BETWEEN:

AMERICAN CYANAMID COMPANY .....PLAINTIFF;

AND

CHARLES E. FROSST & COMPANY .....DEFENDANT.

1964

Mar. 17-20, 23-25

1965

Mar 16

Patents—Infringement—Validity—Disclosure of pending patent applications—Public interest in secrecy of pending patent applications—Infringement where product sold derived from substance made by patented process—Presumption in s. 41(2) of Patent Act—Sufficiency of patent—Meaning of "workman skilled in the art"—Utility of invention—Workability and operability of invention—Judicial approach to invention of great importance and enjoying considerable commercial success—Validity of patent the words of which embrace useless as well as useful substances—Importance of invention date re patent being void for insufficiency or inutility—Sufficiency of description of invention in patent—Patent specification not incomplete if sufficient to permit working of invention—Anticipation—Prior art—Anticipation of patent by conflicting application—Composite French patent as admission of joint patentees that all inventions the same—Patent Act, R S C. 1952, c. 203, ss. 10, 36, 41(2) and 45(1).

This is an action for infringement of two Canadian Letters Patent owned by the plaintiff by way of assignment from the inventors. The first patent, known as the Duggar patent, is No. 497,339, issued on November 3, 1953 for an antibiotic substance and preparation called Chlortetracycline, and the second, known as the Minieri patent, is No 542,622, issued on June 25, 1957 for the production of an antibiotic called Tetracycline.

The Duggar patent is directed to and claims the process for producing Chlortetracycline, a new substance, and the substance itself, which is therefore a process dependent product under s. 41 of the *Patent Act*, whereas the Minieri patent claims only a new process for producing Tetracycline, which was not a new substance at the date of the Minieri patent application.

The evidence disclosed that the antibiotics, Tetracycline and Chlortetracycline are both produced by micro-organisms called streptomyces aureofaciens Chlortetracycline is produced by placing the micro-organisms in a fermentation broth in which there is present a chloride ion Tetracycline can be produced in two ways, indirectly by deschlorinating Chlortetracycline, and directly by placing the micro-organisms in a nutrient broth in which the chlorine content is controlled. The Minieri patent claims the direct process of producing Tetracycline and is therefore a process patent relating to the production of a known-substance in a different manner by a different process

The claims in both the Duggar and Minieri patents which are in suit are process claims only The parties agreed that for the purposes of this suit the defendant will be deemed to have sold in Canada two types of Tetracycline imported from Italy, the first produced from the organism identified as streptomyces lusitanus fermented to produce Chlortetracycline which was subsequently deschlorinated to produce Tetracycline, and the second produced by fermentation of streptomyces lusitanus by a method infringing the Minieri patent if streptomyces lusitanus is an organism of the group consisting of the species

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streptomyces aureofaciens together with natural and artificially induced mutants thereof. The manufacture of both types of Tetracycline was carried out in Italy.

On the question of infringement the main point in contention was whether streptomyces lusitanus is a separate and distinct species from streptomyces aureofaciens or is only a member of this species.

The defendant attacked the validity of the plaintiff's patents, alleging that the specification in the Duggar patent is insufficient and the process is unworkable, that both patents are incomplete, misleading and lack utility and do not disclose when and how the required strains of aureofaciens may be obtained, that the Minieri patent was anticipated by the Duggar and other patents and that the alleged inventor of the Minieri patent was not the first and true inventor.

Held: That under s. 10 of the *Patent Act* the confidential nature of pending patent applications is preserved only if disclosure thereof is not necessary to allow the Court to properly discharge its duty to render judgment and s 10 cannot prevent the Court from dealing with such matters although as little as possible of the confidential information should be divulged.

2. That particularly where the pending patent application is that of the plaintiff, s. 10 of the *Patent Act* does not prevent dealing with such matters in a judgment when necessary, because the practice of not allowing the public to inspect pending applications and documents connected therewith, while necessary for the proper functioning of the public service, is not a public interest which overrides the general principle that in a court of justice every person and every fact must be available to the execution of its supreme functions.

3. That there is infringement of the Duggar patent even if the product imported by the defendant was not Chlortetracycline, the new product invented by Duggar, but Tetracycline admittedly made by the process of making Chlortetracycline and then obtaining Tetracycline by the deschlorination method

4. That when dealing with a new product, i.e. Chlortetracycline from which Tetracycline is made, s. 41(2) of the *Patent Act* creates a presumption in favour of the patentee that the substance imported "in the absence of proof to the contrary" is deemed to have been produced by the patented process.

5. That there is infringement of the Minieri patent on the basis of the agreement made between the parties, and, with regard to the Duggar patent, lusitanus having been found to be an organism of the streptomyces aureofaciens group, it follows that the presumption in s. 41(2) of the *Patent Act* comes into play and establishes that the Chlortetracycline produced in Italy and later made into Tetracycline must be presumed to have been produced by the Duggar process and there is, therefore, also infringement of the Duggar patent.

6. That in the light of the evidence that all the experts who testified at the trial would have no difficulty in producing Chlortetracycline according to the Duggar patent by following its teachings, the patentee has met his obligations under the statute and has properly described his invention so as to make it workable and operable by a man skilled in the art, who, in this case, would be a highly skilled scientist who works in the examination of micro-organisms and the making of antibiotics

7. That the Duggar patent, because of its importance as a break-through in the antibiotic world and the enormous commercial success of the product produced should be approached with a judicial anxiety to support a really useful invention and by a mind willing to understand, not by a mind desirous of misunderstanding, and if this is done there is no question of the sufficiency of the description or the workability of the invention.

8 That if at the date of the patent the words used, i.e. streptomyces aureofaciens, embraced useless as well as useful micro-organisms then the Duggar patent is bad.

9 That the important date with regard to a patent being void on the ground of insufficiency or inutility is the invention date and if at that date all known strains of aureofaciens would produce Chlortetracycline, then the Duggar patent cannot be attacked on these grounds, even if there were known to be at some date subsequent to the date of invention certain strains of aureofaciens that would produce Tetracycline to the exclusion of Chlortetracycline.

10. That the two patents would be void if at the date of issue thereof they embraced useless as well as useful micro-organisms, but such must have existed at the respective dates of the patents.

11 That s 36 of the *Patent Act* requires as one of the considerations for the monopoly grant given the patentee that he give in the patent to the public an adequate description of the invention with sufficiently complete and accurate details as will enable a workman skilled in the art to which the invention relates to construct or use that invention when the period of monopoly has expired.

12 That the person skilled in the art in this case is a highly trained scientist because of the subject matter of the specification and in order that the specification be sufficient it is not required to describe the invention and the manner in which it is to be performed so fully as to instruct persons wholly ignorant of the subject matter.

13. That there is no requirement under the Canadian *Patent Act* or under its rules, in cases of patents which deal with the product of micro-organisms, to deposit the type culture or a strain of such micro-organisms as is required in the United States.

14 That the specification of the Duggar patent is not incomplete because of the absence of a reference to a specific strain of aureofaciens since such absence has in no way prevented the addressee from putting the invention into practice, or deprived the public of all the advantages of working with the invention during the life of the patent and of using it commercially at the expiration of the patent.

15 That in view of the fact that the Duggar patent dealt only with the production of Chlortetracycline by using materials containing a sufficient quantity of chloride to give this product, and because of the uncontradicted evidence of the plaintiff that the production of Tetracycline by fermentation without chloride could not, at the date of the Minieri patent, have been predicted, it follows that the information contained in the Duggar patent can in no way be taken to have given Minieri what he required for his discovery which would have to be the case if the Duggar invention were to be considered to have anticipated the Minieri patent.

16 That in order to have anticipated the invention the prior art must show in clear and unmistakable terms how to put the invention into

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practice, and accordingly the Duggar invention cannot have anticipated the Minieri invention because the teaching of the Duggar patent is to obtain production of Chlortetracycline and if something else is produced, i.e. Tetracycline, the teachings of Duggar are not being followed

17. That although s. 45(1) of the *Patent Act* provides that two applications should be placed in conflict when each of them contains one or more claims defining substantially the same invention, or when one or more claims of one application describe the invention disclosed in the other application, it is only if both applications fall within either one or the other of these provisions that one of the applications can be considered as a possible anticipation of the other.

18. That the existence in France of a joint or composite patent, as apparently permitted by the laws of that country, cannot be considered as an admission that the inventions of the joint patentees are all the same invention.

ACTION for infringement of patents.

The action was tried by the Honourable Mr. Justice Noël at Ottawa.

Harold G. Fox, Q.C. and Donald F. Sim, Q.C. for plaintiff.

André Forget, Q.C. and *Miss Joan Clark* for defendant.

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

NOËL J. now (March 16, 1965) delivered the following judgment:

This is an action for infringement of Canadian Letters Patent No. 497,339 issued November 3, 1953, to its inventor Benjamin M. Duggar, for an antibiotic substance and preparation called Chlortetracycline (hereinafter called the Duggar Patent); and Canadian Letters Patent No. 542,622 issued June 25, 1957, to its inventors, Pasquale P. Minieri, Herman Sokol, Melvin C. Firman, for the production of an antibiotic called Tetracycline (hereinafter called the Minieri Patent), now both owned by way of assignment by the plaintiff.

In order to appreciate the problems involved herein, it may be useful to deal at this stage with a number of characteristics involved in the world of antibiotics. I might first point out that the trade name of Chlortetracycline is the well known drug called aureomycin and the trade name of Tetracycline is achromycin and that both of these, although directed towards the same use, differ in that

Tetracycline or achromycin has a broader application and is more effective than Chlortetracycline or aureomycin.

These antibiotics are produced by living micro-organisms whose essential morphological features are too small to be seen with the naked eye or a hand lens, but instead must be viewed under a microscope and those we are concerned with here are members of the plant kingdom of the division PROTOPHYTA, of the genus streptomyces and of a species called "aureofaciens".

Now, although the two above mentioned antibiotics produced by streptomyces aureofaciens come from or are produced by the same micro-organisms, they are produced in a different manner in that Tetracycline is obtained by placing the micro-organisms in a nutrient broth in which the chlorine content is controlled thereby encouraging the production of Tetracycline and discouraging that of Chlortetracycline whereas in order to obtain Chlortetracycline a chloride ion (a combination of the gas Chlorine with either potassium sodium or calcium) must be present in the fermentation broth or media. Tetracycline can also be produced by taking Chlortetracycline and suspending it in a solvent in the presence of a catalyst such as metal palladium which has the effect of removing the chlorine and substituting hydrogen therefor. However, the use of the fermentation method to obtain Tetracycline has economic advantages over the catalytic hydrogenation method in that around 15 per cent more product is obtained. I might also add that the plaintiff submits that prior to the Minieri patent it was unpredictable that streptomyces aureofaciens would produce Tetracycline if chloride was not present in the fermentation broth.

These micro-organisms are composed of filaments about 1/25 thousandths of an inch in diameter branching and rebranching in a densely textured weft and their ends bear chains of reproductive bodies, called spores. These filaments may be of various forms and the chains of spores may be simply straight or wavy or coiled. They are found everywhere, the soil however being the natural habitat for the various types of streptomyces, and the streptomyces aureofaciens used in the two patents in suit was isolated by Dr. Duggar in 1945 as appears at p. 2, column 4, line 25, of the Duggar patent "from the soil of a timothy field in

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Missouri" in the United States of America after experimenting with 600 samples of soil.

It is only through a pure culture that the organism can be properly isolated from the other micro-organisms that exist in a particular soil and this pure culture must contain only one type of a species. The working of such cultures requires special equipment and laboratories.

The streptomyces will grow on many natural foods, such as cooked potatoes, cooked maize, beef broth, starch and others and in order to observe these cultures, a nutrient broth is used to which is added a substance called Agar-agar, which is liquid when hot but solidifies into a semi-solid condition at a temperature below 37 degrees centigrade. The pure culture is, therefore, obtained in the following manner: a sterile nutrient agar solution is prepared, poured into a sterile flat covered glass dish and allowed to harden and a small drop of a suspension of soil, which is the natural habitat of streptomyces, is streaked across the surface of this nutrient agar or is incorporated therein and some days later micro-organisms begin to grow in the agar material. I might add that it is possible to supply nutrient conditions for growth which may favour one particular type of micro-organism over another and then certain types may be inhibited and kept back or pushed out of the way. The specialists may, by close observation, recognize the streptomyces they are looking for and can reach in and bring out a small bit of the organism which they transfer to another sterile dish of nutrient agar and they keep on doing this until they finally obtain a pure culture of the streptomyces they are looking for.

When an organism has been isolated from its natural habitat where it exists in nature, it is called a natural isolate. When, however, a strain has undergone some sudden heritable change which is such that it cannot be accounted for by the ordinary reproductive mechanisms of the organism, be they sexual reproduction or recombination, then it is called a mutant. Induced production of mutations is a standard part of the development of any one of the antibiotic processes and it may be done by a number of means, one of which would be to take a population of spores from a given organism, by experimentation select a mutating agent, which might be physical in nature, such as the various

radiations, ultra-violet light or x-rays, or chemical such as nitrogen mustard or various ones of the alkaloids, caffeine, which would kill a certain proportion, i.e., 90 to 99 per cent of the spores so exposed. The surviving spores which have been able to survive the effects of the mutogenic agent are able to grow and germinate and they again will form individual colonies. Among the survivors a very high percentage will be unchanged in any way from the parent and a very small percentage will show some differences. The main purpose of creating mutants is to obtain strains of a given organism which will have greater capacity to produce a given metabolic product than the present organism started from. Indeed, by such a process it is possible to make mutant strains which will produce greater yields of the antibiotic than was possible with the organism as it existed when isolated from nature.

It appears from the evidence that once a pure culture is obtained of one of these micro-organisms, no matter how small the quantity, any desired quantity can then be grown in a suitable nutrient.

This pure culture of a given micro-organism is then used to produce an antibiotic by means of fermentation which requires a fermentation broth or what is called in french "le bouillon" which in turn must contain certain nutrient ingredients to support and encourage the growth and reproduction of the micro-organisms and certain constituents from which the micro-organism can make the desired antibiotic. Indeed, in the fermentation process the micro-organisms digest or assimilate the nutrients of the fermentation broth and then elaborate the antibiotic. It appears from the evidence that the usual fermentation broth, which applies here, contains water plus a source of carbon, hydrogen, oxygen in the form of starch or sugar, nitrogen or organic nitrogen such as present in meat, bean extracts or a material called corn steep liquor a by-product of the manufacture of starch as well as certain essential nutrient salts, calcium, potassium, sulphur, certain metals in traces, iron, manganese, copper and a source of chloride which can be a combination from calcium chloride or potassium chloride which is all placed in a container with a cotton plug to allow ingress and egress of air.

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Certain products however, require special constituents and Chlortetracycline in the Duggar patent requires chlorine.

An antibiotic is, therefore, an organic substance produced by a micro-organism which has the capacity of inhibiting or killing other organisms in dilute solution which can be as low as a tenth of a microgram per millilitre which is a tenth of a part per million and to be therapeutically useful must meet certain requirements. It must not harm the human body; it must inhibit or kill the cause of the infection in the body; it must be retained in the human body for sufficient time to cause the infection to diminish; and it must not be inactivated by the body or it must retain its strength.

A number of antibiotics may be produced which kill germs and bacteria but they also kill the patient and therefore they are not a useful antibiotic. Others may not be retained in the body or they may be inactivated by the body and they also are not useful.

It appears from the evidence that it could take two to three years at the least from the time a soil sample is received to the time that a new antibiotic can be confirmed as being therapeutically useful and ready for the market.

The modern antibiotic therapy of infectious diseases began with the discovery of penicillin, by Fleming, Floy and Chain produced by a micro-organism called penicillium NOTATUM in the year 1928. It was not, however, until several years later that penicillin was purified to a stage where it could be used on a human patient. As the action of penicillin was limited, a continuing search was carried out for antibiotics with a wider range and in 1941 the first antibiotic produced from streptomyces was announced at which time it was known as actinomycetes or streptomyces antibioticus and the name actinomycen was then given to the product. This antibiotic, however, was not useful because, while it killed the infection, it would also kill the test animal on which it was used.

The next step occurred in 1944 when streptomycin was discovered, which was the first useful antibiotic made from a streptomyces called streptomyces griseus. However, streptomycin had certain drawbacks in that bacteria seemed to become tolerant to it very quickly and so the dosage had to

be increased and when this was done there frequently appeared to be damage to the eighth cranial nerve, resulting in deafness.

The third important and useful antibiotic was chloramphenicol which was announced in 1947 and was produced by streptomyces venezuelae. The fourth was Chlortetracycline aureomycin announced by Dr. Duggar in 1948 and produced as we have seen by streptomyces aureofaciens.

It may be useful here, in order to properly understand the literature produced as exhibits herein, to deal with the terminology used with regard to these various antibiotics and the changes which later took place. Chlortetracycline of course was known, as already mentioned, under the name of aureomycin; an antibiotic discovered after Chlortetracycline and produced by streptomyces rimosus, was known as oxytetracycline otherwise known by the trade name of terramycin. After the discovery of aureomycin and terramycin, it was recognized that there was a nucleus common to both and the name Tetracycline was proposed for that substance. Aureomycin then became known as Chlortetracycline and that is how the generic name for aureomycin became the plaintiff's trade mark for Chlortetracycline of its manufacture and its trade mark on its production of Tetracycline became achromycin, although the name "achromycin" had been originally applied by the plaintiff to a new antibiotic produced by fermentation of an organism known as streptomyces ALBONIGER which, however, was later changed to puromycin.

The Duggar patent is directed to and claims the process for producing Chlortetracycline, a new substance from streptomyces aureofaciens in a suitable fermentation broth and therefore is a process dependent product under s. 41, whereas the Minieri patent which deals with Tetracycline is not as it contains only process claims. It contains no product claims because, as already mentioned, Tetracycline at the date of the Minieri application February 13, 1954 was not a new substance, the patent being obtained on the basis that, although the substance Tetracycline was produced by the same micro-organisms as Duggar, and although it could be produced by the Duggar method by way of first obtaining Chlortetracycline and then subsequently deschlorinating it to get Tetracycline, it was, however, obtained by Minieri in

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a different manner by a different process, i.e., by direct fermentation of streptomyces aureofaciens in a fermentation medium in which the chlorine content of the medium was controlled so as to discourage the formation of Chlortetracycline and encourage the formation of Tetracycline. This, according to the plaintiff, was the first time that Tetracycline had been produced by a direct method, fermentation, and the contribution of Minieri and his co-workers is submitted to be a pioneer contribution to the art of antibiotic production.

It therefore appears that the continuing search for antibiotics involves a search for micro-organisms, their isolation and classification, and then their use in varying types of fermentation broths or media to produce fermentation products, the testing of these products to determine their antibiotic properties and effects by applying them to actual bacteria, germs and viruses of known diseases as well as the determination of their side effects on the human body to insure that they are useful. The many steps involved here, in the whole process, in so far as the Duggar patent is concerned, must, therefore, be considered in the light of (1) the discovery of a micro-organism that had never been known before; (2) the preparation of the most suitable fermentation broth or media useful in fermenting this particular micro-organism; and (3) the recovery and isolation of a new and useful antibiotic produced from the newly discovered micro-organism and, although step No. 2 hereinabove was a new variation of known fermentation processes, steps No. 1 and No. 3 were absolutely new.

The evidence discloses that both Chlortetracycline and Tetracycline have been therapeutically and commercially very successful. They could be taken not only by injection but also in capsule form and have been successful in treating a much wider range of germs, bacteria and viruses than anything prior thereto such as Rocky Mountain spotted fever, typhus, tachoma, the so-called atypical pneumonia virus, pneumonia mastitus also known as Bangs disease and undulant fever, shigella, a type of dysentry and their side effects are of a minor nature. Their production in the world market has been 513,682,999 daily patient doses for Chlortetracycline and 487,530,000 daily patient doses for Tetracycline from the date of production to August, 1963. A number

of licences and sublicences have been granted by the plaintiff under both the Duggar and Minieri patents.

Before dealing with the defences advanced by the defendent herein, I should point out that, although the Duggar patent has eight claims, the first three, 1, 2 and 3 are product claims and were withdrawn from suit. The Minieri patent has fourteen claims of which, however, only 1, 2, 3, 4, 5 and 7 are in suit and it, therefore, appears that all the claims in suit in both the Duggar and the Minieri patents are process claims only.

An agreement for trial in the present instance was produced, which also shortens the issues herein. This agreement reads as follows:

I. The Defendant agrees to the amendment of the Statement of Claim and Particulars of Breaches herein by the addition of Canadian Patent No. 542,622 thereto. (which latter is the Minieri patent).

II. For the purposes of this suit as amended, the Defendant will be deemed to have sold in Canada two types of Tetracycline imported from Italy as follows:

(*a*) The first type of Tetracycline was produced from the organism identified as Streptomyces Lusitanus which organism was fermented to produce Chlortetracycline which was subsequently deschlorinated to produce Tetracycline. The manufacturing process was carried out by Ferment Farma of Milan, Italy.

(*b*) The second type of Tetracycline sold by the Defendant was also manufactured by Ferment Farma at Milan, Italy and was produced by fermentation of the organism identified as Streptomyces Lusitanus and by a method which infringes Claims 1 to 5 and Claim 7 of Canadian Patent No. 542,622 if Streptomyces Lusitanus is an organism of the group consisting of the species Streptomyces Aureofaciens together with natural and artificially induced mutants thereof, but which method does not infringe Canadian Patent No. 542,622 if Streptomyces Lusitanus is not an organism of the group consisting of the species Streptomyces Aureofaciens together with natural and artificially induced mutants thereof.

III. That the strain delivered to Mr. Austin Phillips by Dr. Tosoni of the University of Toronto, in Toronto, on November 9th, 1962, is the strain of Streptomyces Lusitanus as referred to in paragraphs II (*a*) and (*b*) hereof.

The first point in contention here appears to be whether streptomyces lusitanus, from which the Tetracycline imported and sold by the defendent, was produced, is a separate and distinct species from streptomyces aureofaciens or is only a member of this species.

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The effect of the above agreement would appear to be two-fold and of different impact in respect to both Tetracyclines admittedly imported into Canada. Indeed, with regard to the first type of Tetracycline produced by the deschlorination of the chlortetracycline and, therefore, admittedly made from chlortetracycline, there should be infringement if the facts are such that they do under the law as it now stands, including the presumption provided under s. 41(2) of the *Patent Act*, constitute infringement and providing that lusitanus falls within the aureofaciens group referred to in the agreement as counsel for both parties at the hearing agreed that infringement of both types of Tetracyclines would be dependent upon a prior determination of whether lusitanus is or is not "an organism of the group consisting of streptomyces aureofaciens together with natural and artificially induced mutants thereof" as provided under the agreement. With regard to the Tetracycline produced by fermentation under the Minieri patent, of course, the agreement clearly sets out the fact that infringement here is dependent upon a determination of the speciation of both micro-organisms only.

A specific attack is then made on the validity of the Duggar patent on the basis that the specification is insufficient in that it nowhere discloses the necessity to have chlorine in the broth to obtain chlortetracycline, although as already mentioned, without it the product cannot be obtained.

