COMMISSIONER'S DECISION

S. 2 Medical Treatment. Claims to a non-medical method of locating tumors in a subject by means of radiolabeled antibodies having a high specificity for carcinoembryonic antigens, and detecting with a photoscanning device the uptake of the antibodies, were considered to be directed to a diagnostic treatment. Rejection withdrawn

This decision deals with Applicant's request for review by the Commissioner of Patents of the Final Action on application 372,233 (Class 167-40) filed March 3, 1981. It is entitled TUMOR LOCALIZATION AND THERAPY WITH LABELED ANTIBODIES AND ANTIBODY FRAGMENTS SPECIFIC TO TUMOR-ASSOCIATED MARKERS. The inventor is Milton D. Goldenberg. The Examiner in charge issued a Final Action on July 3, 1984 refusing to allow the claims of the application. At the Hearing on June 3, 1987, the Canadian Patent Agent, Mr. D. Watson represented the Applicant, and Dr. B.D. Saxe, the United States Patent Attorney, presented technical background of the invention. After the Hearing, the Agent submitted a letter that referred to certain Court cases and contained copies of Canadian patents he discussed at the Hearing, and an affidavit of Dr. Saxe.

The application relates to a method of injecting into a living body certain types of antibody substances which have a high specific activity and a high specificity for carcinoembryonic antigens, and that are radiolabeled so that they are capable of detection by scanning devices, and that are specific to a variety of tumors, and to treatment thereof.

In refusing all the claims in the Final Action the Examiner said, in part:

. . .

> ...they are directed to a method which modifies the metabolism of the human body and is equivalent to a method of medical treatment which is outside the definition of invention as given in Section 2 of the Patent Act and judicially declared unpatentable by Tennessee Eastman v. Commissioner of Patents (1974) S.C.R. 111.
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> Applicant's argument is that the method claimed is not a medical treatment. This argument is rejected since the claim defines the step of injecting immunological reagents into a subject (e.g. human body). It is obvious that anything that is injected into a human body will change its metabolism and treats this human body one way or the other.

In the Court decision of Tennessee Eastman Co. v. The Commissioner of Patents (62 C.P.R. 117) p. 130, 154, the judge gave his reasons for holding method of treatment unpatentable when he said:

> Early in the development of patent law in England it was accepted that a manner of new manufacture may be a product or may be a process that can be used in making something that is, or may be, of commercial value, a vendible product. Conturrent with that concept was the principle that a method of treating any part of the human body does not afford subject matter for a patent ... (underlining added).
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> In my view the method here does not lay in the field of the manual or productive arts nor, when applied to the human body, does it produce a result in relation to trade, commerce or industry, or a result that is essentially (sic) economic. The adhesive itself may enter into commerce, and the patent for the process, if granted, may also be sold and its use licensed for financial considerations, but it does not follow that the method and its result are related to commerce or are essentially economic in the sense that those expressions have been used in patent case judgments: the method lies essentially in the professional field of surgery and medical treatment of the human body, even although it may be applied by persons not in that field. Consequently, it is my conclusion that in the present state of the patent law of Canada and the scope of subject matter for patent, as indicated by authoritative judgments that I have cited, the method is not an art or process or the improvement of an art or process within the meaning of Section 2(d) of the Patent Act.

. . .

In responding to the rejection, the Applicant argues, in part, as follows:

. . .

> ...it is only patents for medical treatment in the strict sense that must be excluded. This has led the Examiner to reject the present claims even though they are for a diagnostic method which does not involve the therapeutic treatment of disease.
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> The Examiner has taken the position that the exclusion of methods of medical treatment from patentability under the Tennessee-Eastman decision applies not only to methods of medical treatment, but methods which are considered by the Examiner to be "equivalent to a method of medical treatment". ...There is no legal authority for this extension and it is submitted clearly to be contrary to the decision of the Supreme Court in the Tennessee-Eastman case.
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> The Examiner has furthermore taken the position that if anything is injected into a human body, there will be some change in its metabolism and that there is therefore a treatment of the human body. Apparently this principle is to be applied irrespective of whether

the substance injected has a therapeutic effect. ...This position is unsupported by the case law and contrary to the decision of the Supreme Court in the Tennessee-Eastman case.

