetic preparation used by dentists, and which would avoid after-pain. Alkalinic is, I think, the equivalent of Goldberg's solution. The specification of Goldberg, as I have already stated, defines the term "buffer," as used in his claims, as any salt which on being put into water solution produces a small amount of weak acid and alkali. I think the defendants' buffering agent falls within this definition. It is usually fairly safe to define an equivalent as a thing which performs a function in substantially the same manner as the thing of which it is alleged to be an equivalent. If an important step in advance has been made by an inventor, the law, I think, affords a patentee a range of equivalents commensurable with his invention, and that, I think, should be accorded Goldberg if needs be. However, in my opinion, it is not necessary to invoke that principle because Goldberg in his specification points out that buffering might be accomplished not merely by his preferred buffering agent, but also by that of the defendants, that is, by the use of carbonates. And that I think he claims. I think it is clear that there has been infringement.

In the result, the plaintiff succeeds with the usual consequence as to costs.

Judgment accordingly.