At the beginning of the trial of the present case, counsel for the defendant stated that in the course of research for the preparation of the trial, several matters were disclosed which made it now necessary to add a number of defences. He then submitted that it had been found that within the family of streptomyces aureofaciens there were a number of strains which will not produce chlortetracycline at all and that, therefore, the patent did not meet the promise of the patentee. He also urged that the patent cannot be worked because it was discovered that the strains of aureofaciens, although deposited with certain scientific or governmental agencies, are under conditions which make it impossible for these agencies to deliver it to others and are, therefore, not available to the public at the present time for testing, nor will they be available at the expiry of the patent so that the

monopoly granted by the patent, instead of being limited, will be perpetual.

The above defences apply to both the Duggar and Minieri patents and it was submitted on behalf of the defendant that in this connection the particulars of objection be amended by adding the following:

(1) Both patents are incomplete, misleading and lack utility in that they fail to distinguish between strains of streptomyces aureofaciens which may produce chlortetracycline and other strains of streptomyces aureofaciens which will not produce chlortetracycline for Duggar and strains of streptomyces aureofaciens which may produce Tetracycline and other strains of streptomyces aureofaciens which will not produce Tetracycline for Minieri.

(2) Both patents do not disclose where and how strains of streptomyces aureofaciens, capable of producing chlortetracycline when fermented in the presence of chlorine for Duggar and Tetracycline for Minieri, may be obtained for the purpose of lawful experimentation during the life of the patent and of commercial practice of the invention after the expiry.

A specific attack is made on the Minieri patent in that the process claimed therein is the same as that claimed in the Duggar patent which does not make any mention of chlorine ion and Minieri et al invented nothing in view of the Duggar patent.

With regard to the Minieri patent, a further defence was proposed in that Minieri was not the first inventor as a co-pending application with Minieri was discovered which should have been placed in conflict, i.e., one application made by Martin-Bohonos produced as Ex. D-16 which, however, bears no date but which in respect thereto was dealt with by a statement made by Mr. Sim, one of the defendant's counsels at vol. 2, p. 411, of the transcript as follows:

We will state for the purpose of this action only that whatever that application shows, the Martin and Bohonos application shows, whatever is in it was invented by Martin and Bohonos before Minieri invented what is shown in the Minieri patent in suit and that my friend will not have to go into matters of proof

We will also, of course, agree, if the record indeed doesn't show it, that the Minieri application and the Martin-Bohonos application were co-pending before the Canadian Patent Office at the same time, and I think that is the extent of our agreement.

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It was here submitted by the defendant that the particulars of objection be amended by adding the following:

The alleged inventor of Canadian Letters Patent No 542622 was not the first and true inventor being antedated by Messrs. Martin, Bohonos, Duggar and Devoe as well as Messrs. Heinman and Hooper; patent applications by the said inventors are pending and were co-pending with the application which matured into Canadian Letters Patent No. 542622.

This request for leave to amend by the defendant was strongly opposed by counsel for the plaintiff, firstly on the basis that an amendment of such far reaching importance which would change the nature of the present action, should not be allowed at this stage and, secondly that defendant's attempt to bring in the Martin-Bohonos application, should not be permitted as under s. 10 of the *Patent Act* pending applications are to be kept secret.

I, nevertheless, granted defendant's amendments with costs against it on the basis that the amendments proposed, although tardy, in no way changed the nature of the action and that as far as the production of the Martin-Bohonos application was concerned, it could be handled in such a way that the matters it contained, or the evidence adduced in connection with it, could remain confidential as between counsel for the parties, and myself, as well as (as requested by counsel for both parties) a representative of each party who, through their counsel, gave an undertaking to keep such matters as confidential and the matter was so dealt with.

I might point out that it now appears to me, after closer examination of s. 10 of the *Patent Act*, that as far as the judge is concerned, the confidential nature of such matters can be maintained only if disclosure is not necessary to allow the proper discharge of his duty to render judgment.

If the confidential matters in the application must be disclosed in the judgment, s. 10 of the Act which states that

10 All specifications, drawings, models, disclaimers, judgments, returns and other papers, except *caveats* and except those filed in connection with applications for patents that are still pending or have been abandoned shall be open to the inspection of the public at the Patent Office, under such regulations as are adopted in that behalf.

does not and cannot, in my view, prevent the Court from dealing with such matters although it would seem to be a proper procedure in all cases to try to divulge as little of the confidential information as possible.

It indeed appears to me that particularly in a case such as we have here where the application objected to belongs to the plaintiff, s. 10 of the Act does not and should not prevent the dealing with such matters in a judgment when necessary, because the practice of not allowing the public to inspect pending applications and documents connected therewith necessary for the proper functioning of the public service, is not a public interest which should be recognized as overriding what Rand J. described in *Regina* v. *Snider*[1] at p. 482 as:

> the general principle that in a court of justice every person and every fact must be available to the execution of its supreme functions.

I might add that counsel for the plaintiff after the Court's decision to allow the amendment whereby the Martin-Bohonos application was allowed to be pleaded as prior art in the present case, volunteered to supply and did supply a copy of it. I might also say that the steps taken herein to provide for the secrecy of the contents of the Martin-Bohonos application appeared later at the trial to be somewhat unnecessary when counsel for the defendant stated that these contents could be substantially found in a document produced by the plaintiff in France to obtain a priority date, as appears from a certified copy of same produced as Ex. D-77.

Having set down the position taken by both parties herein and the issues involved, I now turn, firstly, to the determination of the matter of infringement based, as we have seen, on whether the importation into Canada of Tetracycline and its sale in this country (which is admitted by the defendant) infringes the two Canadian patents in suit and if so, whether streptomyces lusitanus, which produces this Tetracycline, should be considered from a taxonomic and speciation point of view as the same species or one different from the recognized streptomyces aureofaciens.

In Rhone-Poulenc S.A. v. *Micro Chemicals Ltd. et al*[2] I had occasion, in referring to the statement of the Supreme Court of Canada in *Hoffman-Laroche* v. *Commissioner of Patents*[3] to state:

[1] [1954] S.C.R 479.
[2] [1964] Ex. C.R. 819 at 831.
[3] [1955] S.C.R. 414.

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That there is infringement of a Canadian process patent by the sale in Canada of a product made abroad by that process would now appear to be accepted by our courts and defendants' submission that the act infringing a Canadian patent must necessarily be done in Canada, cannot therefore be accepted

I might even say that the Supreme Court of Canada in an *obiter dictum* in the *Hoffman-Laroche* case appears to have gone still further and it would seem that the sale of a product made in accordance with a patented process would infringe a process patent, even though the patent contained no claim to the product.

There are also a number of cases which have held that a process patent does not have to be used to produce the precise substance that is imported in order to constitute infringement but may have been used to produce an intermediate product. Now, although it appears to me that to find infringement in such a case could sometines lead to a situation where every person would be held to infringe a process patent who uses or sells an article or product imported into Canada in the course of the production of which the product produced by the process patent has been employed whether such use has been of importance or merely incidental in which latter case we would be going beyond protecting what is ordinarily termed the substance of the invention, there would appear to be some justification to find infringement where the product used as an intermediary is of importance such as we have here. As a matter of fact, infringement was found in a situation very similar to the present case, in *Saccharin Corporation* v. *Anglo-Continental Chemical Works*[1] where Mr. Justice Buckley stated:

> . . . Now the grant in Letters Patent is a grant to a Patentee to make, use, exercise, and vend the invention, to have and enjoy the whole profit and advantage by reason of the invention; and to the end that he may have and enjoy the sole use and exercise and the full benefit of the invention all others are precluded from, either directly and indirectly, making use of or putting in practice the said invention, or any part of the same, or in anywise imitating the same.

And further down he added:

> . . . Does it make it any the less an infringement that the article produced and sold is manufactured by the use of the patented process which is subjected to certain other processes? In my opinion it does not. By the sale of saccharin, in the course of the production of which the patented

[1] (1900) 17 R.P.C. 307 at 319.

process is used, the Patentee is deprived of some part of the whole profit and advantage of the invention, and the importer is indirectly making use of the invention.

It therefore appears that there would be infringement of the Duggar patent even if the product imported was not chlortetracycline, the new product invented by Duggar, but Tetracycline admittedly made by the process of making chlortetracycline and then by the deschlorination method obtaining Tetracycline.

It also appears that in such a situation, dealing with a new product (chlortetracycline from which Tetracycline is made), s. 41(2) of the *Patent Act* which creates a presumption in favour of the patentee that the substance imported "in the absence of proof to the contrary" is deemed to have been produced by the patented process would apply, were it not for the agreement for trial whereby the parties agreed that infringement of both types of tetracycline produced would be dependent upon a prior determination of the speciation of lusitanus which, I believe, has the effect of suspending the presumption and, therefore, the burden of proving that streptomyces lusitanus is a species of streptomyces aureofaciens would rest, under the ordinary rules of evidence, on the plaintiff. Cf. *Terrel and Shelley on Patents,* current edition, p. 327:

The burden of proving infringement (where it is denied) is on the plaintiff, and if he is unable to prove it, there is no necessity for entering upon the question of validity, unless there is a counterclaim for revocation.

I might add however, that if it is found that streptomyces lusitanus is merely a strain of streptomyces aureofaciens then the presumption of s. 41 (2) will be revived and the chlortetracycline produced and later made into Tetracycline will be presumed to have been produced by the Duggar process.

With regard to the Tetracycline imported and sold in Canada by the defendant and produced by means of the fermentation process, and which the plaintiff claims is an infringement of the Minieri patent, there can, of course, be no presumption because Tetracycline at the date of the above patent was not a new product. The agreement for trial, however, provides that there will be infringement of claims 1 to 5 and claim 7 of the Minieri patent "if

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Streptomyces Lusitanus is an organism of the group consisting of the species streptomyces aureofaciens together with natural and artificially induced mutants thereof."

It therefore follows that the matter of infringement will be decided on a question of taxonomy and speciation in determining whether or not streptomyces lusitanus is of the same species as streptomyces aureofaciens.

Taxonomy, according to the Glossary of Terms (Ex. 5) is "the classification of living organisms (although Dr. Henssen would add also fossils) according to their natural relationships. The laws and principles of such relationships" and speciation is "the art of determining the nature of the species or determining to what species a newly collected organism should be associated or assigned."

Now although the question as to whether streptomyces lusitanus is of the same species as streptomyces aureofaciens, appears to be a simple one, such is not the case and this appears clearly from an extract of Ex. 24 which is a recent paper written and presented in Madrid in 1963 by E. Kuster, a well recognized micro-biologist of the University of Dublin, entitled "Morphological and Physiological Aspects of the Taxonomy of Streptomycetes" at p. 195:

> Among these genera the genus *Streptomyces* is the most important one and comprises the greatest number of species. 256 species are considered in Waksman's monography (24) and since that time many new species have been described and named. Much confusion arises when a new species is not sufficiently tested and compared with type cultures. So, it can happen that the same species is named with different designations and many species may be synonyma.
>
> It is often very difficult to fix the borderline between the species; the definition of this taxon is quite unclear in spite of all the regulations in the Code of Nomenclature. Which criteria should be considered important and necessary for a species determination? There are two groups of taxonomists, the "lumpers" and the "splitters". The lumpers using only a few characters collect into one species many types which are designated as different species by the splitters. A good help for taxonomic work is the introduction and use of infrageneric taxa such as "groups", "species-groups" or "series". At present we are not yet able to build up a natural system of classification of bacteria to include the Streptomycetes, based on our knowledge of their phylogeny and evolution. Each classification system and key is only a tool for describing, collecting, and grouping the various naturally occurring types of organisms.
>
> The whole situation of bacteriological work and particularly taxonomy is complicated by the fact that our laboratory experiments do not completely reproduce the conditions and relationships in nature, the original environment of the microorganisms. Uncontrolled mutations or other changes of the genetic substance may also occur in nature, e g. in soil,

which are induced by mutagenic agents, such as metabolic products of microorganisms or substances derived from the decomposition of organic matter If two strains have been isolated from soil which differ in one or two characters, they will be classified as two different species. On the other hand, by a treatment with mutagenic agents mutants can be artificially produced which sometimes differ in more characters and nevertheless belong to the same parent species.

(24) Waksman, S.A. 1961. The Actinomycetes. II. Classification, identification and descriptions of genera and species. Williams & Wilkins, Baltimore.

In Ex. D-16, the Martin-Bohonos application, and this also appears in Ex. D-77, the document presented in France, it is also stated that:

Among mycologists the classification of microorganisms can frequently be a difficult problem, and different mycologists may arrive at different classifications for the identical organism.

In Ex. D-23, at pp. 52 and 53 of a paper printed in 1958 in the review "Applied Microbiology", vol. 6, the problem and difficulties of speciation of streptomycetes are further underlined by T.G. Pridham and associates:

After more than a decade of intensive investigation of streptomycetes, microbiologists are still confronted with the difficult task of identifying strains of these microorganisms. Of particular concern is the problem of characterizing isolates so that they can be readily recognized later. Of further concern is the difficulty encountered in identifying unknown strains using the systems presently available. These difficulties have their origin in the development of keys based principally on physiological criteria. . .

Major reliance on physiological criteria for grouping and speciation in the genus has led to the creation of a large number of "new species" (more than 100 since the discovery of actinomycin in 1940). This trend will continue as long as new antibiotics or other interesting compounds are discovered as metabolic products of streptomycetes unless reliance is placed on more constant taxonomic characteristics. The continuing addition of new species is not surprising when one considers the marked physiological diversity demonstrated in this genus. In our opinion, many of the new species are no more than varieties or physiological forms of valid ones already described. Once studied and compared with valid species, some of the new species could undoubtedly be rejected or placed in synonymy.

It therefore appears that if there are differences of opinion in the scientific world on the proper speciation of streptomyces as we have just seen, such differences of opinion were naturally greater at the trial where a number of bacteriologists, biologists, botanists, taxonomists and chemists confronted each other and where, I may say, they were far from unanimous not only on the matter of species determination of streptomyces lusitanus, but also on the value of the various criteria used for such a determination.

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The question of speciation which I am now called upon to examine and determine occupied the major part of the evidence at the trial and as already mentioned is one on which I have heard divergent opinions. My task, which is not an easy one, will be to consider the evidence of these experts, evaluate them and from that determine which evidence is and should be accepted on the balance of probabilities as more probative than the other. It is with this in mind that I now turn to the evidence of the experts in this case which I intend to analyze and weigh with as much common sense and shrewdness as I may have and with such skill I may have acquired in the course of the trial and during the deliberation.

On the matter of speciation, a Dr. Edward Backus and a Dr. Robert Benedict were heard on behalf of the plaintiff. Dr. Backus is a research microbiologist actually employed by the plaintiff, where he has been heading its Department of Microbiology since September 1956. This gentleman obtained from the University of Wisconsin a Bachelor of Arts degree majoring in botany, in 1937, a Master of Arts degree majoring in botany and plant biology, in 1939, and a Ph.D. degree majoring in botany and mycology, in 1941. Prior to 1956, since 1942, his principal duties with the plaintiff company have been the isolation of micro-organisms from natural sources, their identification and the production of mutations. He is the author of a number of scientific papers in the field of microbiology and is a member of a number of well recognized American scientific societies. From 1955 to 1960 he participated with a group organized by the American Society for Microbiology, now called Society of American Bacteriologists, which endeavoured to study and determine the proper criteria to use in order to determine species of the genus streptomyces and in 1960 he became a member of a study committee which organizes and runs the tests necessary to determine species of the genus streptomyces. He also became a participant of a corresponding group organized on an international basis at the International Congress for Microbiology in Stockholm in 1958, when a cooperative project was set up involving the interested microbiologists particularly those who practised in the taxonomy of the genus streptomyces from all parts of the world and he has continued to be active in this group up to the

present time. Dr. Backus was an associate of Dr. Duggar and has been working with micro-organisms of the genus streptomyces on a more or less continuing basis for the last twenty years and his attention has been focused more or less on the micro-organisms of the species streptomyces aureofaciens because of its importance to his employer, for the last seventeen years. This witness explained how mutant strains were produced, that there were a number of cultures and depositories around the world where interested parties may deposit micro-organisms, so that other people may obtain them and these various cultured collections will receive such organisms, maintain and distribute them upon request. He stated that strain A-377, isolated by Dr. Duggar, was first deposited in the collection of the Northern Regional Research Laboratory in Peoria, Illinois, in the summer of 1949 and it was assigned the number N.R.R.L. 2209. The Northern Regional Research Laboratory is a unit of the United States Department of Agriculture where studies are conducted on the utilization of agricultural products in general. This N.R.R.L. 2209 deposited according to Dr. Backus, was released on September 13, 1949 and from that date anyone could obtain without charge a culture of this organism to study its characteristics and experiment with it. He also stated that a strain of streptomyces aureofaciens known as UV-8 was first produced by a group working under the direction of Minieri, who, at the time, was at the Heyden Chemical Corporation. This strain was first deposited at the American Type Culture Collection (A.T.C.C.) around December 15, 1955 and was released on February 7, 1956, with the only restriction being placed on its distribution being that the plaintiff be informed if an organism was sent outside of the United States. He also testified that streptomyces aureofaciens is generally accepted by scientists as a valid and distinctive species new at the time of Dr. Duggar's original description and isolation of the organism and this seems to be accepted by the other experts.

A strain of streptomyces lusitanus (F. 1617) was delivered to Dr. Backus' laboratory by a Mr. Austin Phillips and the former made a comparative study of streptomyces lusitanus and streptomyces aureofaciens by utilizing strain

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N.R.R.L. 2209, the original Duggar organism, and concluded that this strain of streptomyces lusitanus is none other than a strain of streptomyces aureofaciens. In his written report produced as Ex. 20 he states at p. 2 thereof that:

4. An analysis of the observations on cultural characteristics of the two organisms reveals no significant differences—the minor variations in response to specific media being typical of the variation encountered in different *strains of the same species*. Both organisms gave moderate to good growth on most agar media—exceptions being the thin, light growth which both made on the Czapek-type formulations and on nutrient agar. A majority of media also supported moderate to heavy sporulation by both organisms All appreciable spore masses of both were observed to be brownish-gray shades (*Benzo Brown* and *Mouse Gray* as defined by Ridgway) which fit into the "gray" series of the Pridham et al (Appl. Microbiol, 6, 55, 1958) Guide to Streptomyces classification or the "cinereus" colour group of the key devised by Ettlinger et al (Arch. f. Mikrobiol, 31, 332, 1958). On media which supported good to moderate growth, both organisms produced substrate thalli and reverse colors in shades ranging from pale yellows to deep ruddy browns. No significant differences between the two organisms were noted with reference to soluble pigment production, a characteristic of minor taxonomic significance at best.

5. Morphological characteristics of the two organisms were remarkably similar—both showing hooks, loops or rudimentary spirals intermixed with straight to flexuous sporophores and clearly belonging to the *Retinaculum-Apertum* section of Pridham et al or to the "Spiral" forms as interpreted by Ettlinger et al This total agreement is highly significant since this characteristic is one of the key criteria in Streptomyces classification. No significant differences in spore shape or spore size were observed in the two organisms Likewise both organisms were observed to have smooth, unornamented spore surfaces as viewed by electron microscopy. This again is highly significant since the nature of the spore surface ornamentation has been shown to be a highly stable characteristic of Streptomyces species (Tresner et al, Jour. Bact, 81, 70-80, 1961).

6 The miscellaneous physiological reactions of the two organisms were also remarkably uniform—the chief differences being slight deviations in the amount of growth achieved on various substrate Neither organism was able to reduce nitrate to nitrites when grown on either synthetic or organic nitrate broth. Likewise neither organism was able to liquefy gelatin, while both showed positive starch hydrolysis. Both organisms were non-chromogenic, i e, did not produce melanin-type pigment on protein-rich media. This latter trait again is a highly significant characteristic for determination of Streptomyces species identity, (Ettlinger et al, 1958). *Streptomyces lusitanus* F 1617 grew slowly on purple milk (Difco) and caused neither coagulation nor peptonization at 14 days; however, there was moderate growth and weak peptonization evident after 21 days. *S. aureofaciens,* which grew somewhat better on this medium, caused slight coagulation and weak peptonization at 14 days. Neither organism caused any shift in pH during the growth cycle. Reaction of Streptomyces cultures on milk media is a highly unreliable criterion for species differentiation because of the variability which different strains of the same species have shown in this test This is particularly true of S aureofaciens (Backus et al, Ann. N Y Acad Sci, 60, 90, 1954) The lack of significance of reaction on

milk media for Streptomyces species differentiation in general is also pointed out by Hesseltine et al (Ann N.Y. Acad. Sci., 60, 147, 1954).

7 A highly useful criterion for Streptomyces species differentiation is the pattern of utilization of diverse carbon sources as determined by the technique of Pridham and Gottlieb (Jour Bact., 56, 107-114, 1958). Because of difficulties in interpreting the amount of growth achieved, minor differences in behaviour on specific C-sources are of little significance. Rather, it is the *overall pattern* of similarity or dissimilarity which is meaningful in the comparison of two individual cultures. The data displayed in Table IV shows the remarkably similar C-source utilization patterns of *S lusitanus* F 1617 and *S. aureofaciens* NRRL 2209. The reactions to individual carbon compounds are either identical or differ only in a minor quantitative degree. Growth of *S. lusitanus* in several instances was less vigorous than that of *S. aureofaciens* which reflects its limited ability to utilize inorganic nitrogen compounds. Ammonium sulfate is the sole nitrogen source in this particular medium This limitation, however, was not so severe as to interfere with the observation of the extreme similarity in the C-source utilization patterns of the two organisms.

8 It is reiterated for emphasis that my comparative study of the *S. lusitanus* culture received from Dr Tosoni and *S. aureofaciens* NRRL 2209 revealed almost completely identical characteristics for the two organisms as regards the five critical taxonomic criteria as follows:

(*a*) *En masse* spore colour;

(*b*) Sporophore (spore chain) morphology;

(*c*) Spore shape and ornamentation as determined by electron microscopy;

(*d*) Chromogenicity (melanin pigment production on protein rich media);

(*e*) Carbon source utilization pattern.