The Examiner has sought to sustain his position by relying on a quotation from the trial decision of the Tennessee-Eastman case. ...The quotation is out of context and seriously misleading as it omits the previous paragraph making it clear that this is merely a commentary on the interpretation in England of wording not found in the Canadian Act.

The Examiner has relied on a quotation from the trial decision which is not only out of context as indicated above, but is contrary to the reasoning of the Supreme Court of Canada in that same decision.... ...The law to be considered by the Commissioner in relation to Section 42 of the Patent Act is that of the Supreme Court and not of some lower court in the same case.

The Examiner has taken a position inconsistent with that of other Examiners.... ...Applicant should not be refused patent protection where others are being granted protection for the same type of invention.

. . .

In the decision of the Supreme Court in Tennessee-Eastman (1973) 8 C.P.R. (2d) 202 at page 209, Pigeon J, who delivered the judgment of the Court, was reviewing prior British decisions. He said:

> It might be noted that in the latest reported case brought to our attention, Re Schering A.G.'s Application, [1971] R.P.C. 337, a case dealing with a method of contraception by means of gestagen, the conclusion of the Patents Appeal Tribunal was at p. 345:
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> > Although, however, on a full consideration of the matter it seems that patents for medical treatment in the strict sense must be excluded under the present Act, the claims the subject of the application do not appear to fall within this prohibition and, on the law as it stands today, they should, at least at this stage in our judgment, be allowed to proceed. As Swift's Application (1962) R.P.C. 37 in the Divisional Court of the Queen's Bench Division clearly established, the Office and the Patents Appeal Tribunal are at this stage not deciding the question of "actual patentability", as the phrase was used in that case, and unless there is no reasonable doubt that a manner of manufacture is not being claimed or the application is plainly without justification, it is their duty to allow the claim. The applicants will then have the opportunity in due course, if the matter arises, of having "actual patentability" decided in the High Court. (Emphasis added).

In this quotation, the emphasis added is by the Supreme Court to the proposition that it is only patents for medical treatment in the strict sense that must be excluded. On this basis, a method of contraception by

> means of the administration of gestagen was considered not to be a method of medical treatment in the strict sense. The administration of this product would no doubt have an effect on the metabolism of the body, but would not involve the therapeutic treatment of disease and therefore would not be medical treatment in a strict sense. It is therefore clear that it is only methods of medical treatment in a strict sense that are precluded.
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> . . .

The Applicant refers to Burton-Parsons v. Hewlett Packard (1975) 17 C.P.R. (2d) 97, and pages 109-110, and argues, in part:

> ...It was stated "It is clear that such is primarily and mainly for the taking of electrocardiograms in routine examinations, not necessarily or mainly in connection with the treatment of disease." This shows that the term "medicine" is to be taken as limited to the treatment of disease and does not include substances or methods used in diagnostic procedures.
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> . . .
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> This reinforces the point made above that in discussing previous decisions the Supreme Court distinguished decisions dealing with methods which did not involve medical treatment in the strict sense. The Examiner is applying the prohibition not to medical methods in a strict sense and not even to medical methods in a broad sense, but even to methods which are not methods of medical treatment but which in the Examiner's mind are "equivalent to a method of medical treatment". We submit that in doing so the Examiner is striking out on his own in a direction opposite to that of the Supreme Court.
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> . . .

The Applicant refers again to the Tennessee-Eastman case as follows:

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> ... at the bottom of page 208, Pigeon J, who delivered the judgment of the Court, is commenting on some British decisions and he says:
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> > "In the second place, what was actually decided in those cases is not related to a medical or surgical method. Swift's application dealt with a method of tenderizing meat by injecting enzymes into the animal before slaughtering."
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> This makes it clear that even though substances were being injected into an animal while it was living which would have an effect on its metabolism, it was not to be regarded as a method of medical treatment. It is well established that methods of medical treatment include not only human medicine but veterinary medicine. The only distinction therefore is that in

> Swift's application, the absence of any therapeutic effect disqualified the treatment as being a medical method.