This identity was further supported by identical or highly similar behavior with respect to the lesser criteria such as nitrate reduction, gelatin liquefaction, starch hydrolysis, soluble pigment formation, etc. This abundance of data is consistent with only one conclusion, namely, that *Streptomyces lusitanus* has no characteristics which establish it as a species separable from *Streptomyces aureofaciens.*

This witness described eleven characteristics or tests or criteria employed today for scientific determination of mesophylic species (i.e. organisms such as aureofaciens which grow or exist preferentially at intermediate temperatures (i.e. 25-35 degrees C.)) of the genus streptomyces, commented on their relative importance and the importance and the use made of them by various scientists, these criteria are as follows:

1. The nature of the spore-bearing portion of the aerial mycelium of the micro-organism, which contain chains of spores, their structure, form and shape;
2. The "en masse" spore colour; as the organism sporulates or grows and reaches maturity, the aeromycilum of the surface becomes coloured a distinctive shade and these

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colours (the total colour given to the surface of the well sporulated organism) can be used as diagnostic characteristics;

3. Nature of the individual spores as they may be observed under very high magnification such as provided by an electron microscope;
4. The production of a characteristic blue-black pigment known as melanin pigment, the ability of the micro-organism to produce it or not to produce it;
5. The pattern of utilization by the organism of selected sources of carbon, its ability to use up some types and not to use up others;
6. The range of colour displayed by the vegetative mycelium which grows on the surface of the agar, which is also called substrate thallus colour;
7. The ability of the organism or lack thereof to reduce nitrates to nitrites;
8. Its ability to liquefy gelatin;
9. Its ability to produce pigments other than the melanin which are soluble and may diffuse into the medium and give a distinctive colour called soluble pigment production;
10. Its ability to utilize starch;
11. Its behaviour on litmus milk.

With regard to criteria No. 1 the structure, form and shape of the aerial mycelium of the micro-organism, Dr. Backus produced Ex. 25, taken from the Pridham paper, (Ex. 23), which indicates the different types of sporophores or spore chain arrangements observed in streptomyces. These sporophores are straight, flexuous and fascicled. The first group is called rectus-flexibilis, meaning straight flexuous. The second group encompasses a mixture of sporophores of rectus-flexibilis together with a type described as open-loops, primitive spirals and hooks, which is recognized by the Latin name *retinaculum-apertum,* commonly referred to as R.A. The third category encompasses those organisms in which actual spirals are produced which may be open spirals or tightly wound spirals in almost the form of a little ball which the Pridham group grouped together as spira. Then there is the fourth category, where the spore chains come

out in little whorls along the axis of the hypha, called verticillate or whorls.

He produced Ex. 27, which are photographs of streptomyces aureofaciens strain N.R.R.L. 2209 and streptomyces lusitanus magnified 450 times and where it appears that both organisms produced the hooks and loops and coils of the *retinaculum-apertum* type with a certain amount of flexuous or rectus-flexibilis elements intermixed, and therefore they would both fall within the category of *retinaculum-apertum*.

Dr. Backus stated that all the above eleven criteria were not of equal value in the determination of species within the genus streptomyces and that a number of them were far more stable than others. He admitted that different investigators take different views as to how many of these are more useful, but that, at one time or another, all have been used. He therefore has taken all of them and covered the whole range in the investigation of lusitanus and aureofaciens. He also stated that the Swiss investigators, Ettlinger et al rely upon the first four criteria and consider them definitive for the determination of species, as it appears from a translation of the joint L. Ettlinger, R. Corbiz and R. Hutter paper, produced as Ex. 22. Pridham and his associates, at the Northern Regional Research Laboratory in Peoria, on the other hand, accept the first five criteria as being most useful in the identification of species, as appears from a Pridham article in the review "Applied Microbiology", published in 1958 and produced as Ex. 23. Kuster, another well-recognized scientist, recommended the use of the first six criteria in 1963, as appears from Ex. 24.

In cross-examination on the first criterion (nature of spore-bearing portion of the aerial mycelium of the microorganisms), he was shown p. 128 of a book entitled "The Actinomycetes" (Waksman) where there are three photographs showing on the left side, streptomyces aureofaciens with straight, flexuous and continuous sporophores; in the centre, a photograph of a natural variant of streptomyces aureofaciens with loops and some straight sporophores and, on the right-hand side, an induced mutant streptomyces aureofaciens almost completely looped.

He was asked to explain how aureofaciens could produce these different types of sporophores, which he did by stating

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that strain A-377 used in the first photograph, under the conditions of growth existent at the time, produced straight to flexuous sporophores; that the second one was a strain isolated from nature and the third was an induced mutant strain prepared from A-377.

Here, however, Dr. Backus stated that the difference in sporulation was not necessarily the result of mutations in the strain because the middle one which hooked and looped is not a mutant but an isolate from nature, as well as the first one which on the other hand is straight and flexuous. He is of the opinion that aureofaciens can produce either straight or flexuous or hooked and looped forms and still be aureofaciens, as the latter is usually a mixture of both and that it falls, therefore, within the definition of what the *retinaculum-apertum* group is.

He agreed that the medium used would influence the appearance of the sporophores and that, in certain media, poor sporulation would be obtained and that in order to get proper sporulation and characteristics, the organism must be in a situation where it is growing optimally.

He also admitted that with certain media the sporophores would be of the first type, i.e., straight, and on other media the percentage would tend to shift in the other direction so that we may find here a certain variation. He, however, pointed out that even with variation with regard to the percentage of straight flexuous forms and the loops and coils, it does not vary here out of what Pridham would define as *retinaculum-apertum*. As it was possible that the choice of the medium could affect the proportion of straight mycelium to the proportion of looped mycelium, Dr. Backus stated that he had selected a particular medium for his comparative study and that he had selected this medium because it was one upon which optimal abundant sporulation was developed and that, therefore, in his experience, that was the type of medium which would give the most characteristic appearance of the species and he used the same medium for both streptomyces aureofaciens and streptomyces lusitanus in his investigation.

He also admitted that , at column 4, line 32 and following, in the Duggar patent, a description of the branch hyphae of the aureofaciens mentions the "flexuous and continuous" and does not mention the presence of hooks and loops at all

and that, consequently, the strain used which shows, generally, hooks and loops might have been a mutation.

With regard to the second characteristic, the "en masse" spore colour of the sporulation aerial mycelium, Dr. Backus stated that in order to determine the spore colour, abundant and well-sporulated growth must be obtained; he found here that both organisms, lusitanus and aureofaciens, belong to the grey spore colour group.

He admitted that there were some variations in the scientific world as to the recognized spore colour groups. For instance, Pridham and his associates, as well as Ettlinger, recognize six, although the latter modified them somewhat by combining and splitting. Dr. Backus and his associates recognize seven, the same six recognized by Ettlinger, plus a violet shade group. He also stated that all of these systems contain a group which is regarded as grey but described as ranging from grey to brown, and he affirmed that both lusitanus and aureofaciens would fall into the grey-brown group.

With regard to the third stable characteristic, i.e., nature of the individual spores, as viewed by electron microscopy, the witness produced a number of photographs magnified in the neighbourhood of 40,000 diameters:

Ex. 28: (S. Olivaceous)
Ex. 29: (S. Diastatochromogenes)
Ex. 30: (S. Purpurascens)
Ex. 31: (S. Calvus)
Ex. 32: (S. Albogriseolus)
Ex. 33: (S. Diastaticus)
Ex. 34: (S. Phaeochromogenes)
Ex. 35: (S. Aureofaciens)
Ex. 36: (S. Lusitanus)

From these exhibits, it appears that the spores of a number of streptomyces, viewed under sufficient magnification, have some interesting surface ornamentation useful in classifying these micro-organisms. He states that these characteristics are very constant and are highly reliable criteria. Some of the spores reproduced on the above photographs have little warts on the surface, others have stout thorns, spines or hairs; some have considerably longer hairs

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tangled and twisted around the spores; some have smooth spored forms and others are elongated types.

From the above exhibits it appears that aureofaciens and lusitanus are both smooth spored and have no thorns, spines, hairs or warts on the surface. The cells in both cases tend to be somewhat elongated and are further marked by curious thickenings at the ends of the cell with an electron-dense area running through the centre which gives this chain of spores a phalangeal appearance like the bones in the finger.

With regard to the fourth stable characteristic, i.e., the production of melanin pigment, which is a test for the presence in the organism of an enzyme, tyrosinase, which has the capacity to stimulate the chemical change of the aminoacid tyrosine to melanoid type of pigments, the witness produced Ex. 37 which illustrates that the two types of streptomyces, bikinienses and lavendulae, give a positive melanin production and reaction, whereas both lusitanus and aureofaciens do not.

The fifth criterion, i.e., the ability or lack thereof of the organism to utilize certain carbon sources in a defined medium can, according to Dr. Backus, supply something of a fingerprint as to its identity as certain patterns of utilization can be determined in particular species and are useful in identifying particular organisms. Certain species appear to be variable with reference to certain carbon sources, whereas concerning other carbon sources there is a very firm pattern of utilization or a constant lack of utilization. He stated that this technique was described by Pridham and Gottlieb and further expanded by Dr. Benedict in later years. Having applied this test to both lusitanus and aureofaciens, and having used a series of carbon sources indicated in his report (Ex. 20) in a defined medium, he stated that the results indicate that there is here a similar pattern of utilization. A key carbon source, in the opinion of this witness, is sucrose and both lusitanus and aureofaciens utilize sucrose as well as fructose and dextrose, although essentially all organisms utilize dextrose.

He added that, on the other hand, they both are essentially unable to utilize mannitol, raffinose, rhamose and salicin.

He affirmed that, although generally the results of the test used by him in his investigation would depend somewhat on the strains and medium used, the carbons he used are very constant and therefore, in his opinion, his test was most useful. As far as the strain used in his test is concerned, it was a type culture derived from the original A-377.

He also added that even if the strain he had used for his comparative study was a mutant, it would have exhibited no differences from its natural isolate predecessor in respect of the first five stable characteristics hereinbefore mentioned as well as in respect of the other six characteristics, so long as the strain used corresponds to the characteristics shown by the original.

According to this witness, the first five characteristics we have just seen are the most suitable for determination of the species and he has used them in studying approximately 600 nature isolates of various streptomyces and has found no strains of streptomyces to have identity with streptomyces aureofaciens on all five of the above-stated characteristics which were, in his opinion, a distinct species from streptomyces aureofaciens.

He also stated that he went through the six other criteria because they have been used by other investigators and he wished to confirm that his conclusions, based on the first five, which he believed most useful, would also be confirmed by these other criteria, adding that these other tests also confirmed his opinion that the two organisms belong to the same species.

With regard to the substrate thallus colour, both organisms produced a colour ranging from a creamy yellow to a deep ruddy brown (i.e., in a yellow brown area) depending on the nature of the substance upon which it is growing.

Neither of them were able to reduce nitrate to nitrites, nor did they liquefy gelatin to any degree.

As to the soluble pigment produced other than melanin, although somewhat erratic, the test produced in both cases the same soluble pigment in a yellow-brown shade.

Both organisms were able to hydrolyse starch.

With regard to the litmus milk test, which is one where an indicator of acidity, alkalinity, has been added to skimmed milk, growth in both cases was very slow, neither organism

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liking this medium particularly, lusitanus however growing somewhat more slowly than aureofaciens. During the period of incubation, there was no difference, neither being able to produce any change in the pH (acidity) of the medium in which there had been any mixture of the acidity of the alkalinity.

With regard to the use of mannitol, they, according to his test, would not support growth in aureofaciens and that part of the Duggar patent, column 5, line 32, which states that it will support growth, he explained by saying that in the patent it is being utilized in an entirely different sort of medium in which there are other types of compounds present supplying nitrogen, perhaps supplying even other carbon sources, and that a good deal depends on the medium although if the test is carefully prepared, according to the formula employed, it can be very meaningful.

In other words, with regard to the mannitol utilization, different media would give different results.

He also added that the difference in the result obtained in his test and that described in the Duggar patent revolves around the use of a specific Pridham-Gottlieb medium which is a chemically defined medium with precise determination of the ingredients contained therein. In contrast, the medium to which Professor Duggar was referring to in the patent contained natural materials which may well bring along with them miscellaneous carbohydrates other than the one he also added as a major component and, therefore, it would be unsuitable for use in determining whether or not a specific carbon source would or would not be utilized because of the nature of the other ingredients put into it.

In the case of both lusitanus and aureofaciens, he used the exact same media and identical mannitol, which incidentally is a sugar alcohol, and therefore he was comparing like with like.

In cross-examination he was referred to a paper prepared by Professor Waksman entitled "The Actinomycetes" and where the latter referred to Dr. Duggar, Dr. Campbell and Dr. Backus (the witness) in respect to the question of speciation. At p. 100 of vol. 1 of the above writing it is stated by Professor Waksman:

They (Dr. Duggar, Dr. Campbell and Dr. Backus) are willing to use as a basis of species differentiation minor or single variations of morphological or developmental features, of responses to environmental changes, of differential election of nutrients or of metabolic differences.

Dr. Backus admitted that he was part of a study that Professor Waksman was conducting at that time adding, however, that Professor Waksman has put a few interpretations of his own into that writing which are contrary to what Dr. Backus claims his and his colleagues' writings were and that Professor Waksman's statement did not interpret accurately what he, Dr. Campbell and Dr. Duggar had employed or written in that paper and that actually some of the quotations are couched in such a manner in Waksman's interpretation that they present an almost exactly opposite idea to what Backus states "we were trying to put forward". At p. 481 of the transcript he stated:

Rather than accepting that as a basis of the species, we pointed out that to do this would result in the creation of thousands of species where tens exist, and in so doing, of course, that would be exactly the thing which we in the line previously had agreed was unsound practice, so I am sure that it has never been my concept to accept this idea of using small differences to create species, and it is my general recollection that Professor Duggar was of the same view.

Having stated that in his opinion streptomyces viridifaciens and streptomyces aureofaciens were one and the same thing, he was asked whether he would change his mind after looking at Ex. 23 "A Guide for the Classification of Streptomyces According to Selected Groups" by Pridham, Hesseltine and Benedict, p. 65, under the heading "Epithet", where both aureofaciens and viridifaciens are listed individually. He said he would not, stating at p. 387 of the transcript:

...The mere fact that they are both listed here does not necessarily mean that these authors accepted all of these organisms so listed as valid and separate species.

They indeed indicate earlier in this treatise, at p. 53, that it is their opinion that many of these may be reduced to synonymy. He then stated that he had had occasion to examine S. viridifaciens and conduct studies in respect of it in the same manner he had done for S. lusitanus and in his opinion viridifaciens is also only a strain of aureofaciens.

Dr. Backus was then referred to Canadian patent 658,503, granted to American Cyanamid Co. on February 26, 1953, p. 6, line 5, where in connection with the mention of S. viridifaciens, it is stated at p. 407 of the transcript:

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. . . The published morphological data on these microorganisms is insufficient conclusively to determine whether or not they are new species or merely strains of S. aureofaciens.

He was then asked whether the above would be a correct statement of the art of taxonomy of streptomyces at the date of this patent, i.e., 1963, to which he replied, at p. 407 of the transcript:

> A. Certainly the organisms you have mentioned there are inadequately described and one could not, simply by reading these descriptions, arrive at a determination since certain of these descriptions do not supply the majority of the key characteristics we were discussing this morning.

And later, when asked whether he would agree with the statement or not, he stated he would not disagree with certain portions of the statement, adding, however, at p. 408 of the transcript:

> A. Well, I certainly agree with these references to alleged distinct species, because I do not think these are distinct species. I would agree with this passage where he says that these are alleged to be distinct species. In other words, he is not committing himself to this point. But they are alleged in the literature to be different species. And the published morphological data on some of these is insufficient; in other words, we are not told what the structure is, whether it is flexuous or whether it is coiled, or whatever it is, and with reference to the other characteristics we are not told.

He then concluded by saying that he had conducted studies similar to the comparative study contained in his report, Ex. 20, on all of the following streptomyces: viridifaciens, sayamaensis, feofaciens, and that they are in his opinion merely strains of aureofaciens.

Dr. Robert Benedict, a fermentation expert and microbiologist, was also heard on behalf of the plaintiff.

This gentleman received his Bachelor of Science degree from Michigan State College in 1936; A Master of Science degree in biology from Virginia Polytechnical Institute in 1938; and a Ph.D. degree in agricultural bacteriology from the University of Wisconsin in 1942. He is the author and co-author of a number of technical articles and papers in the field of fermentation and microbiology. From July 1942 until September 1960 he was employed by the Northern Regional Research Laboratory in Peoria, Illinois, which, as we have seen, is a division of the United States Department of Agriculture. During the years 1942 to 1946, he maintained bacterial cultures of the N.R.R.L. and also did research work on penicillin and other antibiotics. From 1946

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to 1953 he was with the Survey and Development Section of the N.R.R.L. where research on antibiotics produced by moulds, bacteria and actinomycetes was carried on, during which period he received the Superior Service Award from the United States Department of Agriculture in 1950; from 1953 to 1956 he was engaged in a special project for the United States Army Chemical Corps; from 1956 to 1958 he headed the Microbiological Technology of Polymer Unit where research work was carried out in dextrine and polymers from yeast and bacteria; in 1958 he was engaged for six months in a special project concerning the microbiological synthesis of rubber, and from 1958 to 1960 he was the head of the new product's exploration and reactions investigation group where work was being carried out in the production and isolation of fermentation product from fleshy fungi. From October 1960 to date, he has been associated with the College of Pharmacy, the drug plant laboratory of the University of Washington in Seattle, studying the chemical constituents of a variety of fleshy fungi and he is now an associate professor nominate in that University; he is a co-author, with Pridham, of "The Guide for the Classification of Streptomyces According to Selected Groups" (Ex. 23); he is a member of the American Society of Microbiology and is listed in the American Men of Science.

Dr. Benedict dealt with the N.R.R.L., its culture collection and the reputation it enjoys in the scientific world. It is composed of several divisions, one of which is the fermentation division where a culture collection of yeasts, moulds and bacteria is maintained. He affirmed that the above culture collection is known throughout the world and that any qualified microbiologist interested in taxonomy would know if he saw the initials N.R.R.L. that they stood for Northern Regional Research Laboratory.

Dr. Benedict has isolated three different strains of aureofaciens from samples of three Japanese soils and in addition to that, in the course of several years, has personally investigated about 4,000 samples. He has isolated actinomycetes from these samples, studied them culturally and has done fermentations in attempts to produce antibiotic substances of medicinal value.

He stated that Ex. 23, which is "The Guide for the Classification of Streptomyces According to Selected

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Groups", prepared by Pridham, Hesseltine and himself, should serve as a guide to both experts and novices interested in the taxonomy evaluation of strains of streptomyces.

He affirmed that where a spore has both R.F. and R.A. characteristics, the proper classification of such a micro-organism is to place it in the slightly more complex category and, in the present instance, with regard to lusitanus and aureofaciens, they should be referred to as R.A. types instead of R.F. types.

From the strain of S. lusitanus (F-1617) obtained from Dr. Backus, Dr. Benedict made a study of this micro-organism and compared it with S. aureofaciens, using two strains of the latter, number N.R.R.L. 2209 and the other from the Lederle Laboratories. He stated that as far as the two last mentioned strains are concerned, there was no difference between their morphological or other characteristics.

His conclusion also was that S. lusitanus is none other than a strain of S. aureofaciens, as appears from a report prepared by him and produced as Ex. 40, which is based on the following considerations taken therefrom at pp. 2, 3 and 4:

10. Although *S. lusitanus* grew somewhat more slowly and sporulated less vigorously than *S. aureofaciens* NRRL 2209 the habits of growth of the two were similar. Despite minor differences in shading due to differences in the total quantity of accumulated spores, there is no doubt that the spores of both strains should be grouped into color series 6 of Pridham *et al* (Appl. Microbiol., 6, pps. 52-79, 1958). This is the gray series (light gray to mouse gray to brown-gray to gray-brown). Likewise, there is no doubt that both organisms would belong to the "cinereus" colour grouping of Ettlinger *et al* (Arch. f. Mikrobiol., 31, page 332, 1958).

11. *Sporophores* (Spore-chain Morphology): This is one of the most significant criteria for Streptomyces species differentiation. Media which afford optimal sporulation conditions provide material which reveal the characteristic sporophore structure of the organisms. The various sporophore types have been defined and illustrated in the Pridham *et al* Guide previously cited (Appl. Microbiol., 6, pps. 52-79, 1958). Well sporulated cultures of *S. lusitanus* revealed the presence of substantial numbers of sporophores which were hooked, looped and coiled into primitive spirals. Therefore, the morpholigical section in the Pridham *et al* Guide into which *S. lusitanus* falls is *Retinaculum Apertum* (RA) wherein the species *Streptomyces aureofaciens* also belongs.

12. *Soluble Pigments:* No significant differences were observed in the soluble pigment formation by *S. aureofaciens* and *S. lusitanus,* both producing light yellow or no pigments on the agar media used. No particular significance is attached to the production of soluble pigments as a criterion for species differentiation.

13. *Physiological Tests: Carbon utilization tests.* Within the past ten years, numerous investigators have employed carbon-utilization tests as an aid in species differentiation of Streptomyces. The majority of these workers have found the tests to be of value when combined with other characteristics which have been found to be most stable and uniform in behavior. For example, Benedict *et al* (Appl. Microbiol., 3, pps. 1-6, 1955) found that four strains of *S. aureofaciens* (natural variants) gave a fairly uniform carbon utilization pattern. Actually, if one eliminates from contention those C-sources commonly used by practically all Streptomyces species, he finds that relatively few C-sources are metabolized by strains of *S. aureofaciens*. One of the normally "difficult to utilize" C-source (Table 2, page 3, Benedict *et al*, Appl. Microbiol., 3, pps. 1-6, 1955) is sucrose, in contrast to the readily metabolized sugar alcohol, manitol. Both *S. aureofaciens* NRRL 2209 and *S. lusitanus* F-1617 gave identical reactions.

14. *Miscellaneous Tests:* Although chromogenicity (melanin pigment production) still ranks high as a link in species differentiation, far less importance can be attached to the results of such tests as nitrate reduction, gelatin liquefaction, etc. It should be noted, however, that both *S. aureofaciens* NRRL 2209 and *S. lusitanus* F-1617 gave identical reactions.

He accepted Dr. Backus' statement that the first five criteria or characteristics mentioned by the latter were stable and added that they were accepted by a number of scientific people as determinative of the species streptomyces.

He compared the sporophore morphology of lusitanus and aureofaciens and both exhibited a combination of R.F. and R.A. types, which according to his classification should place both of them in the more complex group of *retinaculum apertum* (R.A.).

With regard to the second stable characteristic, the "en masse" spore colour of the micro-organism, although there are six colour groups in which streptomyces may fall, he observed that both lusitanus and aureofaciens fell into what is called the grey group, or the grey colour.

With regard to the melanin pigment production, he stated it was a valuable diagnostic too and he found that both aureofaciens and lusitanus were negative.

The carbon source utilization test (Pridham-Gottlieb) is, in his opinion, valuable as a diagnostic tool for these micro-organisms and, having compared lusitanus and aureofaciens on a number of different carbon sources, he observed that the pattern of utilization between the two is similar.

Dr. Benedict stated that none of the streptomyces strains he studied which showed identity with streptomyces

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aureofaciens in respect of the five criteria were separate and distinct species.

He also conducted additional physiological tests with both lusitanus and aureofaciens, including the ability to hydrolyse starch, where both cultures were positive; the ability to break down gelatin, where both cultures were negative; and the ability to reduce nitrate to nitrite, where both cultures were also negative.

He also had occasion to conduct studies of streptomyces aureofaciens and streptomyces viridifaciens and concluded that the latter is none other than a strain of streptomyces aureofaciens.

Dr. Benedict admitted that various strains of aureofaciens would not respond similarly in the same medium, and, in his opinion, that explains Ex. D-1 which was discussed with Dr. Backus and which on the left side shows a photograph of filaments of a straight and flexuous type whereas the variant and the mutant aureofaciens shown opposite are full of loops.

Asked by the Court as to whether he used the best medium to obtain the best morphological development of the spores, he answered "yes", adding at p. 531 of the transcript:

> A. I might explain that Doctors Pridham, Hesseltine and myself have done a considerable amount of this work in the last ten years. We have made a study of a variety of different media. In one of our publications we have about 30 different types of media listed. We have found in studying and analysing the various types of media that there are certain ones which are better than certain others. Therefore, the ones which I used in the present study, I believe, are ones generally accepted to be of value in producing the stable, morphological, sporophore types that we have been talking about. Also in producing spore colours en masse, that are reproduceable from one time to the next.

Asked how many species there are today of streptomyces he answered that it would be very difficult to say exactly but that Ettlinger *et al*, the Swiss investigators, recognized about thirty-four different species.

Dr. Benedict was referred to Ex. 23, a paper of which he is a co-author, and particularly to certain colour series contained therein indicating that there are white, olive buff, yellow, blue, red and grey series. He also stated that he was familiar with a paper prepared by doctors Tresner and Backus, entitled "System of Colour Wheels for Streptomyces

Taxonomy" (Ex. D-15) in which the colours of streptomyces are divided into a number of actual colours and sub-divided into what are called hues or codes. He also agreed that these colour divisions of the spores are an important factor and a diagnostic aid when involved in an analysis such as conducted in Ex. 23.

In his report (Ex. 40), he produced four sheets, two of which are entitled "Section IA" for lusitanus and the two others, "Section IB" for aureofaciens. It is possible, by looking at these tables, to compare the amount of growth, the aerial mycelium and/or spores, the soluble pigment and the reverse colour, of both streptomyces lusitanus and streptomyces aureofaciens when grown in a number of media.

With regard to some growths, or colours, or pigments, there appears to be some differences which Dr. Benedict was called upon to explain in cross-examination. For instance, on a medium of tomato paste oatmeal, lusitanus has fair growth whereas aureofaciens has good growth and Dr. Benedict agreed that aureofaciens grows better in that medium than lusitanus. With regard to the aerial mycelium it appears that it is whitish becoming light olive grey with lusitanus and whitish becoming mouse grey with aureofaciens which Dr. Benedict explains in that in his colour guide when reference is made to the grey series, they are not speaking of a single colour but that there is meant colours ranging from light grey to mouse grey to grey-brown and to brownish-grey. In other words, there is a range of colours in the grey series which he compared to the Ridgway colour guide which has been used by scientists for a number of years in matching colours.

With regard to the words "sporulation areas becoming benzo-brown" in his report of lusitanus grown on tomato paste oatmeal, he pointed out that brown is just a preliminary stage in the development of the final colour. He admitted that he had not mentioned the colour of the aureofaciens spores "en masse" and could not say why but that he is sure the colours would be close to mouse grey. He agreed that there was a difference between lusitanus and aureofaciens in the reverse colour with regard to the medium tomato paste oatmeal, in that for lusitanus it was walnut brown and for aureofaciens it was deep olive, adding,

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however, that he did not attach special significance to the so-called reverse colour, nor does he attach a great deal of significance to the soluble pigment.

With regard to the second medium used in these tables, oatmeal agar, the amount of the growth of lusitanus is fair and that of aureofaciens is good. The characteristics of the aerial mycelium are, for lusitanus, "aerial: white to deep greyish olive in central colony zones to mouse grey at margins. Sporulation moderate", whereas for aureofaciens, on the same medium, he has "aerial mycelium: whitish becoming benzo-brown in sporulation areas. Sporulation moderate." He stated that he does not attach any significance to the above small differences as the significant colours here are those that have to do with the colour of the spores at maturity and those in the grey series range from light grey to mouse grey or a brownish-grey, and grey is the predominant colour in the series.

The same applies to the differences which appear with regard to both organisms in a medium called Hickey and Tresner agar, the important thing being the colour of the spores at maturity.

With regard to the medium yeast extract agar, which for the aerial mycelium reads: "From white to deep olive, grey to mouse grey in sporulation areas at margins. Sporulation moderate" for lusitanus, and "Aerial mycelium white becoming mouse grey, sporulation heavy" for aureofaciens, he explained what happened inside the body of the spores in lusitanus where the sporulation at margins is mentioned by saying that there is a tendency in some of these media for the colours on the outer edges to develop more sporophores than some of the colours inside. At p. 544 of the transcript he added:

> A. . . . Why this is so I don't know. Often you will see it in the colonies out at the edge of the plate, on the periphery, and later it will develop towards the centre.

Asked why he did not make the same observation in connection with aureofaciens, he stated, at the same page:

> A. We do not claim that lusitanus and aureofaciens are exactly the same thing; no two strains of any microorganism are the same. We simply referred to these as within the limits you would expect.

This table, with regard to lusitanus on a medium called inorganic salt starch agar, indicates that from a colour point of view, after ten days of growth the aerial mycelium is

"none to white". The table indicates that he did not analyse aureofaciens after ten days and he explained this by saying that he had found that lusitanus grew somewhat more slowly than aureofaciens and, therefore, the lusitanus plates had to be looked at sometime after the N.R.R.L. plates had fully developed insofar as sporulation is concerned. According to Dr. Benedict this was simply a matter of lusitanus in this particular case being unable to utilize inorganic nitrogen sources as rapidly as aureofaciens. He attached, he said, no importance or significance to the slow growth of lusitanus in this medium, nor does he attach significance to the fact that lusitanus went through capucine buff to light olive grey before getting to mouse grey, whereas aureofaciens become greyish olive and then deep greyish olive and then mouse grey, as those colour changes were intermediate changes, he also stated that he attached no importance to the fact that in Czapek's sucrose the growth of lusitanus is scant whereas the growth of aureofaciens is fair and that aureofaciens has "aerial mycelium scant, whitish becoming grayish white, sporulation none," and lusitanus has "aerial mycelium scant, white, sporulation none" because here again lusitanus cannot utilize inorganic nitrite quite as rapidly as aureofaciens N.R.R.L. 2209 and consequently the growth is somewhat slower and perhaps a little lighter.

With regard to the growth of the organisms in asparagine dextrose, where lusitanus grows fairly and aureofaciens likewise, but where the aerial mycelium in aureofaciens is whitish changing to benzo-brown, and it is whitish becoming dark olive buff in lusitanus, no significance should be attached to these differences according to Dr. Benedict because, as he stated at p. 558 of the transcript:

> A. Here again strain variation, of course, does occur, it is a phenomenon which qualified scientists accept, or in this particular case I believe it is simply slight differences in colours, and to me they are not significant.
>
> Q. So that a difference in strain you think accounts for these differences in colour?
>
> A. I believe that is right.

In the medium potato dextrose agar, the colour for the aerial mycelium in lusitanus is "aerial mycelium whitish becoming dark olive buff in centre but mouse grey to benzo-brown in sporulation areas" and for aureofaciens it is

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"whitish, later becoming benzo-brown (first mouse grey to benzo-brown) in sporulation areas".

The difference here again with regard to the deep olive buff and the benzo-brown is not, in Dr. Benedict's opinion, of any significance. He was asked whether the olive buff mentioned with regard to lusitanus was not the olive buff mentioned as No. 2 series of colours as contained in Ex. 23, a guide of classification of which he is a co-author, to which he replied that such was not the case and that in the development of the aerial mycelium of these actinomycetes it often happens that the initial colour is white. It may then go through a series of colour changes on its way to the final colour of these spores "en masse". He indicated that he was simply pointing out in his report that one of the colour phases gone through, for example, would be olive grey, but the colour of the spores at maturity would be mouse grey or benzo-brown or some shade in between and olive grey would not be the colour of the spores at maturity.

He agreed that there was a difference in the lusitanus grown on yeast extract agar between his test and that of Dr. Backus where in the case of lusitanus the growth was moderate whereas in the case of Dr. Benedict it was fair and where the aerial mycelium in the case of Dr. Backus was "yellowish white becoming benzo-brown in isolation zones" and where in Dr. Benedict's it was white to deep olive grey to mouse grey. Although here the spores are at maturity, Dr. Benedict does not find this difference significant because, as he states at p. 570 of the transcript:

> THE WITNESS: Here again, as we pointed out before, our gray series has a range of colours, and brown, grayish-brown can be included in that series the way we have defined it in our paper, and the mere fact that I observe, for example, a mouse-gray colour of the spores in contrast to perhaps Dr. Backus' benzo brown is not of particular significance to me. That is, there is not the difference—I would not attach a great deal of significance to that minor difference.

Dr. A. M. Henssen then testified on behalf of the defendant. She studied natural sciences in the summer of 1944 at Freiburg, Germany, which she interrupted for war service but resumed in the winter of 1945 at the University of Marburg, when she studied botany and chemistry. In 1949, she started her doctorate thesis in plant physiology at the University of Marburg, which thesis was accepted in June 1953, when she obtained her Ph.D. She first did research

work as an assistant at the Institute of Fruit Culture at the University of Bonn from September 1953 to April 1954 and then worked for two years in the Berlin-Dahleim Institute of Bacteriology from April 1954 to April 1956, where she became interested in the taxonomic study of thermophilic actinomycetes. From 1945 on she was interested especially in small plants such as mosses, lichens and fungi and worked seven months in Berlin in the Botanical Museum in the department of lichens.

In 1955, she was invited to take part in a Finnish expedition to Lapland where she studied for two months lichen flora, mosses and liverworts. In 1956 she went to Helsinki, Finland, to arrange the collections she had made in 1953 where she had the function of determining lichens. In 1957, she returned to Marburg where she obtained in May of that year a two-year fellowship for the taxonomic study of the lichens she had collected in Lapland. This was interrupted for one year when her professor asked her to take a year of assistantship at the University of Marburg, which lasted from 1958 to 1959, after which she continued the fellowship and went to Upsala, in Sweden, where she stayed two years until 1961. She then obtained a second fellowship and left Germany in 1961 for America, where she first went to the University of Colorado, and then six months later, to Harvard University, where she stayed until May 20, 1961, during which time she continued collecting lichens in different parts of the United States. In 1962 she went to Toronto as a research assistant at the Botany Department of the University of Toronto, where she worked with Dr. Roy Cain and where she became involved in the studies for the present trial. In July 1963 she was appointed curator of cryptogamic plants at the University of Marburg, which position she presently holds. She is a member of the International Association for Plant Taxonomy to the Deutsche-Botanische-Gesellschaft to the Svenska-Botaniska-Forennigen, to the British Mycological Society and the Mycological Society of America. She stated that she belongs to the group of specialists referred to by Dr. Backus as working on actinomycetes on account of the paper she wrote earlier and is considered as an expert in this group. She is an expert in lichens and has been invited to take part in 1965 in an antarctic expedition organized by Dr. Lamb, of Harvard

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University. She has established three new genera of streptomyces: termonospora, thermopolyspora and pseudonocardia and has established two thermophilic species of the genus streptomyces: thermociolaceus and rectus. She also wrote a paper which is a contribution to the morphology and taxonomy of thermophilic actinomycetes.

Miss Henssen, after pointing out that there is even divergence on the definition of taxonomy in that some authors call it a science whereas others call it an art, added that the proper classification of micro-organisms requires a diagnosis to characterize and identify the particular object which is a science where description is absolute and objective, and then this taxonomic classification which, however, is an art, and is subjective.

She then referred to Ex. D-20, which is p. 437 of an article taken from "The Microbial Species" which points to the subjectivity of taxonomy in stating that "just as no two observers see the same rainbow, so no two biologists conceive exactly the same species". She also indicated that "a microbial species" is a population and not a particular specimen and that like any other population, it is made up of many different individuals, each of which may show certain features. It therefore appears that for Dr. Henssen there are two problems in taxonomy, (1) identification of the organism and then (2) its classification, and that in order to identify an organism, she would study it very carefully and when she knew its characteristics, she would try to find a name for it. She stated that there are many books written on the subject of identification of micro-organisms containing keys for such identification but she added that they are difficult to use. She indicated that when dealing with bacteria we are not dealing with a single specimen but a culture in which there are many spores containing a population and therefore, the taxonomy of actinomycetes because of this culture, can change. She declared that it is much more difficult to identify an actinomycetes than any other plant.

In order to properly classify an organism, all of its characters must, according to this witness, be studied and a decision has to be taken as to what species it is and of what genus. This, in her opinion, is not a mathematical science, but is really the creative part of taxonomy.

Asked how many species there are in her opinion, she replied, at p. 673 of the transcript:

> A. I don't know. To see how many species a genus has, I have to study this very carefully and make a monographic treatment and because it is so extremely difficult nobody has done it for streptomyces before. You have to regard every species which is described in the literature, and in order to find all this literature it is a difficult task and then you try to study, you have to rely in many cases upon descriptions. You see you don't have all the type cultures of the species that have been described earlier.

According to Dr. Henssen, one has to study ten years to make a monograph of the streptomyces and she added "we did not have that long to prepare this evidence."

Dr. Henssen made a comparative study of streptomyces lusitanus, streptomyces aureofaciens, strepcomyces feofaciens and produced her report as Ex. D-29, parts of which are hereafter set out:

Sporophores are defined as the hyphae which produce spores, at least normally. In *Str. feofaciens* the spore production is depressed, and the sporophores mainly develop fragments. Sometimes spore formation is observed along with the production of fragments (fig. 23). In the other species, the sporophores produce fragments occasionally (fig. 39).

The sporophores in all species are at first straight and alternately branched (fig. 2, 17). A verticillate branching is common later in *Str. aureofaciens* and *Str. viridifaciens* (fig. 9, 14, 16, 39), more rarely seen in *Str. feofaciens* and *Str. species* (fig. 12, 23), and not yet observed with certainty in *Str. lusitanus*.

Under optimal growth conditions, the sporophores are circinate or finally coiled in *Str. lusitanus*, (fig. 5, 44, 45), *Str. viridifaciens* (fig. 14, 16, 18, 39, 48, 49) and *Str. feofaciens* (fig. 22, 23, 25, 26, 41, 52). Occasionally coiled sporophores are developed in one of the two strains of *Str. aureofaciens* (fig. 11b). Usually, the sporophores of this species are straight or flexuous (fig. 9, 11a, 40, 47) as in *Str. species* (fig. 30, 33-35, 43, 51).

Aerial hyphae bearing sporophores were observed in *Str. species*, *Str. foefaciens* and *Str. lusitanus*. They disintegrate completely, form partly spores, or break down into fragments (fig. 1, 22, 34, 35, 46, 51, 52, 53).

Large systems of aerial hyphae not producing spores or fragments are developed by *Str. species* on starch and dextrose-asparagin agar (fig. 32, 50) and by *Str. viridifaciens* on Czapek agar. Coils of unknown function are formed abundantly by the hyphae in *Str. spec.* (fig. 42). Such coils of single or several aerial hyphae are also observed, but rarely, in the other species.

The aerial hyphae can fuse with each other or with substrate hyphae. Furthermore, connections arise where the hyphae twist around each other. The fastened hyphae becomes straightened and stretched (fig. 46, 50, 51, 53).

Long aerial hyphae, when developed abundantly, give the aerial mycelium a tomentous appearance. The production of spores or fragments on the contrary produce a powdery one.

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The border of the colonies may be straight or fringed, depending on whether the substrate mycelium forms a closed circle or is divided into little branches (three of them seen in fig. 48, covered here by the aerial mycelium).

The colors, produced by the *Streptomyces,* are very characteristic for each species. Coloration can be observed in the substrate as well as in the aerial mycelium, furthermore, pigments can be secreted into the nutrient medium.

In the species studied, the substrate mycelium itself was colored yellow to orange, red or brown, best seen in culture tubes, when observed from the side. The color can be masked by a thick layer of aerial mycelium. Colonies, actually orange-brown, may appear to have a red tinge seen from below through a thin layer of agar.

In media where pigments are strongly developed, it is difficult to judge if the colony coloration arises from the soluble pigment or by the coloration of the substrate mycelium itself.

The aerial mycelium is white. When spores or fragments are produced, grayish or brownish colors were developed in the species studied. The coloration is either uniform or variable in circular patterns.

Relationships between the species. The five species studied can be united into two groups, the first contains *Str. aureofaciens* and *Str. viridifaciens,* which produce orange pigments on Czapek's agar. On starch agar they develop single sporophores which soon branch verticillately and completely break down into spores. The second group contain *Str. lusitanus* and *Str. feofaciens* and *Str. species,* which grow very faintly on Czapek agar without production of pigments. On starch agar they produce aerial hyphae which can form sporophores or fragments along with single sporophores.

Str. aureofaciens and *Str. viridifaciens* are very closely related and scarcely warrant being retained as separate species. *Str. aureofaciens* may have originated from *Str. viridifaciens.* The orange pigment is produced more slowly, and the coiling of the sporophores is retarded (strain 2209) or completely suppressed (strain 10762).

The three species of the second group are not so closely related. *Str. lusitanus* stands nearer to *Str. feofaciens* than to *Str. species,* in having coiled sporophores and in producing fragments by aerial hyphae. *Str. feofaciens* differs from all other species in the abundant production of fragments and almost complete loss of spore production. *Str. species* is distinct in having its sporophores formed either singly by substrate hyphae or more or less clustered on the aerial hyphae but never coiled.

For the purpose of this study, she used three types of characteristics, some that can be observed through the eyes such as the substrate or the vegetative mycelium and the pigmentation in the substrate and in the medium, and produced Exs. D-22, D-23, D-24, D-25 and D-26 to illustrate this where one can see the aerial mycelium which can be either continuous or broken and in contrast to which, however, there can be a ring formation.

In D-25 there is a continuous growth in the lower picture (aureofaciens on dextrose) and in the upper picture (lusitanus on dextrose) there is a ring formation.

In the upper picture of D-26 (Lusitanus on cornmeal agar) there is a very fine extending aerial mycelium and the growth is produced in little white spots. In the middle picture (aureofaciens on cornmeal agar) there is a feathery growth. In the lower picture (S. species on cornmeal dextrose agar) there is the formation of aerial mycelium and this is very characteristic for this species.

Then she pointed out that there are the colours. In D-22 there is the orange colour on the lower picture (S. aureofaciens) which shows the orange soluble pigment in the agar. Then the colours of the aerial mycelium in D-25, where there is a change to grey in the uppermost one (lusitanus on dextrose) and in the lower picture (aureofaciens on starch agar) and in D-24 there is this greyish brown colour. In the lower picture D-26 (S. species on dextrose agar) there is a white aerial mycelium. She pointed out here, however, that the colour of the aerial mycelium can be changed by the photographic reproduction.

The second category of characteristics used by Dr. Henssen are those that can be seen with a microscope. The aerial as well as the substrate mycelium can be studied by looking at them on an agar plate. A good way to study the substrate hyphae is by making hanging drop cultures and thereby study the different branching type of the substrate mycelium which is a good means of identification for the species. Ex. D-21 contains aerial mycelium where there are hyphae which do not produce spores. Those that do produce spores are called vegetative and generative mycelium and they can form very long systems of hyphae which cover the whole colony. These sporophores can range from long branches to short ones.

The third means employed by Dr. Henssen is to observe the characteristics of the spores with the aid of an electron microscope.

In Dr. Henssen's opinion the important characteristics for the identification and the description of the species are (a) the type of branching of the substrate hyphae (straight or curved) and then (b) the shape of the sporophores, (c) the shape of the spores and (d) the pigmentation of the colonies

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or more properly the pigmentation of the substrate and aerial mycelium.

She made a comparative study of aureofaciens and lusitanus using aureofaciens strain 2209 of N.R.R.L. and another strain obtained from Dr. Cain (10762) and she had a lusitanus strain, a culture obtained from Dr. Tosoni. She studied both sets of strains side by side (two of aureofaciens and one of lusitanus) upon the same media to see if they were the same or different and in the process used the following media for these cultures: starch agar, dextrose agar, czapek, iron agar (to study the melanin pigment) and dextrose asparagin agar. She also used at one stage potato dextrose agar, malt extract agar and oatmeal agar prepared by Difco.

She then produced a number of living plates of both lusitanus and aureofaciens on the above nutrients and compared them. These plates are produced as Ex. D-30 to D-50. The comparison of these organisms on the same nutrient disclosed a number of differences which in her estimation has brought her to conclude that lusitanus and aureofaciens are to be considered as different species. On starch agar, the colours are brown in the substrate mycelium in lusitanus and reddish in aureofaciens. In this same nutrient, lusitanus has a brown soluble pigment whereas aureofaciens has none. The colour of the aerial mycelium in lusitanus is grey whereas in aureofaciens it is brown or grey and sometimes a little bit olive. On dextrose asparagin agar lusitanus has brown pigmentation whereas the pigmentation in aureofaciens is reddish. The substrate mycelium in lusitanus is brown whereas in aureofaciens it is reddish purple. The aerial mycelium in lusitanus is grey and poorly developed whereas in aureofaciens it is nicely developed with an olive greenish or brownish green shade. On the same nutrient, but on the cultures in tubes, the substrate mycelium of lusitanus is of a brownish tinge whereas in aureofaciens it is of a reddish colour. The aerial mycelium in lusitanus is grey whereas the aureofaciens is olive and lusitanus grows much slower on this media than aureofaciens.

On czapek agar, lusitanus has poor growth of aerial mycelium whereas aureofaciens has splendid growth.

On oatmeal agar, lusitanus has a reddish brown culture which later becomes black whereas aureofaciens is greenish blackish from the beginning. Lusitanus has no aerial mycelium and the colour of the aerial mycelium in aureofaciens is mouse-grey-brown-grey. On oatmeal, lusitanus has a brown colour whereas it is black on aureofaciens. The aerial mycelium for lusitanus is scarce whereas it is white and well developed in aureofaciens. On czapek agar, lusitanus has very faint colour whereas aureofaciens has a thick layer of aerial mycelium. On potato dextrose there is not too much difference between the two micro-organisms; on malt extract agar, lusitanus develops no aerial mycelium whereas aureofaciens does.

She then studied with a microscope and with the aid of the hanging drop cultures the morphology of the substrate mycelium and the aerial mycelium and produced drawing Ex. D-51 which indicates the substrate and aerial mycelium of S. lusitanus and Ex. D-52, that of aureofaciens. From this it appears that the substrate mycelium in both cases is very similar, which, however, she claims cannot be of any help for the purpose of identification.

She then studied the type and the morphology of the aerial mycelium and she produced four separate sheets, Ex. D-53 (lusitanus), three magnified photos on starch agar; Ex. D-54 (lusitanus) three magnified photos on cornmeal dextrose; Ex. D-55 (aureofaciens), four magnified photos on cornmeal dextrose (1) on starch agar (2); Ex. D-56, (aureofaciens), three photos on malt extract agar (1) on cornmeal agar and czapek (1). She pointed out that Ex. D-56 shows aureofaciens with a system of the long hyphae without any sporophores and which, according to Dr. Henssen, is only produced in aureofaciens. She pointed out that on Ex. D-55, two pictures on the left side and Ex. D-56, the two uppermost pictures, she observed a special type of hyphae which applies only to aureofaciens where the sporophores look like stars with substrate hyphae. At. p. 723 of the transcript she stated:

> A. . . . If you have young sporophores they always look straight and flexuous, and later you can have spirals if they are produced in the the species.
>
> HIS LORDSHIP: You say that the young ones have a tendency to grow straight?