... .

The issue before the Board is whether or not the claims are directed to patentable methods in view of Section 2 of the Patent Act. Claim 1 reads:

> A non-medical method for detecting and localizing a tumor which produces or is associated with a cytoplasmic, intracellular or cell-surface marker substance, without medically treating said tumor, which method comprises one of the following procedures:
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> (a) injecting a subject parenterally with an antibody specific to a cell-surface marker and radiolabeled with a pharmacologically inert radioisotope capable of detection using a photoscanning device; concurrently injecting said subject with normal immunoglobulin from the same or different species as that used to prepare said specific antibody, said normal immunoglobulin being radiolabeled with a different pharmacologically inert radioisotope from that used to label the specific antibody and emitting at an energy capable of independent detection by said photoscanning device, said labeled normal immunoglobulin having substantially the same kinetics of binding, distribution and metabolism as the labeled specific antibody; and subsequently scanning the subject with said device, the level of activity of the labeled normal immunoglobulin being used to determine the distribution of background activity due to non-targeted specific antibody, said background distribution being subtracted from the total activity of specific antibody, whereby the activity and the location of substantially only the targeted tumor-associated antibody is determined; or
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> (b) injecting a subject parenterally with an antibody specific to CEA and radiolabeled with a pharmacologically inert radioisotope capable of detection using a photoscanning device and subsequently scanning the subject with said device to determine the location of the resultant uptake of said labeled antibody by said tumor; wherein said anti-CEA antibody is a substantially monospecific antibody having a CEA-specific immunoreactivity prior to labeling of at least 70% and a cross-reactivity to other antigens of less than 15%, said antibody being radiolabeled to an extent sufficient to reduce its CEA-specific immunoreactivity by from 5 to 33%; or
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> (c) injecting a subject parenterally with an antibody specific to an intracellular marker substance and radiolabeled with a pharmacologically inert radioisotope capable of detection using a photoscanning device, and subsequently scanning with said device to detect and locate the site or sites of uptake of said labeled antibody by said tumor; or
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> (d) injecting a subject parenterally with at least one marker-specific fragment obtained by cleavage of an antibody specific to a cytoplasmic, intracellular or cell-surface marker substance and radiolabeled with a

pharmacologically inert radioisotope capable of detection using a photoscanning device, and subsequently scanning with said device to detect and locate the site or sites of uptake of said labeled antibody fragment by said tumor; or

(e) injecting a subject parenterally with at least two marker-specific fragments, at least one fragment being a marker-specific fragment obtained by cleavage of a first antibody specific to a first tumor associated marker and at least one other fragment being a marker-specific fragment obtained by cleavage of a second antibody specific to a second tumor-associated marker, each of said at least two fragments being radiolabeled with a pharmacologically inert radioisotope capable of detection using a photoscanning device, and subsequently scanning with said device to detect and locate the site or sites of uptake of at least one of said labeled fragments by said at least one tumor; or

(f) injecting a subject parenterally with a multivalent hybrid containing in chemical combination at least one marker-specific fragment obtained by cleavage of an antibody specific to a first tumor-associated marker and at least a second, different marker-specific fragment obtained by cleavage of an antibody specific to the same or different tumor-associated marker, said hybrid being radiolabeled with a pharmacologically inert radioisotope capable of detection using a photoscanning device, and subsequently scanning with said device to detect and locate the site or sites of uptake of said labeled hybrid by said at least one type of tumor.

We look first to the application for an understanding of the invention. Certain substances are disclosed which are radiolabeled and have low intensity and are intended to be parenterally injected into bodies solely to enhance tumor localization and detection. Other kinds of radiolabeled isotopes that gather at tumors are described as having an effective strength that permits them to treat tumors. Several examples are given of the substances which have been radiolabeled, including a table of those that may be used for both detection and therapy. Mention is made of mixtures of radiolabeled antibodies specific to antigens that may enhance detection, localization, and/or therapy. Specifically it is stated that radiolabeled marker-specific antibodies or fragments provide tumor therapy. It is noted that antibodies having a high marker-specific immunoreactivity will generally be targeted at tumors, and that the therapeutic aspect of the invention makes use of highly marker-specific antibodies. Various radionuclides useful in certain concentrations for therapy are given.