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THE WITNESS: Yes.

HIS LORDSHIP: If they are not in the best condition they develop loops.

She admitted that this was a very complicated morphology and in Ex. D-55, which is aureofaciens on different media in the lower picture on the right the starch agar, it has loops between the straight stars whereas in the upper picture of Ex. D-56, which is also aureofaciens, the stars are distributed uniformly.

An examination of Ex. D-53 (lusitanus), the lowest picture on cornmeal agar and Ex. D-54 (lusitanus), the middle picture on cornmeal dextrose agar, in Ex. D-53, the uppermost middle picture and Ex. D-54, the upper and the lowest picture, one can see that these sporophores are really complex. Dr. Henssen pointed out that in aureofaciens we get these stars with relatively few branches in contrast to lusitanus which has real thick coils. There is also this ring formation in lusitanus in contrast to the continuous growth in aureofaciens. She stated that in lusitanus a substrate hyphae always produces rings of aerial mycelium.

On Ex. D-52, (aureofaciens), the stars at 11a are usually straight or flexuous and this is strain 10762 whereas at 11d, which is strain 2209, there are some loops.

Dr. Henssen did not personally study the shape of the spores seen in an electron optical microscope as this was done by a Dr. Shnep, although she was present during the taking of most of the photographs. This was the first time that she had looked at the species through an electron optical microscope. She produced Ex. D-57, three photos of lusitanus on starch agar and Ex. D-58 three photos of aureofaciens 10762 on the same medium.

She stated that the spores in Ex. D-58, picture 164, are the same as can be seen in Ex. D-57, picture 132, although she claims that the size of the spores in lusitanus are a little larger than in aureofaciens. She admitted that the spores in both cases, lusitanus and aureofaciens, are smooth.

Dr. Henssen based her decision that lusitanus and aureofaciens are to be considered as different species on the fact that she found differences in the pigmentation of the substrate mycelium, although the latter is, in her opinion, not too convincing a characteristic, as well as differences in the growth; this is the continuous growth which she has

found in aureofaciens and the ring formation in lusitanus on the same medium. There is also the difference in the type of sporophores where she found clear stars in aureofaciens and thick balls in lusitanus. She also found a difference in the hyphae system in aureofaciens which was not observed in lusitanus; on the other hand, she found aerial hyphae with short sporophores in lusitanus which she did not observe in aureofaciens. She stated that in using certain media she had differences in lusitanus and that in using other media she found other differences and it is based on these differences, the number of differences on the culture and in the sporophores that she has concluded that they are different species. She added that the growth of the sporophores in lusitanus is slow and it is difficult to culture it whereas in aureofaciens it is fast and very easy to culture, although she admitted that she had difficulty when she started with strain 2209.

In addition to the two strains of streptomyces aureofaciens and the one strain of lusitanus, she also studied three other species, S. psammoticus which is S. feofaciens (strain 11654) received from A.T.C.C.; two strains of S. Viridifaciens one from Dr. Cain and the other strain, No. 11989, the original strain received from A.T.C.C.

She conducted tests on these strains similar to those conducted on S. aureofaciens and S. lusitanus on the following media: czapek agar, iron agar, starch and dextrose asparagin, potato dextrose and malt extract agar and oatmeal from which she concluded that S. viridifaciens is so very closely related to S. aureofaciens that she considers both as varieties and sub-species of the same species; she considers S. psammoticus and streptomyces species as distinct species and she is of the opinion that lusitanus is more related to S. psammoticus and streptomyces species than S. viridifaciens.

She produced Ex. D-59, a living plate of culture of viridifaciens 11989 and comparing it with plates D-36 (S. aureofaciens) and Ex. D-34 (S. lusitanus), she found the same colour colony in aureofaciens and viridifaciens whereas in S. lusitanus there is only a faint growth in the aerial mycelium. She finds the long hyphae system very similar to what is found in aureofaciens, the same colour in the aerial colony as well as the same colour in the product pigment.

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She produced Ex. D-60, a sheet marked "Streptomyces Viridifaciens" being four photographs of sporophores of S. viridifaciens and compared it with Ex. D-55 and Ex. D-56 which shows the sporophores of aureofaciens and Ex. D-53 and Ex. D-54 which show the sporophores of lusitanus.

It appears that S. viridifaciens is different from S. aureofaciens because of the shape of the sporophores and that S. viridifaciens and S. lusitanus are similar with regard to the coils. On the other hand, S. viridifaciens has the same continuous growth as S. aureofaciens and has the same star-like sporophores and, therefore, she does not consider that S. viridifaciens is a different species from S. aureofaciens, basing her conclusion on the fact that there is agreement on most characters. Her explanation as to how it happens sometimes that different scientists obtain different results after preparing tests on the same organisms, is that there is often contamination inside of the actinomycetes; there is also the possibility of getting a spore of another species into the culture or, as this is a population, i.e., a mixture of different spores within the organism itself, of getting a mutant during culturing, which is different. She explained this by sketching black and green spores in a particular culture. These spores would belong to the same species but as the strain is a population it could be that the black spores would produce coiled sporophores and the green ones little stars. She also pointed out that if a different medium was used it might happen that the black spores would develop much better than the green spores on a particular medium, which would result in having many coiled sporophores and very few flexuous ones. If another medium was taken, however, such as starch agar, then only the green spores in a star shape would develop as they grow much better than the black ones on this medium and, therefore, because of this, there is a possibility of selection.

With regard to pigmentation, she stated that it is never a good character because it is something to be looked at and that is subjective. With regard to the lack of pigmentation, she maintains that it does not indicate that it is a different species, and that two scientists starting with the same strain might later obtain a different pigmentation of the cultures.

It appears from her evidence that there is no valid type of culture for S. lusitanus and that she made no attempt to get

this type culture or to ascertain what the type culture was before conducting her taxonomic study because she was told that this was the type culture she was to study. She stated that the two strains of aureofaciens that she investigated behaved identically in that she first got a light color and then an orange one and then a dark reddish one, adding, however, that sometimes she got slow growth. Her report, Ex. D-29, however, records a number of differences of behaviour of these two strains which is peculiar as the two strains, 10762 A.T.C.C. and 2209 N.R.R.L. are one and the same. With regard to the evidence given by Dr. Backus and Dr. Benedict that the first five criteria were determinative of the species within the streptomyces, she agreed that the first four were important but that she did not check the carbon source utilization as she had never used this test. She added that these tests are not stable because all of these characteristics can vary and that in addition to the above tests she would add any other character which she thinks is important, reiterating that there is no such thing as a stable characteristic in taxonomy.

She admitted, however, that the first five criteria are useful tools for species determination of streptomyces with the exception of carbon utilization of which she knows nothing as she has never used it. It appears from her evidence that she made her studies and tests and then checked the literature.

She does not agree with Dr. Backus and Dr. Benedict that the sporophores of S. lusitanus and S. aureofaciens both exhibit a combination of straight flexuous and primitive loops, hooks and coils because, according to this witness, the sporophores of S. lusitanus are coiled and looped and the final shape of S. aureofaciens, so far as she has studied this micro-organism, is normally flat and flexuous and only occasionally looped. Although she admits that Pridham in the case of a micro-organism, displaying both the straight flexuous and primitive loops, hooks and coils places it in a more complex group, she does not agree with this opinion.

She also disagrees with Dr. Backus and Dr. Benedict that both S. lusitanus and S. aureofaciens fall into the same group with respect to spore colour. On the basis that if she uses Pridham (Ex. 23, p. 55, the colour groups at the bottom of the page) with regard to the colour of aerial mycelium,

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she would place her spores study of S. lusitanus in the sixth group of grey (light-grey to mouse-grey to brown-grey to grey-brown) and aureofaciens, according to Dr. Henssen, belongs to this grey group and sometimes to the second group which is olive buff (buff to tan to olive-buff), not taking into consideration, however, as pointed out by Dr. Backus and Dr. Benedict, that the Pridham colour chart referred to deals with the colour of sporulating aerial mycelium at maturity and not their colour at an intermediate stage as stated specifically at p. 55 of the above exhibit. Furthermore, at p. 4 of her report, Ex. D-29, when speaking of all the micro-organisms she observed, she states that: "When spores or fragments are produced, grayish or brownish colours were developed in the species studied," which confirms Dr. Backus and Dr. Benedict. She explained this, however, by saying that since her report of December 12, 1962, she had had an opportunity to study further and has revised her observations and conclusions in this regard.

The electromicroscopic examination and the photographs taken were made in the *last days of October, and the beginning of November, 1963* and, therefore, did not figure in her initial report, Ex. D-29. She admitted that the spore surface, when viewed by electromicroscope, displays a smooth surface in both cases. She agreed that melanin pigment production or the ability of the micro-organism to produce melanin pigment is an old criterion but only one of several physiological criteria used. She has had very little experience with this criterion and in her comparative study all the strains were negative. With regard to the carbon source utilization, she stated that it was a difficult test to run because it is necessary to have pure substances and technical assistance for the test and that she did not have this as she had to do everything herself. She considers this test of converting nitrates to nitrites as very insignificant, although admitting that it is mentioned in the literature. On czapek agar where aureofaciens grows and lusitanus has only a faint growth, she was asked if that did not indicate that there seemed utilization by lusitanus and she replied that it was only faint and indicated nothing except that "the organism draws on its own reserves which explains the faint growth but no utilization of the medium."

She is familiar with the literature in respect to the ability of the micro-organisms to liquify gelatin and considers this test insignificant, although she admits it is used extensively by taxonomists and bacteriologists. She did not, however, run this test. She did, however, run the "Hydrolysis of Starch" test as she used starch agar and she found that both S. lusitanus and S. aureofaciens grow well on starch and that the other strains cannot utilize it. She did not try the litmus milk test, although she admits it is mentioned in the literature, considering it also as insignificant.

She admitted that it is important to compare the characteristics on a medium which permits maximum growth of the micro-organisms studied adding, however, that on czapek agar there was no growth on S. lusitanus, for instance, whereas, aureofaciens grew (although even here she did not obtain sporophores but only long hyphae systems) and according to Dr. Henssen this is as good a character for the determination of the species as whatever characters can be seen from both growing on a productive nutrient. She later admitted, also, that she had used a cornmeal recipe which is a well-known medium for fungi but which is not used for streptomyces and that no qualified investigator had ever before used it for the determination of the latter. She insisted upon the importance of the characteristic of S. lusitanus not really growing and S. aureofaciens and S. viridifaciens growing on czapek. This, in her opinion, is one of the keys that can be used for the determination of the species streptomyces. She added that the keys which have been made to date are very difficult to use and are not useful and that is why everybody is trying to make new keys. She added that she would make one or two and identify the test keys that she could find and in the present case she is relying on her own keys for the five species dealt with in her report. According to Dr. Henssen the classification of the species is a very difficult task and at p. 850 of the transcript, she explains the difficulties as follows:

> A. For these five species, you see, I have a key. Before I can make a really good key for streptomyces, I have to make a monograph and it should last at least ten years.

She attaches considerable importance to the differences in S. aureofaciens and S. lusitanus in respect of the soluble pigment production and she considers it a very helpful

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criterion, admitting, however, that in dealing with a mutant which does not produce the same pigment it no longer is helpful. She agreed that Ettlinger, in Exs. 21 and 22, states that he does not like to consider the soluble pigment production in the classification of the species, but pointed out that there were many other scientists, such as Baldacci, Bergley and Waksman, who show that this characteristic is a useful one in taxonomy within the genus streptomyces. She, however, was unable to produce any writings of these authors in support of her contention. She was also impressed by the physiological characteristics of the substrate mycelium which she maintains appears in the living cultures produced as Exs. D-22, D-23, D-24 and D-25. The colour of the substrate mycelium in S. lusitanus is different from the reddish tinge in that of S. aureofaciens. With regard to Exs. D-31 and D-32, she admitted that although these plates were prepared at substantially the same time, because S. lusitanus grows more poorly or more slowly than S. aureofaciens, the micro-organisms are not being compared at the same stage of development. With regard to the ring formation in S. lusitanus and the continuous growth of S. aureofaciens, she admits that no one in the literature recognizes this as useful or valid. At p. 862 of the transcript, she was questioned as follows in this connection:

> Q. Is it not possible that what you are observing there is the difference between the RF and RA type of structure when you are observing the fringe, because you have loops, hooks and coils.
>
> A. No, in aureofaciens the same continuous growth is observed as in viridifaciens for example, you have in viridifaciens these nice coils, and in aureofaciens you have these little stars.
>
> . . .
>
> Q. What do you think it is due to?
>
> A. It is a good character for determination, I think.
>
> Q. What do you think causes it?
>
> A. This is difficult to say. I have to study yet that.

Dr. Roy Cain, a biologist, mycologist and botanist, was also heard on behalf of the defendant. He received from the University of Toronto a Bachelor's degree in biology in 1930, a Master's degree in mycology in 1931 and a Ph.D. in mycology in 1933, at which time he became the curator of the cryptogamic herborium at the Department of Botany of the University of Toronto. He later, in 1946, became assistant professor and eventually, in 1955, Associate Professor

at the same Herborium. In 1959, he became acting chairman of the Department of Botany of the University of Toronto and in 1961 became full professor at the herborium. He is a member of the Mycology Society of America and at present (1964-1965) is a member of the council. He is a member of the American Biological Society of which he was vice-president in 1949-1950 and president in 1960-1961; he is also a member of the Ecological Society of America, the American Society of Plant Taxonomy, the American Institute of Biological Sciences, the International Institute of Plant Taxonomy, the British Mycological Society and the Swedish Botanical Society and he is included in the publication "American Men of Science". He is also the author of some 28 papers dealing with the taxonomy of fungi.

This witness also explained why different scientists may and have obtained different results when testing micro-organisms and particularly species of streptomyces. When a culture is obtained from the soil, there is always the possibility of getting hyphal fragments or even groups of spores that contribute to the single colonies insulated to make the one culture. He explained that it has been demonstrated for a considerable number of species of streptomyces that a single filament always contains numerous nuclei. The nuclei are the carriers of genes which are the heritable factors, i.e., the only characters pertinent, according to this witness, to the determination of the classification of organisms as the characteristics induced by the environment should not be considered. He stated that it has been shown in at least five different species of streptomyces that when filaments come together, there is the possibility of a fusion taking place and the movement of one or more of the nuclei going from one filament over to the other. If there are any gene differences in the nuclei that have moved from one filament over into the other, then the filament with the two groups of nuclei will have nuclei of a different gene composition. He also pointed out that in culturing, in order to be exact, it is necessary to purify the culture before it can be related to anything because if there is a mixture of heritable characters in the culture, the results obtained will be mixed depending upon the mixture one starts with. If the filament contained only one nucleus in each spore, it would be a

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simple matter of sorting out the characters. However, in the genus streptomyces, several of the species have not only one nucleus in the spore but some of them have two nuclei so one cannot be absolutely sure in plating out these spores that one is getting one nucleus only. In order to insure that there is one nucleus in the spore, the spore is grown and a new colony is produced on a plate. After having so purified the filament, the culture will then remain consistent with no changes except those one might get due to environment. Now, if this culture, however, is bombarded by some type of rays, something may happen to it and we may obtain a mutation. Some mutations may take place with the organism growing in the laboratories but it can be speeded up immensely by irradiating, by ultra-violet light and various mechanical means where it is possible to produce a mutation which might take possibly hundreds of years under natural conditions. He also pointed out that another factor may enter here. It is when growing the original filament which had two types of nuclei in it, the balance between the two could be shifted by merely growing it in a different medium and one nucleus could be favoured over the other. The name for such a process is, according to Dr. Cain, selection which is a method for shifting the genetics composition. He then stated that a process called fusion might also take place and this, according to him, has been demonstrated in five species of streptomyces. In a selection method the two nuclei in the filament have remained intact, one only taking over the other in the selection, but with a fusion we obtain a new and different culture from anything we had before. It will be the essential parts of the same characters but in a different combination. This is also called mutation by reduction. He pointed out that it will be difficult to distinguish between the results of the mutation obtained by means of the reduction division and by means of the reduction by bombardment in the nucleus concluding, however, that a new combination would be a new culture.

He also pointed out that there is vegetative reproduction and sexual reproduction although, actually, there are no structures in streptomyces that can be identified as sexual; they have, however, so far as the heritable characters are concerned, a sexuality. In his opinion, this is the way species originated through the sexual mutations and evolution until

one gets a product which can be used, sufficiently different from the original to be regarded as a different species adding "But in that evolution as it occurs in nature there is no pearly gate which the species go through and come out a new species. It is a gradual development."

Dr. Cain referred to the literature which indicates there has been at least five species reported in which recombinations have been demonstrated. He produced Ex. D-67, a photocopy of pp. 854 to 861 inclusive, of the Annals of the New York Academy of Scientists, vol. 81, which shows that re-combinations of streptomyces coelicolor was dealt with by Sermonti and Spada-Sermonti. He also referred to Ex. D-68, pp. 914 to 949 of a paper entitled "Genetics of Organisms Producing Tetracyclines" by a Russian called Alikhanin et al. However, here, although the possible recombinations of aureofaciens is discussed, it was not demonstrated in this paper. Dr. Cain stated that in all probability, most of the species would eventually be found to exhibit the sexuality he mentioned before, the only open question remaining in his opinion is whether it is the reduction division or the parasexual cycle which is involved. His explanation as to why different scientists when studying the same cultures of the species streptomyces get differences, can be found at p. 904 of the transcript:

> A. This demonstrates that given a mixed population to begin with in any culture you have the various mechanisms by which you can get out of it different combinations of these characters so that you get a series of combinations which will not match exactly the original; and even when you have a single set of genetic factors, any subsequent mutations might still give you some differences in the culture, so that the two cultures that have had the same origin, if kept separately, as they would be in different laboratories, with no subsequent remixing, could ultimately come to exhibit different characteristics by either these two mechanisms with either having started with an original mixture or the mixture having its origin in the culture itself by a mutation giving a different factor to work on, and once you have the two factors, out of it you can get quite a number of different-appearing cultures, and this explains why, when you make the original isolation from the soil, you may get out, as, indeed, they have reported in streptomyces aureofaciens cultures which vary slightly from others and, depending on the proportions of the various genetic types, you will get a somewhat different-appearing culture with considerable—if you have several mutations within a species such as aureofaciens, then with all the permutations and combinations it would be unique if from the soil you would get exactly the combination in one field that you have got from a few feet away in another field, because the chance of getting the same grouping would be very slight.

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And at pp. 905-906 when asked what classification he would make in a case such as here where he would have some differences and some similarities between aureofaciens and lusitanus, he answered:

> A. In a population such as streptomyces aureofaciens you will get recombinations of the same sets of factors, so you will always have some common characteristics, but you will get a few that are different in each of the different isolates. But this will give you a random assortment and completely unbiased mixing of the various genetic types that are included in the species aureofaciens. But in the case of lusitanus you get a different combination of factors which are not common to all that are present in aureofaciens, and of these cultures that you isolate from the soil you don't get the exact copy of the lusitanus, because we consider this a separate entity, and being a separate entity in our opinion it would not mix with this population even if it did occur in the same area, so there is no mixing. If it were a mixing completely between aureofaciens and lusitanus, then you would have a complete integration right through of all characters, including those of lusitanus, which we have not seen; lusitanus doesn't fit into this picture.

Dr. Cain maintained that the thing to do in differentiating the organisms is to deal with characters known as heritable and to rule out all of those that are simply, from appearance, due to the environment. He added that while the actual appearance of a character might be inherited, the expression of the characteristics may be an influence of the environment and he used as an example aureofaciens and lusitanus growing on czapek, where aureofaciens grows well and where there is practically no growth of lusitanus. This, he says, is inherited but one would not see it unless it was placed in this particular environment. He admitted streptomyces would appear different at different stages of development and that on some of the medium it can be grown to an optimum growth whereas on others it would stop far short of that and, therefore, one does not obtain by this method all the morphological features which are inherited in the heritable characteristics. He also pointed out with regard to spore chains and the discrepancies found in the observations of the tests made in this case that this might be due to the humidity or the amount of moisture in the medium or to the fact that the observations were made in the air which might influence the tightness of the spiral or whether it is pulled out, loose or compact and, therefore, a different investigator working in different areas might

conceivably obtain different results due to atmospheric conditions.

Dr. Cain referred to a published article by Dr. Kuster entitled "Results of a Comparative Study of Criteria Used in the Classification of Actinomycetes" which deals with a conference of scientists which decided to distribute a certain number of cultures to 34 different specialists and they were asked to record their observations with respect to these different cultures. The people who made these tests were Baldacci, Kuster, Backus, Nomi (Japan), Hutter, Pridham and Krassil'Nikov. These cultures were taken home by these scientists where they were tested and a chart was subsequently published in the International Bulletin of Bacteriology Nomenclature and Taxonomy, pp. 133 to 160, produced as Ex. D-73 in this case, where it appears that the various investigators, although showing similarity, showed also different spore colour groups for the same culture. The observations in the above tests had to do with two features, the morphology of colony changes and the spore colour and it therefore appears that the results obtained are far from uniform.

Dr. Cain's definition of the rectus flexibilis is "where the sporophores are straight and wavy, the number of hooks forming complete turns is small, the occurrence of real spiral is very rare, though possible with other strains", adding that the observance of one or two spiral sporophores cannot be decisive in typifying. He however admitted that there is no clear cut operation so far as the species are concerned with respect to the form and shape of the sporophores and that out of the same species one may obtain considerable variations from the flexuous through to some spirals and hooks to some spirals.

Dr. Cain's method of classifying any group of organisms, similar in this respect to that of Dr. Henssen, is to not rely on an arbitrary system but to first make observations on the specimens themselves, record every conceivable difference, all the characters, going into as many minute details as is practical and as he put it at p. 945 of the transcript:

> It is a question of being able to see all of the features that are exemplified by a particular organism quite irrespective of what some other author has said should be the criteria that you are going to set up by which you are going to identify these unknown organisms.

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He stated that Dr. Henssen and himself had three sources of lusitanus, the original transfers made by Dr. Tosoni, one of the original tubes and one of the transfers that Dr. Henssen used in making her own set of experiments.

Dr. Cain conducted tests on streptomyces aureofaciens and streptomyces lusitanus with five different media, dextrose, asparagin, beef extract czapek and alphacel beef extract plus starch. His conclusions from his first set of experiments are that the characters he obtained were sufficient to recognize lusitanus as a species distinct from aureofaciens adding that viridifaciens showed very small differences from aureofaciens. He explained his conclusions by saying at p. 950 of the transcript:

> There was a considerable number of different characters by which I could distinguish between lusitanus and aureofaciens, and from experience in working with other groups I know that the degree of relationship between any two species is not determined by the extent—that is the quality of any particular difference—but actually the number of differences is more significant, even though the differences themselves may be very slight.

Dr. Cain agreed that there is no question as to the status of aureofaciens as a separate species. He also admitted that as far as he knows, there is no legal publication of lusitanus so that the type referred to and the culture used in making the description is not yet described and there is no type culture for streptomyces lusitanus at the present time. He agrees that the question of speciation, of placing an unknown organism in one species, involves the evaluation of the differences observed in the physiological and morphological characteristics of the two micro-organisms adding that all the information available should be taken inclusive of that obtained from a cytological examination as species in the black flies, for instance are now being examined by the arrangement of the genes on the chromosomes. He admitted also that although they are rare, there were some loops, hooks and coils in respect of the aureofaciens he tested. He also admitted that one can obtain S. aureofaciens strains which produce an abundance of loops, hooks and coils. He would not agree to the suggestion based on the literature that if a colony has even one loop, hook or coil, it should be classed in the more complex group consisting of loops, hooks and coils. Asked by the Court what he would do when he had a combination of both, he replied at p. 979 of the transcript:

It is a question of what is inherited. I have to find out what are the differences in the observations which are due to environment, and considering only the heritable characters, I see whether there is actually any difference between the one and the other that I am comparing. I don't care what somebody else has said how you are going to classify them.

He admitted that some authors in the literature classify them in the more complex group whereas others, he stated, do not. He was not, however, able to produce one reference in the literature which states that it is not valid to place it in the higher or more complex group, as suggested by Pridham.

He also admitted that in the "en masse" spore colour of both these micro-organisms on medium which promoted optimum growth they both fell in the grey grouping. He did not study these micro-organisms under the electron microscope. He admitted observing that neither of the two organisms produced melanin pigment but with regard to the utility of the melanin pigment test he stated:

. . . a difference would indicate the different species, but similarity wouldn't give you any clue.

He however admitted that there is a recognized grouping based on the ability or not to produce this melanin pigment. He then agreed with an article by Kuster, Ex. D-72, which says at p. 91:

Likewise the melanin reaction is an unequivocal characteristic and can be applied in a classification.

He admitted running no tests with respect to carbon source utilization as he did not have the facilities to do that adequately and that he was familiar with the fact that the literature indicated that this was a useful criterion.

He did not study the ability of these organisms to produce gelatin liquefaction nor did he run the litmus test.

He produced no written report of his study and then gave the factors in which he found differences in both aureofaciens and lusitanus as follows: there was a difference in the colour that diffuses into the agar medium by the production of soluble pigments; there was a difference in the colour of the mycelium observed in reverse; there are slight shades of difference in colour of the aerial hyphae spores which he qualified as minor differences; there were differences in the structure of the substrate mycelium and in the manner the aerial hyphae branched and the way the chain of spores came off; there were differences in the size of the hyphae.

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He stated that so far as he recalls, the two strains of aureofaciens the N.R.R.L. and the A.T.C.C. performed identically throughout his taxonomic study and that, therefore, there were no recombinations here. He also agreed that there is no literature reference that says that recombination has occurred in streptomyces aureofaciens, and that to his knowledge the genetic aspect of aureofaciens has not been investigated and so, therefore, his theory on recombination is based not on his own observations because he had two cultures that behaved identically and not on direct work conducted on aureofaciens but on conclusions that he draws from the work and report of others in respect of streptomyces. He admitted that when faced with differences between two different organisms then it becomes a personal matter of evaluation as to what category it is to be placed under, adding at p. 1001 of the transcript:

> . . . There are none of the species that we have all of the information as to similarities and differences, so we just have to work with the information that we have, depending on how much information we have we can make a more refined or a very loose classification.

It appears from this detailed and exhaustive review of the expert evidence adduced in this case that the taxonomic classification of the genus streptomyces is a very complex problem, one which admittedly requires, on the part of the investigator, considerable experience and an intelligent personal evaluation of the morphological and physiological characteristics of the micro-organisms investigated. It is also clear that these same characters may vary from strain to strain and from culture to culture due either to the environment in which the micro-organism is cultured, or the medium on which it is developed and even because of a natural or induced mutation.

There is also, as pointed out by both Dr. Henssen and Dr. Cain, the possibility of allowing the nuclei of a different species into the culture due to the difficulty of isolating a pure culture of this species. Dr. Cain has even gone farther than that in asserting that in a particular strain, a pure culture, the spores may have two different nuclei, one for instance giving flexuous sporophores and the other looped or coiled ones.

It follows, therefore, that the person most competent to arrive at the best possible classification of the species would be not only one who has had considerable experience in

studying the species, but also and especially one who has had considerable experience in studying various strains of Streptomyces aureofaciens as it is only by so doing that a reasonable evaluation of its variations can be made and a reasonable classification of a micro-organism can be determined in relation thereto; as a matter of fact the only real difference between the experts on both sides is the importance or effect of the differences they found between the micro-organisms in the studies they conducted.

In this respect there can be no question of the qualifications of both Dr. Backus and Dr. Benedict over both Dr. Henssen and Dr. Cain on this particular point. Indeed Dr. Backus has spent the last twenty years investigating organisms of the streptomyces type and the last seventeen years investigating and working on many micro-organisms of the Streptomyces aureofaciens species. He has produced isolates from the soil, he has produced and investigated mutants and has investigated 600 isolates of Streptomyces with reference to the first five criteria mentioned in his evidence affirming that he has not found one that could not be correctly classified on the basis of these five criteria. Dr. Benedict, whose profesional career has been mostly spent with a U.S. Government agency in charge of deposited cultures of micro-organisms, is the co-author with Pridham of a guide for the classification of Streptomyces according to selected groups (Exhibit 23) and is now a Professor at the University of Washington; he has been working on Streptomyces for over eighteen years and has investigated 4,000 samples, including various strains and cultures of aureofaciens.

On the other hand, although both Dr. Henssen and Dr. Cain are no doubt competent scientists, their personal experience with regard to the genus streptomyces herein, has not been of the same magnitude. Dr. Henssen admitted that she knew nothing about antibiotics, had never studied them and had never run fermentation studies. She has never isolated any aureofaciens and never tried to, nor has she ever done any mutations or mutation studies of this micro-organism. She received her Ph.D. degree in relation to duck weeds which is a member of the spermatophyta division, whereas Streptomyces is a member of the Protophyta division, and her habilitation in respect of lichens related to the Thallophyta division of the plant kingdom and not to the

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Protophyta with which we are concerned here. Her studies in Streptomyces prior to April, 1954 and her investigations at that time, were restricted to the thermophylic forms (found in compost and manure piles) whereas Aureofaciens and Lusitans are of the mesophylic form. She only started to study Streptomyces of the mesophylic form in 1962 for the present trial for the purpose of giving evidence and preparing her report, Ex. D-29.

Now, although the taxonomic study of lichens (fungi and algae) and of thermophylic streptomyces has some similarities, she admitted that generally speaking it was quite different from that of the mesophylic streptomyces.

Dr. Cain's background is mainly in connection with the taxonomy of fungi which are not streptomyces. He has never conducted any mutation studies of Streptomyces aureofaciens, nor has he ever attempted to produce chlortetracycline by Streptomyces aureofaciens. There have been fermentations run in his laboratory of these micro-organisms to produce antibiotics, but he does not recall that he actually did all the work. I must also add that his evidence was not supported by a written report and the examination of the criteria he examined and his discoveries in respect of each media used could, therefore, not be verified.

At page 985 of the transcript, when asked for the factors or criteria in which he found differences in the behaviour of both aureofaciens and lusitanus he stated:

> A. Well, I don't have my notes here. I couldn't give you a scientific answer. I wouldn't try to commit from memory a scientific document.

He did, however, later describe a number of factors very similar to those described by Dr. Henssen.

It also appears that both Dr. Henssen and Dr. Cain tested only the aureofaciens A.T.C.C. and N.R.R.L. strains which turned out to be the same strain which, of course, would give no information as to what the permissible variations might be within this given species.

There, therefore, is no question in my mind that the background of both Dr. Backus and Dr. Benedict, as contrasted with that of Dr. Henssen and Dr. Cain, is the one most conducive to evaluating similarities and differences and permissible variations and most likely, in the present state of the art, to assist in arriving at a proper conclusion as

to the significance of these similarities, differences and variations and a proper determination of the speciation or classification of the species involved, having regard to the reference set down in the agreement for trial, i.e. "as to whether lusitanus is an organism of the groups consisting of the species streptomyces aureofaciens, together with natural and artificially induced mutants thereof".

There is an additional reason for accepting the evidence of the plaintiff's experts in that their studies were founded on a scheme of classification supported by the literature, were enclosed in a written report which listed the method and media used and the results obtained inclusive of some which indicated differences but which both Dr. Backus and Dr. Benedict stated and, in my view, established as being permissible variations allowed for the species.

On the other hand, Dr. Henssen, instead of going to keys already published by well recognized investigators stated that she did not find these published keys to be useful and decided upon her first investigation into the determination of the species involved herein to find keys of her own, using in one instance at least a medium (cornmeal) that had been used on fungi, but that never before had been used on streptomyces. Now, although it would appear to me to be a good thing for investigators of streptomyces to go to new media for the purpose of determining the species and making new keys which would add to its scientific determination, it would seem more practical and more helpful and possibly also more scientific when dealing with a problem such as the present one, to use mainly the methods used by prior and well recognized investigators in this field. Moreover, Dr. Henssen, in my view, admitted the weakness of the personal keys she used in her study of streptomyces when she stated at page 850 of the transcript:

> A. For these five species you see I have a key. Before I can make a really good key for streptomyces, I have to make a monograph and it should last at least ten years, I say.

Under these circumstances, one wonders what credence should be attached to the differences she found by the unproven methods she adopted and which she considered important in the determination of the species.

Furthermore, in several cases she was unable to support the differences she found as indicating to her a difference in

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species between the species she studied, (including aureofaciens and lusitanus) as having been found useful or determinative by any prior qualified investigator. This occurred, for instance, in relation to the differences observed in the soluble pigment production which Dr. Henssen considered very important and which Ettlinger (Exhibit 21 and Exhibit 22) does not think much of, and although she referred to a number of investigators in support of her view, she produced no documents to substantiate it. The same applies to her contention as well as that of Dr. Cain's that the micro-organisms which display a combination of flexuous and loops, hooks and coils, should be placed in the group where the majority lay (which is nowhere supported by the literature) and not in the more complex group as Dr. Backus and Dr. Benedict have done, which latter position, however, is supported by the literature in Pridham Exhibit 23 and Exhibit D-73 produced by the defendant, the article entitled "1961 International Bulletin of Bacteriology Nomenclature and Taxonomy, Krassil'Nikov where at page 139 he states:

> We believe that if any strain has even a single spiral sporophore on any medium, it should be classed as a spiral culture.

Dr. Henssen, at one point in her evidence, stated that in order to make a proper taxonomic study of an actinomycetes she would require and need a type culture. However, later at page 784 of the transcript she admitted that there is no such thing for lusitanus when she stated:

> A. There is no description, no valid description of Lusitanus and therefore we don't have a type culture.

It also appears that she made no attempt to get the type culture of lusitanus or to ascertain what the type culture was before conducting her taxonomic study because she was told this was the type culture she was to study. With regard to the Melanin pigment production which all the experts agreed, (including Dr. Henssen,) was a well recognized criterion and where both organisms showed identity she found unimportant. She admitted that she did not use the carbon source utilization test as she had never studied nor used it, although she had heard of it and knew that some investigators found it useful. She stated that it was a difficult test to run because one must "have pure substances and technical assistance for the preparation to make the

work for you, but I had to make everything with my own hands".

With regard to the aerial mycelium of both lusitanus and aureofaciens which she described in her report, D-29 at p. 4 as developing "greyish or brownish colours" in the species she studied, which went counter to her verbal evidence at the trial that lusitanus should be placed in the sixth Pridham group, "grey, light grey, mouse grey, a brown-grey and grey-brown" and aureofaciens in the second Pridham group, "olive-buff" (buff to tan to olive-buff), she explained by stating that this is her report (D-29) of December 12, 1962 and that in the meantime she had had an opportunity to study further and had revised her original observations and conclusions.

The ring formation on lusitanus and the continuous growth on aureofaciens which Dr. Henssen felt was an important difference in both species and determinative of species she agreed was not recognized in the literature and she could not explain how these characteristics are caused as appears from her evidence at page 862 of the transcript:

Q. Is it not possible that what you are observing there is the difference between the RF and RA type of structure when you are observing the fringe, because you have loops, hooks and coils?

A. No, in aureofaciens the same continuous growth is observed as in viridifaciens, for example, you have in viridifaciens these nice coils, and in aureofaciens you have these little stars.

. . .

Q. What do you think it is due to?

A. It is a good character for determination, I think.

Q. What do you think causes it?

A. This is difficult to say. I have to study yet that.

Dr. Henssen had the species she was studying examined as already mentioned by a Dr. Snep under Electron magnification and the spores of some of the species examined showed spikes, others showed long hairs and warts, whereas both aureofaciens and lusitanus showed characteristic smooth phalangeal configurations. She produced a number of magnified photographs which from an examination of same indicate to me that there is practically identity between the shape of the spores of aureofaciens and lusitanus, both indeed showing the same smooth phalangeal effect and whatever differences Dr. Henssen pointed out as indicative of these being of a different species, such as the size and the foldings and thickenings, I must say I could not perceive.

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With regard to Dr. Cain, although as already mentioned, he conducted a taxonomic study investigation of species including aureofaciens and lusitanus, he did not prepare a written report. He states that he observed the sporophore morphology of the two micro-organisms. (cf. page 977 of the transcript):

A Not in any great detail I just observed some differences.

With regard to the matter of placing a micro-organism in a more complex group, i.e. RA in the event it shows even a minor amount of loops, hooks and coils, he stated that the authors in literature disagree, some say they should be so placed and others that they should not. However, when asked to indicate one reference in the literature which is in Court which says it is not valid to place it in the higher or more complex group as suggested by Pridham, he answered:

A No I am afraid I can't. I would have to search the material

With regard to the conversion from nitrate to nitrite test when asked whether growing the micro-organism on Czapek Agar proves an ability to utilize nitrates or nitrites, he said:

A I don't know.

He then stated later at page 986 of the transcript:

Well, the ones that impress me most was the fact that it (Lusitanus) wouldn't use the nitrate, in the Czapek.

It however appears as pointed out by Counsel for the plaintiff, Mr. Sim, if reference is made to the Minieri Patent column 1, bottom of column 7, line 17 that the patentee refers there to the characteristics of two isolates of aureofaciens derived from the type culture used in the production of Tetracycline which is exactly what both Dr. Cain and Dr. Henssen observed in respect of lusitanus and which is described in the following words:

Czapek Agar, poor growth, flat colourless mycelium no aerial hyphae.

and this is one instance which indicates that Dr. Cain and Dr. Henssen, because of their restricted experience with aureofaciens, did not and could not appreciate the variations permissible within this species. When asked for the criteria in which he found differences in the behaviour of the two micro-organisms, Dr. Cain first answered at page 985 of the transcript:

A Well, I don't have my notes here I couldn't give you a scientific answer I wouldn't try to commit from memory a scientific document

He then attempted to give some of the factors reiterating as far as I can see the same differences previously listed by Dr. Henssen.

Now contrasting the methods used by the plaintiff's experts using accepted tests and keys, and those used by the defendant's experts who had never done a study in this field before and using as they did personal unrecognized keys, here again there can be no hesitancy in preferring the former to the latter.

It, therefore, follows that if the proper classification of the species in the present case is to be conducted on a proper assessment of the significance of the differences observed and a proper determination as to whether they are sufficient to warrant the creation of a new species or that they are so small that they should be considered as within the same species, the explanations given by both Dr. Backus and Dr. Benedict of these differences based on their experience in working not only on all the species examined but also on various strains or cultures or mutants of aureofaciens, would place them in a better position to determine the permissible variations within the latter species than both Dr. Henssen and Dr. Cain who dealt only with one strain of aureofaciens and who first became interested and studied streptomyces of the mesophylic form in 1962 for the preparation of their evidence in the present case.

I must, therefore, of necessity accept the evidence of both Dr. Backus and Dr. Benedict on this matter of speciation and find that there is here a preponderance of evidence which drives me to the conclusion that the lusitanus dealt with here is not a separate and distinct species from streptomyces aureofaciens and is, therefore, "an organism of the group consisting of the species streptomyces aureofaciens together with natural and artificially induced mutants thereof," as set out in the agreement for trial.

It therefore follows that there is infringement of the Minieri Patent on the basis of the agreement of the parties already referred to and with regard to the Duggar Patent having found that lusitanus is an organism of the streptomyces aureofaciens group, it follows that the presumption of section 41(2) now comes into play and establishes that the Chlortetracycline produced in Italy and later made into Tetracycline must be presumed to have been produced by

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the Duggar process and there is, therefore, also infringement of the latter patent.

I now turn to the question of validity and to the first attack made on the Duggar Patent that the specification is insufficient in that it nowhere discloses the necessity to have chlorine in the broth to obtain Chlortetracycline and without it the product cannot be obtained and, therefore, the process is unworkable and inoperable. It may be of some use to point out here that Chlorine is the element and as such is a poisonous gas and chloride is chlorine after it has entered into combination with, for example, a metal like sodium.

It indeed appears that although chloride is not essential to the growth of the micro-organism which produces Chlortetracycline, it must however be present in the fermentation broth if Chlortetracycline is to be achieved and this necessity for a content of chloride ion is not specifically referred to in the Duggar Patent and the question here is whether the absence of such a specific reference could be such as to defeat the Patent. It is urged by the defendant that in the formula at column 1 of the Duggar Patent, although there is a Cl. atom indicated as being present in the molecule, this does not necessarily show that chlorine must have been present in the fermentation broth to obtain the product Chlortetracycline; furthermore, again, according to the defendant, the absence of a specific chlorine requirement in the Patent for the broth might lead one to use instead a chlorate or chlorite (where in both cases chlorine is united to a metal together with oxygen) and in which event, as stated by Dr. Petty, this might kill the organism and the process would, therefore, be useless. Now although this chlorine can be found in nature as submitted by Dr. Petty, other essential constituents of the fermentation broth here can also be found in nature such as carbon and nitrogen and yet they are specifically set out in the patent, whereas chlorine is not and I must say that the absence of such a reference in the Duggar Patent is somewhat surprising. What the defendant, of course, is saying here is that the patentee has not, with respect to the Duggar Patent, complied with his obligations under s.36 of the Act to

> (1) . . . correctly and fully describe the invention and its operation or use as contempated by the inventor, and set forth clearly the various steps in a process, . . . in such full, clear, concise and exact terms as to enable any person skilled in the art or science to which it appertains,

or with which it is most closely connected, to make, construct, compound or use it; . . . in the case of a process he shall explain the necessary sequence, if any, of the various steps, so as to distinguish the invention from other inventions; he shall particularly indicate and distinctly claim the part, improvement or combination which he claims as his invention.

This section then requires that:

(2) The specification shall end with a claim or claims stating distinctly and in explicit terms the things or combinations that the applicant regards as new and in which he claims an exclusive property or privilege.

Dr. A. L. Tosoni, a chemist, was heard on behalf of the defendant. This gentleman became a bachelor in chemistry in 1942, a Master in organic chemistry in 1944 and obtained a Ph.D. in chemistry in 1947 from the University of Toronto. He has done some work in connection with antibiotics and has written a thesis on the purification and preparation of Penicillin and its derivatives. He is a Research Member at the Connaught Laboratories owned by the University of Toronto which deals with vaccines, toxoids and materials used in preventive medicine, polio vaccine products, dyphtheria and tetanus.

At page 578 of the transcript Dr. Tosoni asked by Counsel for the defendant, Mr. Forget, if, after having analysed the Duggar Patent in connection with this chlorine problem, he could say whether he could use a medium which would be chlorine-free among the various media indicated in the patent, stated:

A. No, I think if I were trying to repeat the Duggar Patent I would use the things he prefers, corn steep liquor, and that contains considerable quantities of chloride ion.

Q. Have you analyzed the possibility that by selecting from his list of ingredients you may get a chloride-free medium?

A. I think you could get a medium which was extremely low in chloride content almost to the point that you could say it was chloride free.

Q. What would be the effect of such medium on the production of chlortetracycline?

A. There would be chlortetracycline produced to the extent of the chloride content. If it was very low the production of chlortetracycline would be very low, and to the extent that the organism produced a tetracycline, the remainder would be tetracycline.

He then later, at page 640 of the transcript, reiterated that if he wanted to carry out the teachings of Duggar and produce Chlortetracycline in accordance with same, he would not use a chlorine-free medium.

A. I would use the ones recommended by Duggar as being the ones he prefers.

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Q. Which are not chlorine-free?

A. That is right.

Q And which are not even extremely low in chlorine content?

A. That is correct.

Dr. Milton Petty a biologist who testified on behalf of the plaintiff and who is the author and co-author of a number of technical papers in the field of microbiology and fermentation research, confirmed the chlorine content of the Duggar broth when in cross-examination he stated at page 422 of the transcript in answer to the following question:

Q If you used the Duggar Patent but happened to take a broth that was chlorine free, I think you would agree that you could not produce chlortetracycline?

A. No. One. The Duggar Patent does not teach a chloride-free medium and therefore I would not be following Duggar if I took a chloride-free medium.

Q. But does it teach that the medium must be chloride?

A The patent teaches this, that we want to make Chlortetracycline which contains chlorine The patent teaches what the organism requires for its growth and for the production of the desired substance, may be used with natural materials and a source of essential salts, and if I use natural materials I will have chloride present in the medium.

Q Show me where the patent says you use natural materials

A P 3 column 6 first paragraph:

"Suitable sources of nitrogen for the fermentation process include a wide variety of substances such as amino acids" (which may or may not contain chlorine, some do, others don't) "casein" (could go up as high as 5% sodium chloride) "both hydrolyzed and unhydrolyzed, fish meal, soy bean meal, meat extracts, liver cake, and various other substances of vegetable or animal origin."

Dr. Petty affirmed that the above ingredients all contain chlorine and that he has not run into any nitrogenous substances of vegetable or animal origin for instance, which have not contained chlorine varying in quantity from very small to large amounts.

Now although Counsel for the defendant in cross-examination attempted to get Dr. Petty to agree that if one used the ingredients mentioned by Duggar in his patent in their pure form, one would not have any chlorine, the witness would not agree that such a result could ever be obtained in Duggar because the ingredients mentioned in the patent were specifically described as not being in their pure form but were natural materials containing in most instances sufficient quantities of chlorine to obtain the result contemplated by Duggar.

It indeed appears from the evidence that only ten parts per million of chlorine are required in the fermentation medium to permit the reaction to proceed in the manner indicated by Duggar and all the witnesses agree (including Dr. Tosoni) that there is more than sufficient chlorine in the preferred materials listed by Duggar in his patent, such as corn steep liquor, caseine, artificially chlorinated water and even natural water which may even be chlorinated, to produce Chlortetracycline, I might add that the very name of the product achieved, Chlortetracycline, and its formula in the Patent, indicate that it has chlorine in the molecule and the extent of the skilled knowledge I have acquired as a result of the evidence adduced in the present case, of which the defendant has the burden on this matter of validity of the Patent, would indicate to me that if the end product is Chlortetracycline and there is chlorine in the formula of this product, it must have come from somewhere and this would be from the fermentation broth.

In the light of the above circumstances and the statements of all the experts including Dr. Petty, and even Dr. Tosoni, that they would have no difficulty in producing Chlortetracycline according to the Duggar Patent, by following the latters teachings as therein contained, it would appear to me impossible to hold that the patentee has not met his obligations under the statute and has failed to properly describe his invention so as to make it unworkable and inoperable as if the man skilled in the art which here appears to be a highly skilled scientist, one who works in the examination of micro-organisms and the making of antibiotics finds no difficulty in producing the product, then that should and will determine sufficiency and operability.

In *British Ore v. Minerals Separation*[1] Lord Justice Fletcher Moulton clearly set down the correctness of such a solution when he said at p. 138:

> In the first place, the patentee is entitled to say that his Specification is addressed to those who are skilled in the art, and that if its directions are adequate to guide them he has sufficiently "described the manner in which his invention is to be performed", even though they might seem utterly inadequate to one unacquainted with the subject matter.

I also feel that there is no substance to the allegation that the Duggar process would be useless in that some one might use a chlorate or a chlorite instead of a chloride and thereby

[1] (1909) 26 R P C. 124

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not be able to produce Chlortetracycline in view of the fact that such elements could kill the organism; it indeed appears to me that if such a result would occur and even this is not entirely certain in view of Dr. Petty's uncertain answer to Counsel for the defendant in this regard, no person skilled in the art to whom this invention is addressed would use such a radical. I cannot, indeed, see how a competent workman in the art would use in a patent such as here, whose object is to grow organisms on a nutrient in order to obtain an antibiotic, would use an element which would kill the very organism which produces the desired result.

In my view, this Duggar Patent, because of its importance as a break-through in the antibiotic world and of the enormous commercial success of the product produced and sold on the market, should be approached as stated by Sir George Jessell in *Hinks & Son v. Safety Lighting Co.*[1] at p. 612, "with a judicial anxiety to support a really useful invention and by a mind willing to understand not by a mind desirous of misunderstanding" and if this is done there can be no question, in my view, of the sufficiency of the description nor the workability of the invention which here leads the competent workman to success.

It therefore follows that the attack made by the defendant on the sufficiency of the Duggar patent must and does fail.

I now come to a two-fold attack made on both the Duggar and the Minieri patents and they may, therefore, be dealt with together here.

This attack is to the effect that the patents,

(1) are incomplete, misleading and lack utility in that Duggar fails to distinguish between strains of Aureofaciens which may produce Chlortetracycline and other strains of Aureofaciens which will not produce Chlortetracycline and Minieri fails to distinguish between strains of Aureofaciens which may produce Tetracycline and other strains of Aureofaciens which will not produce Tetracycline, and

(2) do not disclose where and how strains of Aureofaciens capable of producing Chlortetracycline when

[1] (1876) 4 Ch. D. 607.

> fermented in the presence of chlorine ions may be obtained, nor where and what strains of Aureofaciens capable of producing Tetracycline may be obtained for the purpose of lawful experimentation during the life of the patent and of commercial practice of the invention after its expiry.

The position taken by the defendant with regard to (1) above, is that aureofaciens being a broad term embraces, as we have seen, a great many strains some of which it submits refuse to produce chlortetracycline and, therefore, the patentee in his patent, to use an expression current in patent cases, has spread his net too wide and has thereby embraced strains which will not and do not achieve the result of producing chlortetracycline with any strain of streptomyces aureofaciens and he has, therefore, claimed too widely.

The defendant produced Ex. D-11, a Canadian patent No. 678,153, issued January 14, 1964, entitled Tetracycline Fermentation by John Andrew Growich Jr. and Nicholas Deduck and Ex. D-78, a U.S. patent issued August 29, 1961 entitled Production of Tetracycline, by Terry Robert Daniel McCormick, Newell Oscar Sjolander and Ursul Hirsh, both of which now belong by assignment to the plaintiff company which deals with strains of aureofaciens which it submits will not produce chlortetracycline under the Duggar patent, but which will only produce Tetracycline. Exhibit 11, at p. 1, reads as follows:

> This invention relates to the production of tetracycline by fermentation and, more particularly, is concerned with certain novel mutant strains of *Streptomyces aureofaciens* which possess the property of producing tetracycline to the exclusion of chlortetracycline irrespective of the chloride ion content of the fermentation medium.

Now it is clear that if at the date of the patent the words used (and here we are dealing with streptomyces aureofaciens) embraced useless as well as useful micro-organisms then the Duggar patent is bad. There is considerable authority for this proposition, the main one being, of course, the *Minerals Separation Case* which came before this Court, was heard by the Supreme Court of Canada[1] and then by the Judicial Committee of the Privy Council[2].

The facts of this case dealt with a froth flotation process for the concentration of ores where the claim in issue

[1] [1950] S.C.R. 36.

[2] 12 Fox P.C. 123.

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claimed xanthate, a chemical, as part of the process of froth flotation for the concentration of ores. It was established at the trial that there were some 90 known xanthates at the time of the patent of which 14 only were effective, the balance being ineffective. On the basis that many xanthates were known to the patentee which were not effective or of no value to the process, the patent was held invalid by the Supreme Court and later confirmed by the Judicial Committee of the Privy Council.

Now before dealing with the legal aspects of this matter, it would be in order to deal firstly with the defendant's assertion that Growich et al and McCormick et al cover patents dealing with aureofaciens which will not produce chlortetracycline.

Dr. Backus questioned in this respect and when presented with the Growich and Deduck patent (Ex. D-11) agreed that it appeared to be based upon the discovery that certain novel mutant strains of aureofaciens produce by fermentation Tetracycline to the exclusion of chlortetracycline and that they do this regardless of the concentration of chloride ion in the medium.

At p. 357 of the transcript, in view of the fact that certain strains of aureofaciens would not give chlortetracycline, he was asked the following question:

> Q. Am I right in saying that when an inventor of your company says he makes chlortetracycline with streptomyces aureofaciens he is not giving enough information to allow a person wanting to make tetracycline or chlortetracycline with aureofaciens to proceed; he would have to indicate the strains?
>
> A. On the basis of my personal knowledge, I have never dealt with a strain which did not produce—

At pp. 357 and 358 of the transcript he was then asked:

> Q As an expert in this field, from your personal knowledge in this field would you not admit that unless we knew the strain involved we could not be sure of getting chlortetracycline with aureofaciens?
>
> A. All of the strains of streptomyces aureofaciens which exist in nature to my knowledge produce chlortetracycline.
>
> . . .
>
> Q I didn't ask you to construe the document, doctor. Your learned counsel objected strenuously to that, and I agree with him But would you not agree, on the basis of your own general knowledge of the subject and as an expert that there are strains of aureofaciens that will not, even in the presence of chloride ion, produce chlortetracycline.
>
> A. As of this date, yes
>
> . . .

HIS LORDSHIP: What was the answer?

THE WITNESS: I said that as of this date perhaps it was true, but I was not sufficiently familiar with whether or not the determinations had been run in such a manner that it was absolutely certain that there was no chlortetracycline There might have been a very small amount, but I could not speak from my own experience with reference to it.

As for Dr. Benedict, his evidence is to the effect that even today he knows personally of no strains of aureofaciens which will not produce chlortetracycline.

As far as I can see this is the extent of the evidence submitted by the defendant on this matter. There is indeed on the one hand the production of these patents (Exs. D-11 and D-78) which appear to say that some strains of aureofaciens have been discovered which produce tetracycline to the exclusion of chlortetracycline and a statement by Dr. Backus in cross-examination to the effect that there might still be a small amount of chlortetracycline produced even with the McCormick and Growich strains. Now, although the fact that these patents were assigned to the plaintiff corporation might give this evidence some stature on the basis that the plaintiff would not have acquired these patents had they been useless, it still, in my view, falls short of the cogent evidence required and which would have been met, for instance, if a scientist had stated that he had used these strains and had effectively produced tetracycline to the exclusion of chlortetracycline. This question, however, of whether such strains exist or not today appears to me to be of an academic interest only in the present case due to the fact that the important date with regard to a patent being void on the ground of insufficiency or inutility is the invention date and if at the date of the invention all known strains of aureofaciens would produce chlortetracycline, then it cannot be successfully attacked on the above grounds.

The law appears indeed to be that if at the date of the patent, 1953 for Duggar and 1957 for Minieri, both embraced useless as well as useful micro-organisms, then the patents are bad and void. However, these useless micro-organisms must have existed at the date of the patent to avoid it as the patentee is not required to have the gift of prophecy and this appears to have been always recognized by our courts as well as by the authors.

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Now, as evidence clearly discloses that as of the above dates there existed no strains of aureofaciens that were unworkable and if the law is such as is hereinabove indicated, then this should dispose of this attack made on both patents. I might point out that with regard to the attack on this basis made on the Minieri patent, no evidence at all was adduced of the existence of strains of aureofaciens which would not produce Tetracycline.

That the state of knowledge must be considered at the date of the patent appears clearly in a reference contained in *Frost on Patents,* 4th edition, at p. 204:

> It must not, however, be forgotten that the meaning of words is liable to change with the progress of science and discovery, and a term which, for the purpose of the specification, is sufficiently accurate, may, in future years, include that which will not answer the purpose the patentee has in view. In such a case the specification will be read with reference to the state of knowledge at the time it was prepared, and if the term used include nothing then known that would not answer, it will not be held to be ambiguous, though the use of the same term subsequently might be. This is only equitable, for a patentee is not entitled to a monopoly of ingredients and materials which were unknown at the date of the specification, and which, viewed in the light of the knowledge at the date of the specification, would not be perceived to be the equivalents of materials mentioned, even though the language used be sufficiently wide to include them. It would be manifestly unfair to hold that language which, by the advance of knowledge, has come to include more than the patentee contemplated should vitiate the grant.
>
> Thus, for instance, when the directions given in a specification for the preparation of the article, which is the subject-matter of the patent, necessitate the use of a practically chemically pure substance, and, at the date of the patent, the person to whom the specification is addressed would, by using the knowledge of the period, obtain the substance sufficiently pure and would succeed, it is no valid objection to the utility of the invention and the sufficiency of the specification that, at a subsequent date, the same person using the then commercial article (*which has only come into existence as a commercial product after the date of the patent*) would fail.

The above, in my opinion, applies to both the plea of insufficiency of the specification and lack of utility. Further authority in this regard can be found in the *"Z" Electric Lamp case*[1] a decision of the Court of Appeal, where Lord Fletcher Moulton stated:

> . . . For the purpose of considering this point, I must go back to the state of knowledge at the date of the Letters Patent, for I think it perfectly good law to say that you have to judge of the validity of Letters Patent at the date of the grant, and that if they are then valid, no subsequent increase of knowledge can affect that validity in any way.

[1] (1910) 27 R.P.C. 745.

And *Terrell and Shelley on Patents* at p. 67 confirms this in stating that :

> A specification is to be construed with reference to the state of knowledge at the time it is published.

This notion is also clearly indicated in the *Minerals Separation case* (*supra*) where as indicated by counsel for the plaintiff, Mr. Fox, the judges of the Supreme Court at pp. 50, 52, 59, 67 and 70 when inquiring as to the common knowledge known or contained in dictionaries refer always to the year 1923 which was the date of the patent in that case. Indeed, Mr. Justice Rand at p. 52 states:

> On the plain language of this claim, it is bad: there *were known to Keller* many xanthates which were of no value to the process. (the emphasis is mine).

And at p. 59, Mr. Justice Kellock states:

> In 1923 the only xanthate in commercial use according to the evidence was cellulose xanthate which was used in the rayon industry.

The same applies to the decision of the Judicial Committee of the Privy Council (*supra*), p. 133 where it is stated:

> . . . It has already been said that in their Lordships' judgment the word "xanthate" as ordinarily used by chemists at the date of the patent included cellulose xanthates and indeed cellulose xanthates were the only xanthates at all widely known.

It therefore follows that the attack on the basis that all strains of aureofaciens will not produce chlortetracycline or tetracycline must and does necessarily fail.

I now turn to the next attack made on both patents in that they do not disclose where and how strains of S. aureofaciens, capable of producing chlortetracycline when fermented in the presence of chlorine ions (for the Duggar patent) and Tetracycline (for the Minieri patent) may be obtained for the purpose of lawful experimentation during the life of the patent and of commercial practice of the invention after the expiry.

It indeed appears that the Duggar American patent (Ex. D-3, September 13, 1949) in addition to a description of the growth of the micro-organisms clearly states that the strain of aureofaciens can be obtained from the Northern Regional Research Laboratory, at Peoria, Illinois, U.S.A. under the designation N.R.R.L. 2209 whereas the Canadian Duggar patent is silent in this regard, although for the purpose of designating the organism it contains a complete

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description of its growth at p. 2, column 4, line 23 of the patent as follows:

The organism which produces chlortetracycline was isolated from the soil of a timothy field in Missouri. Structurally and functionally this organism, *Streptomyces aureofaciens* as found naturally in the soil and as represented by spontaneous or induced mutants, belongs to the genus currently distinguished as Streptomyces. It is typically aerobic, with limited growth when submerged. A mycelium is formed, and when young, discrete colonies in asparagine-meat extract-agar (hereafter referred to as AMD agar) display branched hyphae, rapidly intermeshed, producing a dense, button-like colony with the free ends of the hyphae generally flexuous and continuous. Surface colonies are raised, often slightly depressed at the center. Agar slants sown with well distributed, numerous spores yield a confluent growth, that is, a continuous and "prostrate" mycelial stratum in the exposed or outer layer of the nutrient matrix, a growth type commonly called surface growth. Colonies in this state of growth on AMD agar are commonly hyaline for at least 48 hours, gradually changing to orange yellow (dull to bright), and in the several forms that may be selected out, pigmentation of the hyphal mass may be described as a hygrophanous Persian yellow, apricot yellow, maize yellow (Oberthur et Dauthenay, Répertoire de couleurs), yellow buff, or turbid variations of the clearer qualities.

The AMD agar is only slightly, if at all, pigmented with the growth of Streptomyces aureofaciens recently isolated from soil. On the AMD agar a continuous growing surface on a slant culture exhibits aerial hyphae with conidia white at first, becoming dark grey and abundant as sporing proceeds (7-10 days). The reverse view at this stage is tawny. Fragmented hyphal remains are also gray.

Young hyphae are gram-negative (older hyphae variable) and not acid fast; these younger hyphae measuring about 0 7-0.8 u in diameter and up to twice as much when differentiating conidia. The conidia are speroidal to ovoidal, measuring up to 1 5 u in the longer diameter.

Growth on AMD agar is very good and conidial production abundant, with favorable temperature.

Growth on nutrient broth agar is good but production of aerial hyphae and conidia is inhibited. With added $NaNO_3$ there is no improvement, and only a slight betterment with the addition of dextrose.

Growth on corn steep liquor agar is very good, conidial formation slow but ultimately (15 days) heavy.

Growth on synthetic (Uschinsky's asparagin) agar yields a heavy hydrophanous yellow-tan prostrate mycelium, no conidia, and the medium displays a cloudy amber pigmentation.

Growth on steamed potato slants in orange yellow (to brownish yellow in certain mutants), considerably raised, surface eventually nodulate.

Gelatin stabs display no liquefaction in 15 days at about 26°C

Nutrient broth affords a collar of almost hyaline growth at the glass surface; with added nitrate growth is similar, but with either dextrose or starch added the collar is yellowish-brown.

Litmus milk also supports a slight growth collar, yellow brown above, but in 15 days there is neither significant pH change nor apparent peptonization.

In fermentation tubes (with phenol red as indicator, pH 6.8-7) there is no gas accumulation with the addition to the nutrient broth of either xylose, glucose, galactose, sucrose, maltose, lactose, glycerol, or mannitol. Acidity is indicated over a period of about 5 days with only glucose or sucrose, this color change being gradually succeeded by a slow change toward alkalinity. In the presence of the other carbon sources either no change occurred (maltose, glycerol) or increasing alkalinity developed, this being strongest with mannitol.

Among other carbon-furnishing substances, dextrose, sucrose, maltose, lactose, dextrin, starch, glycerol, and mannitol support growth.

Dispersed in agar, soluble starch is hydrolyzed in a zone around the colony (pH = 5.8 to 6.0). Hydrolysis of starch is also induced when the dispersion is in nutrient broth.

The defendant here takes the position that the Canadian competent workman (and here we are talking about a microbiology and fermentation scientist, because the subject matter of the specification is such that no one but a person possessing a very considerable amount of scientific knowledge could at the date of the specification be considered a competent workman) has not in the present patent the information he needs to either work this patent experimentally or even after its expiry to produce the product, whereas his American counterpart has a reference to a strain, i.e., N.R.R.L. 2209 with information as to where it is deposited and, therefore, the patentee here has not made a full disclosure of his invention as required by s. 36 of the Act.

The American Duggar patent, at column 3, lines 70 to 75 inclusive and at column 4, line 2 inclusive, indeed refers to the organism as follows:

The organism which produces the new antibiotic substance of the present invention was isolated from the soil of a timothy field in Missouri. Cultures of the living organism have been deposited with the Fermentation Division of the Northern Regional Research Laboratory at Peoria, Illinois, and have been added to their permanent collection of microorganisms as N.R.R.L.-2209.

There is no question that s. 36 of the Act requires as one of the considerations for the monopoly grant given the patentee that the latter give in the patent to the public what Mr. Fox at vol. 1, p. 328 *Canadian Patent Law on Practice*, 3rd Ed. 1948, describes as:

. . and adequate description of the invention with sufficiently complete and accurate details as will enable a workman, skilled in the art to which the invention relates, to construct or use that invention when the period of the monopoly has expired

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In *Minerals Separation North American Corporation* v. *Noranda Mines, Limited*[1], Thorson P., as he then was, with respect to the obligation of the patentee, in this regard stated at p. 316:

> Two things must be described in the disclosures of a specification, one being the invention, and the other the operation or use of the invention as contemplated by the inventor, and with respect to each the description must be correct and full. The purpose underlying this requirement is that when the period of monopoly has expired the public will be able, having only the specification, to make the same successful use of the invention as the inventor could at the time of his application.

And at p. 317 he added:

> When it is said that a specification should be so written that after the period of monopoly has expired the public will be able, with only the specification, to put the invention to the same successful use as the inventor himself could do, it must be remembered that the public means persons skilled in the art to which the invention relates, for a patent specification is addressed to such persons.

It would be apposite to reiterate that the person skilled in the art here is a highly trained scientific person because of the subject matter of the specification and in order that the specification be sufficient it is not required to describe the invention and the manner in which it is to be performed so fully as to instruct persons wholly ignorant of the subject matter.

Frost on Patents, vol. 1, pp. 210 and 211 clearly explains this as follows:

> The often repeated statement to the effect that the specification is insufficient unless it be comprehensible to the "ordinary workman" in the trade to which the invention relates is apt to lead to great confusion, if it be not clearly borne in mind that the "ordinary workman" is to be regarded as a person of very different knowledge and skill according to the nature of the field of invention with which the patentee in a particular case is dealing. Thus, if the invention is merely the construction of a mechanical combination of parts for a purpose readily understood—e g., a bicycle—then the "ordinary workman" is, no doubt, a mechanic used to the construction of machines; but if the invention is the production of something by a process, or series of processes, to understand which the highest scientific knowledge and attainments are requisite, the "ordinary workman" then becomes a highly trained scientific person, who may be called upon to give the necessary instructions to his less highly instructed and skilful subordinates to enable the process to be carried out by them—e.g., if the invention relates to the production of a chemical product by a process, or series of processes to the understanding of which a knowledge of the most recent developments of chemical theories and ascertained facts is indispensable, then the "ordinary workman" becomes a highly trained

[1] [1947] Ex. C.R. 306.

chemist, who may be properly called upon to bring his special knowledge of the particular branch to which the invention relates into play, for the purpose of giving minute directions to his less skilful subordinates so as to enable them to perform the operations necessary to the carrying out of the process, which they, by their lack of knowledge, may not be able to fully appreciate.

Have the patentees (Duggar and Minieri) fulfilled the requirement of s. 36 of the Act of describing the invention and its operation or use and of setting forth clearly the various steps in their process in such full, clear, concise and exact terms as to enable *any person skilled in the art or science to which it appertains* to make, construct, compound or use it, when such as here, having deposited a culture of the micro-organism used in the patent under an identifiable number in a U.S. depository, they have not (at least in so far as the Duggar patent is concerned) indicated it in the Canadian patent, and by so doing have they deprived Canadians from all the advantages of working with this invention during the life of the patent and of using it commercially thereafter because it appears to me that it is only in the event that the absence of a reference to a culture has this result that s. 36 of the Act can be taken not to have been complied with. There indeed is no requirement under the *Canadian Patent Act*, nor under its rules, to deposit in the case of patents which deal with the product of micro-organisms the type culture or a strain of such micro-organism such as required in the United States as appears from an extract of a letter addressed by the plaintiff to the Northern Regional Research Laboratory, dated August 11, 1949, and produced as Ex. D-7 where it is stated:

> We are placing these live cultures in your possession in view of a requirement by the U.S. Patent Office that the aureomycin producing mold S. Aureofaciens be made available to the public as a condition to the allowance of our patent application covering aureomycin and a method of producing this material by fermentation filed by Dr. B. M. Duggar.

Counsel for the plaintiff here takes the position that there was no obligation on the part of the patentee to indicate a deposit in his patent at all and that as Dr. Duggar, in his patent, describes how to obtain aureofaciens, lists the steps he took, where and how he obtained the micro-organism, describes its structure, together with the nutrients on which it is grown and sporulates, which is sufficient to enable a skilled man in the art to work his invention, the patentee has sufficiently complied with the requirements of the

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Patent Act. Dr. Tosoni, one of the defendant's witnesses stated at p. 578 of the transcript that as of June 1953 and reading the Duggar patent, the latter teaches one to try to obtain it by looking in the soil and he added that one may be fortunate and find it soon, or it may take a long time. Now, although this method might mean the examination of a great number of soil samples, there is no evidence in this case that by following the Duggar teachings one does not obtain streptomyces aureofaciens. The question here might therefore well be whether Duggar has disclosed everything that is necessary for the certain procurement of the commodity for which the patent was granted or reiterating what Thorson P. said in the *Minerals Separation* case (*supra*) at p. 317:

> When it is said that a specification should be so written that after the period of monopoly has expired the public will be able, with only the specification, to put the invention to the same successful use as the inventor himself could do, it must be remembered that the public means persons skilled in the art to which the invention relates, for a patent specification is addressed to such persons.

The answer here would appear to be in the affirmative if the evidence of Dr. Benedict is considered as it appears at p. 502 of the transcript where he states that by following Dr. Duggar's teachings in his patent, he was able to isolate three strains of aureofaciens from the soil in Japan and produce chlortetracycline and as he was not cross-examined on this point, I may take it that he had no trouble in finding the organisms:

> MR SIM: What, if any, work have you done in the production of chlortetracycline?
>
> A I have isolated strains of aureofaciens from samples of Japanese soil.
>
> Q How many?
>
> A. Three strains, three different strains from three separate soil samples. These were isolated, studied, and using the teachings of the Duggar patent I have been able to produce chlortetracycline with each of these strains.
>
> Q. How did you know that the strains that you had isolated were streptomyces aureofaciens?
>
> A. I compared very carefully using the teachings of the Duggar patent . . . I can't recall the exact column there, but I think it goes from No. 34 to 51. If I may have it. At column 4, starting at about line 24 and going over to column 5, about line 53.
>
> Q You are referring now, of course, to the Canadian Patent?
>
> A. Yes

Q. Now, at that time what would you have done?

A. At that time I would have referred to patent No. 2,482,055.

Q Is that the corresponding United States patent?

A. Yes.

Q If, Dr. Benedict, on November the 3rd 1953, you had been given a copy of the Canadian Duggar patent which you have just looked at, and using only the ordinary knowledge available to you as an expert in this field you had been asked to carry out the teaching of the patent, what difficulty, if any, would you have experienced in producing chlortetracycline?

A. None.

The evidence moreover discloses that the N.R.R.L. and A.T.C.C. depositories in the United States are scientific places well known to all the experts heard in this case and would, according to the latter, be well known and recognized also by all those competent workmen in the art who would, during the life of the patent, like to work on it or after its expiry use it. They could indeed write to these depositories and obtain the organisms.

Dr. Backus, at p. 132 of the transcript, dealt with the availability of these deposited organisms as follows:

Q. When was this N.R.R L. 2209 released?

A. It was released on September 13th, 1949.

Q. And what is the effect of the deposits being released, what does that mean?

A. It means that anyone can obtain a culture of this organism, to study its characteristics, to carry out the teachings of Professor Duggar in the patent which he had written. It was released to those who requested it.

Q. What charge was made on a request for a strain?

A. There was no charge made.

Q. Would you tell the court what, if any, restriction was placed on the supply of N R.R.L. 2209 after it was released?

A. None.

Q. Are you familiar with the strain of streptomyces aureofaciens known as UV8?

A. Yes, I am.

Q. By whom was UV8 first produced?

A. UV8 was produced by a group working under the direction of Minieri, who at the time was with the Heyden Chemical Corporation.

Q Would you tell the court where UV8 was first deposited and released?

A I would say the first deposit at the A.T C.C, American Type Culture Collection, was about the 15th of December, 1955, and it was released on February 7th, 1956, I believe.

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Q. What is the A.T.C.C.?

A. The A.T.C.C. is the American Type Culture Collection, and this is one of the major culture collections of the world where an extensive collection of micro-organisms is maintained and available.

Q. What restrictions were placed on the supply of the A.T.C.C. deposit of the micro-organism UV8, if any?

A. The only restriction placed to my knowledge was that American Cyanamid, who had deposited the organism, were informed if an organism was ever sent outside of the United States.

This witness stated that to his knowledge the plaintiff company never refused permission for this strain to be sent outside the United States by the A.T.C.C. He also stated that from the records of the plaintiff company it appears that strains of N.R.R.L. 2209 were sent to Canada, one to a Dr. R. H. Haskins from the Prairie Regional Laboratory, in Saskatoon, in May 1951 and in April of 1952 a Dr. Stewart of the University of Alberta, in Edmonton, obtained a similar transfer.

Dr. Benedict stated at p. 501 of the transcript that if one wrote to the N.R.R.L. and merely asked for aureofaciens, although one could have obtained the exact number of a particular strain because the evidence shows that the literature was full of reference to the deposits, one would get aureofaciens and probably aureofaciens 2209. There was also a deposit at A.T.C.C. of A.T.C.C. 10762 and here, although it was necessary to get permission to send it out of the United States, there was evidence that permission to send it out of the United States was never refused. The evidence clearly shows that to the skilled scientist in the art, the micro-organisms were well known and easily available upon demand and could be used if one did not wish to have recourse to the soil, and, therefore, the invention could have been put to the same successful use as the inventor if such means had been adopted. This also, in my view, could be an answer to the alleged incompleteness of the specification of the patent in not specifying the strain or its location. Support for such a view can be found in *Blanco White on Patents*, at p. 160, line 5, where it is said:

> Thus a general instruction to use "any suitable material" or "known methods" or to use chemical reagents of a general class (leaving it to the addressee to determine which members of the class will operate satisfactorily), will be sufficient if it enables the addressee to put the invention into practice.

It, therefore, follows that the absence of a reference to a specific strain in the patent has in no way prevented the addressee from putting the invention into practice, or deprived the public of all the advantages of working with this invention during the life of the patent and of using it commercially at its expiry and this attack made on the Duggar patent must, therefore, fail.

The attack made on the Minieri patent on the basis that there is no mention therein as to where or how strains of aureofaciens, capable of producing Tetracycline, can be obtained, is urged by counsel for the defendant to be more serious than in the case of Duggar because here, although Minieri mentions strain UV-8 which, according to the evidence, is deposited with A.T.C.C. under number 12416, the evidence discloses that instructions were given by the plaintiff company to the culture depository not to send the strain to a foreign country without the plaintiff's consent and that, therefore, the Canadian scientist would thereby be at the mercy and will of the plaintiff corporation with regard to the procurement of the micro-organism.

Dr. Petty testified that the question of the strain UV-8 (which is 12416) being available or not was a matter of policy of the company and that although the plaintiff wanted to know what strains of UV-8 were sent out of the United States, permission to send it out was never refused. The evidence discloses that Dr. Cain tried to get strain No. 12416 but did not, although in this case, as appears from his letter to the American Type Culture Collection dated September 14, 1962, and produced as part of Ex. D-75, he had suggested an alternative (10762) which is also aureofaciens and had no trouble obtaining it.

Now it also appears from the Minieri patent that the latter is not limited to the UV-8 strain. It is, indeed, mentioned in the patent only as one organism which is found to be useful as the patentee made it clear that any S. aureofaciens can be used as appears at p. 4, column 8, line 59 of the patent:

> The present invention is not limited to UV-8 or any particular organism but includes any S. aureofaciens organism or variant or mutant, either naturally occurring or artificially induced, which produced tetracycline in concentrations making possible the recovery of the therapeutic product.

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Under these circumstances I fail to see how it can be said that the Canadian scientist, who knows about the depositories, is at the mercy and will of the plaintiff when, as it appears from the evidence, Dr. Cain had no trouble at all after referring to the literature in obtaining an aureofaciens organism capable of producing Tetracycline under the Minieri patent even if it was not the UV-8 strain, and this attack fails also. As stated by *Frost on Patents*, vol. 1, at pp. 204 and 205:

> It is always a question for the jury, or the Court acting as a jury, to say whether or not the specification describes with sufficient accuracy the ingredients or materials which the patentee directs to be used, but a patentee is not obliged, in referring to materials and ingredients, to enter into minute details as to them if they are known in commerce and can be readily procured under the names which he gives them.

I now turn to the attacks made on the Minieri patent on the basis that the latter is invalid because it was anticipated by the Duggar patent by the Martin, Bohonos, Duggar and Devoe application as well as by the Heineman and Hooper patent application.

As no evidence was presented nor argument expressed in relation to the Heineman and Hooper application, I need not deal with it.

With regard to the Duggar patent, the defendant submits that if Duggar is followed and if the ingredients indicated by Duggar are chosen without a chlorine content or very little, the Minieri result will be obtained and that, therefore, it is possible by following exactly the directions of Duggar to obtain Tetracycline instead of chlortetracycline.

This attack on the Minieri patent as set down by the defendant in his particulars of objection reads as follows:

> B I. The process claimed therein is the same as that claimed in Canadian Letters Patent No. 497,339 also in suit which does not make any mention of chloride ions.

Now there is no question but that chlortetracycline or (aureomycin) is a valuable antibiotic as recognized by the experts, including Dr. Tosoni, who at p. 632 stated in answer to the following question:

> Q Would you agree with me that chlortetracycline and tetracycline are very valuable products?
>
> A. I certainly would.

The difference between chlortetracycline and Tetracycline is that the chloride ion that appears in chlortetracy-

cline was taken off and a hydrogen substituted and so chemically it is a different product. Now the evidence discloses that although Tetracycline has about the same effectiveness as chlortetracycline as an antibiotic, it has fewer side effects and, therefore, is more easily tolerated by the patient. It is, therefore, an improved product.

Dr. Duggar's contribution was therefore the discovery, isolation and identification of streptomyces aureofaciens and the production of chlortetracycline as a new product using aureofaciens in a fermentation medium which contains chloride. On the other hand, Minieri deals with the production of Tetracycline and his contribution was to discover that Tetracycline (not a mixture of chlortetracycline and Tetracycline) could be produced by the same micro-organisms aureofaciens, not by the method of deschlorinating chlortetracycline which, as already mentioned, had been discovered before, but by fermentation, if the chlorine content in the medium were controlled in one way or the other.

Dr. Petty's evidence at p. 98 of the transcript explains Minieri's method of producing Tetracycline as follows:

> Q What is the relationship, if any, between the process of producing tetracycline by deschlorination and that of producing tetracycline by using the organism streptomyces aureofaciens in a medium or broth in which the chloride is controlled?
>
> A. The deschlorination of chlortetracycline is a chemical process. It was unpredictable that the micro-organism streptomyces aureofaciens would produce this molecule in the absence of chloride.
>
> HIS LORDSHIP: What was that again?
>
> THE WITNESS: It was unpredictable that the microorgainism streptomyces aureofaciens would produce tetracycline if chloride was not present in the fermentation broth.

This witness then explained that following Duggar's work in 1953, the production of Tetracycline by fermentation of aureofaciens in a medium from which the chloride has been removed or stripped or held back, has economic advantages over the chemical method of knocking it off with a catalytic agent, because using the fermentation method results in an increased production of 15 per cent of the product chemically speaking.

Dr. Petty was the only person skilled in the art of fermentation who spoke of the skilled person in the art at the relevant date, which here is September 28, 1953 (date of the Minieri invention) and it is at this date that this matter

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of anticipation by Duggar or Martin-Bohonos or even of the invention of Duggar over Minieri must be looked at.

This witness appears to have been the only one heard on the matter of anticipation and inventiveness in Duggar, Minieri and Martin-Bohonos and he was not cross-examined on these subjects. I had occasion in *Dominion Auto* v. *Defrees*[1] to point out the heavy onus one has who attacks the validity of a patent in instructing the judge and making him sufficiently skilled in the art to enable him to appreciate the problems involved in assessing the relevance of the prior art cited either as anticipation of, or of establishing the obviousness of a patent, when at p. 351 I said:

> I do believe that whether the presumption of validity is a heavy or easy one to displace remains a question of fact in each case although I must say that in patent matters it would seem that as the alleged infringer has the burden of not only attacking the validity of the patent in issue, but of also placing the judge in the position of a man skilled in the prior art it is not too surprising that the President of this Court has stated on numerous occasions that the onus is not an easy one to discharge.

From an examination of both the Duggar and Minieri patents, and using whatever knowledge the evidence has supplied, it now appears to me with reference to claim 1 of the Minieri patent that the latter's contribution to the art consists in using any aureofaciens and placing it in a fermentation broth which is substantially free of chloride and thereby recovering tetracycline instead of chlortetracycline. This claim deals with a broth which is free of soluble chlorides. Claim 2 deals with a broth being substantially free of available chloride ion. In the case of claim 1, if the broth is free of soluble chlorides, it means there is not much chlorine there. If, however, it is free of available chlorides, it may mean that there is chlorine there, but it is not available for participation in the reaction. Minieri appears to cover also a medium in which chlorine, although present, is in some way restricted or tied up so that it cannot take part in the reaction.

It, therefore, follows that Minieri's contribution consists in discovering a process of producing Tetracycline by direct fermentation in a medium in which the chloride is controlled or restricted or inhibited, with a conventional culture of streptomyces aureofaciens and is quite different from the Duggar patent which, as already mentioned, uses as a

[1] [1964] Ex. C.R. 331.

requirement for the production of chlortetracycline a minimum quantity of chlorine which, as we have seen, can be found in large quantities in the nutrient materials listed by Duggar.

In view of the fact that Duggar dealt only with the production of chlortetracycline by using materials containing a sufficient quantity of chloride to give this product, and because of Dr. Petty's uncontradicted evidence that the production of Tetracycline by fermentation without chloride could not, at the date of the Minieri invention, have been predicted, it follows that the information contained in the Duggar patent can in no way be taken to have given Minieri what he required for his discovery which would be required if Duggar is to be considered as a valid anticipation of Minieri and, consequently, I fail to see how Duggar could have anticipated Minieri.

Counsel for the defence, however, submitted that notwithstanding the fact that Duggar's object was to produce chlortetracycline by following his teachings, a medium could be selected which would be substantially free of chlorine and Tetracycline would be obtained and not chlortetracycline and that if such is the case, Duggar would have anticipated Minieri because one could, by following the teaching of Duggar, get Tetracycline in what turns out to be the Minieri method.

The requirements for a valid anticipation of a patent were set out clearly by Thorson P., as he then was, in *The King* v. *Uhlemann Optical Company*:[1]

> ...The information as to the alleged invention given by the prior publication must, for the purposes of practical utility, be equal to that given by the subsequent patent. Whatever is essential to the invention or necessary or material for its practical working and real utility must be found substantially in the prior publication. It is not enough to prove that an apparatus described in it could have been used to produce a particular result. There must be clear directions so to use it. Nor is it sufficient to show that it contained suggestions which, taken with other suggestions, might be shown to foreshadow the invention or important steps in it. There must be more than the nucleus of an idea which, in the light of subsequent experience, could be looked on as being the beginning of a new development. The whole invention must be shown to have been published with all the directions necessary to instruct the public how to put it into practice. It must be so presented to the public that no subsequent person could claim it as his own.

[1] [1950] Ex. C.R. 142 at 157.

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It is not even sufficient that a prior art reference in order to be an anticipation contains, as expressed by Thorson P., in the same decision:

> . . . suggestions which taken with other suggestions might be shown to foreshadow the invention or important steps in it. There must be more than the nucleus of an idea, which in the light of subsequent experience, could be looked on as being the beginning of a new development.

The prior art, indeed, must show in clear and unmistakable terms how to put the invention into practice. Now it appears that the teaching of Duggar is to obtain the production of chlortetracycline and if something else is produced, the teachings of Duggar are not being followed. Indeed, if pure materials are used and the chlorine is kept down and Tetracycline is obtained, the latter was not obtained by following the teachings of Duggar, but by going against those teachings and, therefore, Duggar cannot be considered as solving for Minieri the production of a material different from that produced by the Duggar patent and by a process discovered several years after his original production of chlortetracycline. It follows that the Duggar patent can in no way be considered as having anticipated the Minieri patent.

I now turn to the attack made on the Minieri Patent under B-3 of the Particulars of Objection which reads as follows:

> The alleged inventor of Canadian Letters Patent No. 542,622 was not the first and true inventor, being antedated by Messrs Martin, Bohonos, Duggar and Devoe as well as Messrs. Heineman and Hooper; patent applications by the said inventors are pending and were co-pending with the application which matured into Canadian Letters Patent No. 542,622.

What the defendant is saying here is that both Minieri and Martin-Bohonos cover the same invention and that if such is the case conflicts should have been declared between the two as according to the admission made by Counsel for the plaintiff and referred to at the beginning of this judgment, the Minieri Patent as an application was, at one stage, co-pending with the Martin-Bohonos application. The above admission also recites that whatever was disclosed in Martin-Bohonos was disclosed prior to whatever was disclosed in Minieri and it, therefore, follows that if Martin-Bohonos is an anticipation of Minieri it will invalidate the latter. The defendant urges that the examples given in Martin-Bohonos show the same media as those shown in Minieri. This,

however, is not the case and Dr. Tosoni, one of defendant's expert witnesses, in cross-examination at p. 609 clarified this point when he stated that from the examples given in Martin-Bohonos, whatever he meant by "controlled conditions" he did not mean that the medium was to be free of available chloride (which, of course, is the teaching of Minieri) as there is in Martin-Bohonos substantial chloride in every example varying from 20 parts to a million in one example to 3 and 550 parts to a million in another. It, therefore, can hardly be said that both media are the same. Minieri's teaching is, therefore, to keep the available chloride low and Martin-Bohonos teaching is that even with 3 or 550 parts to a million and more of available chloride, Tetracycline can still be obtained or a portion thereof by using certain selected strains.

Now looking at the Martin-Bohonos application again with whatever skill I have acquired as a result of the evidence submitted at the trial, it appears to me that although, as mentioned by Counsel for the defendant, the Martin-Bohonos application contains very broad claims, some of which even dominate the Minieri invention, this is not sufficient to place two applications in conflict under section 45(1) of the Act because the above article covers only two situations where applications should be placed in conflict which are (1) "when each of them contains one or more claims defining substantially the same invention," (2) "when one or more claims of one application describe the invention disclosed in the other application." It is indeed only if both applications fall within either (1) or (2) above that consideration can be given to the Martin-Bohonos application as a possible anticipation of Minieri, although compliance with section 45(1) (a) and (b) is merely one obstacle to overcome in order to make the application available as an anticipation, the latter being determined on an examination of the fundamental principles which apply to all prior art citations and which was referred to above in re: *The King v. Uhlemann Optical Company* (*supra*).

I do not think it necessary to go into an examination of the claims of both Minieri and Martin-Bohonos in order to determine whether they should be placed in conflict or not, because in my view even if they should have been placed in

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conflict (which, however, I refrain from determining although I might say that a cursory comparison of both claims in the light of the knowledge I have acquired from the evidence adduced herein, would indicate to me that they should not have been placed in conflict), Martin-Bohonos cannot be considered as a valid anticipation of Minieri.

Dr. Tosoni's evidence and the Martin-Bohonos Patent, D-16, indicate to me that the latter's discovery is that certain selected strains of streptomyces aureofaciens in a conventional fermentation broth will produce Tetracycline as well as Chlortetracycline, whereas Minieri, as already mentioned, discovered that any conventional strain of aureofaciens in a special medium will produce only Tetracycline and, of course, these are two different inventions.

Counsel for the defendant then introduced a copy of the United States Martin-Bohonos application deposited with the French Patent office in support of a request for priority under the International Convention as Exhibit D-77 as well as D-76 the French joint Minieri, Martin-Bohonos and Duggar and Devoe patent, which were allowed in under reserve of Counsel for the plaintiff's objection that these documents were not pleaded or listed in the affidavit on production and no notice was given which, in my view, should be sufficient to reject them entirely. However, even if they were admissible they do not, as urged by Counsel for the defendant show that Minieri and Martin-Bohonos are one and the same thing. They merely show that as apparently permitted in France a composite patent can be obtained involving work from different inventors and this can in no way be considered as an admission that Minieri, Martin, Bohonos and Duggar are all the same invention, nor does the evidence establish that such is the case.

There appear to be, in fact, three important differences between Minieri and Martin-Bohonos:

(1) Minieri used any conventional strain of Streptomyces aureofaciens. Martin-Bohonos used certain selected strains only with peculiar characteristics. Martin-Bohonos deals apparently with new or selected micro-organisms discovered and bred strictly for their capacity to produce in a chloride containing medium a substantial amount of Tetracycline as well as amounts of Chlortetracycline.

(2) Minieri used a special medium in which chlorine is controlled, restricted or inhibited; Martin-Bohonos used a conventional medium containing large quantities of chlorine.

(3) Minieri teaches that with proper control of the chlorine Tetracycline can be produced to the exclusion of Chlortetracycline; Martin-Bohonos teaches that with his process a mixture of Tetracycline and Chlortetracycline can be produced with a slightly larger proportion being Tetracycline.

It, therefore, follows that whether the Martin-Bohonos application qualifies as a reference within the meaning of section 45, subsection (1)(a)(b) or not, it certainly does not, in view of the above, meet with the requirements necessary to make it a valid anticipation of Minieri.

The essential ingredients and materials essential in Minieri for its utility cannot, in my view, be found in Martin-Bohonos and this is not too surprising as the processes invented are, as already mentioned, fundamentally different, Martin-Bohonos dealing with selected strains of aureofaciens in a conventional fermentation broth producing Tetracycline as well as Chlortetracycline, whereas Minieri deals with conventional strains of S. aureofaciens producing Tetracycline by direct fermentation in a medium in which the chloride is controlled, restricted or inhibited.

Under these circumstances, it is impossible to say paraphrasing the dictum in *Pope Appliance Corporation* v. *Spanish River Pulp and Paper Mills Ltd.*[1] that Minieri in attacking the problem he solved would have found what he wanted in Martin-Bohonos and, therefore, it cannot be said that Martin-Bohonos anticipated Minieri.

I now come to the last attack made on the Minieri Patent in that the latter invented nothing in view of Canadian Letters Patent 497,339, which is the Duggar Patent. The defendant is saying here that in the light of Duggar, Minieri was obvious and does not therefore possess one of the necessary attributes of a valid patent, i.e., inventiveness. In order to find here that this attribute is missing in Minieri, I would have to come to the conclusion that the new process in Minieri, in view of Duggar at the date of the Minieri

[1] [1929] A.C. 269; 46 R.P.C. 23 at 54.

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invention of 1953, was so easy that very little reflection would have been required to find it. This I am not prepared to say because, having regard to what was generally known at the date of the patent in suit, it was not obvious without considerable experiment and research that the new process invented by Minieri could give Tetracycline by direct fermentation and consequently I must, and do, hold that the attack made on this basis must and does also fail.

During the presentation of argument, Counsel for defendant submitted also that Minieri was obvious in the light of the Martin-Bohonos application; it however appears that this application, although pleaded as an anticipation of Minieri, was not pleaded as establishing non-inventiveness and, therefore, strictly speaking, should not form part of the issues involved in the present case. Now, although this would be sufficient in my view to dispose of this attack, I might add that even if this issue had been properly pleaded, I would still find no substance to it as, in my opinion, there is no doubt that here again Minieri's process could not have been and was not obvious in view of what Martin-Bohonos disclosed, which I dealt with in some detail on the matter of anticipation and, consequently, this attack must also fail.

I find, therefore, that all the attacks on the validity of the claims in suit fail. It follows, of course, that I find that as between the parties the claims in suit are valid.

There will, therefore, be judgment in favour of the plaintiff as against the defendant that as between the parties the claims in suit of the two patents are valid and that they have been infringed by the defendant as contended and that the plaintiff is entitled to the relief sought, except as to damages. If the parties are unable to agree on the amount of the damages or the amount of profits, if the plaintiff elects an account of them, there will be a reference to the Registrar or a Deputy Registrar to determine the amount of such damages or profits and judgment for the amount found on such reference. The plaintiff is also entitled to costs to be taxed in the usual way. The defendant's counterclaim must also be dismissed with costs.

Judgment accordingly.