Mr. Watson discusses the significance of the Supreme Court's decision in the Tennessee-Eastman case. He reasons that its decision establishes the law in dealing with subject matter similar to that of his client, not the statements from the lower Court that are interspersed in the Supreme Court's decision. From our reading of the Tennessee-Eastman case, we believe the Supreme Court, by commenting on the assessment by the Exchequer Court, did not express disfavor with those or other statements made by the lower Court. For example, the Supreme Court, 8 C.P.R. 2(d) page 204, includes a passage by Kerr J. given in the lower Court which reads, in part, as follows:

> ...The method lies essentially in the professional field of surgery and medical treatment of the human body, even although it may be applied at times by persons not in that field. Consequently, it is my conclusion that in the present state of the patent law of Canada and the scope of subject-matter for patent, as indicated by authoritative judgments that I have cited, the method is not an art or process or an improvement of an art or process within the meaning of s. 2(d) of the Patent Act.

We compare the above opinion to that expressed by Pigeon J. of the Supreme Court on page 207 as follows:

> Having come to the conclusion that methods of medical treatment are not contemplated in the definition of "invention" as a kind of "process", the same must, on the same basis, be true of a method of surgical treatment.

We see no diversion of opinions in the above passages. The findings by both Courts is that medical and surgical treatments do not merit patent protection under Section 2 of the Act which reads:

> "invention" means any new and useful art, process, machine, manufacture or composition of matter, or any new and useful improvement in any art, process, machine, manufacture or composition of matter;

Of particular interest as to how the Tennessee-Eastman case is viewed by the Federal Court is the recent case, Imperial Chemical Industries Ltd. v. Commissioner of Patents (1986) 9 C.P.R. (3d) 289, hereinafter ICI. On page 296 of ICI, Heald J. set out his understanding of Mr. Justice Pigeon's pronouncement, as follows:

> Coming now to the decision of the Supreme Court of Canada, Mr. Justice Pigeon delivered the Court's decision. He commences his reasons by setting out the agreed statement of facts and issues. At page 204 of the report, he reproduces, with approval, that portion of the reasons of Kerr J. set out supra. It is true that he does discuss the impact of Section 41, presumably since that case was a subsection 41(1) case. However, after that discussion, at page 207 of the report, he states:
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> > Having come to the conclusion that methods of medical treatment are not contemplated in the definition of "invention" as a kind of "process", the same must, on the same basis, be true of a method of surgical treatment.
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> In my opinion, this is a clear and unequivocal statement that "...methods of medical treatment are not contemplated in the definition of "invention" as a kind of "process...". That was the sole issue before the Court and it is here answered in unmistakeable and unambiguous language. Accordingly, in my view, the force of that pronouncement cannot be restricted merely to factual situations where subsection 41(1) of the Act applies. It follows, therefore, that the Commissioner did not err in considering himself bound by the ratio of Tennessee Eastman. (our emphasis)

Mr. Watson discusses other passages in the Tennessee Eastman case. Among them is that taken from the British decision in Re Schering, namely, "patents for medical treatment in the strict sense must be excluded", to which the Supreme Court added particular emphasis. He reasons that Court's assessment of Schering is that the administration of gestagen, an agent for contraception, although having an effect on body metabolism, would not be a therapeutic treatment of disease, and therefore would not be medical treatment in a strict sense.

Mr. Watson compares the Supreme Court's comments in the Tennessee Eastman case about Swift's application, to the Applicant's method of localizing tumors, by referring to the following passage from page 208:

> In the second place, what was actually decided in those cases is not related to a medical or surgical method. Swift's application dealt with a method of tenderizing meat by injecting enzymes into the animal before slaughtering.

Mr. Watson argues the Applicant's claimed method of localizing tumors is not directed to a medical treatment, just as Swift's method of injecting enzymes was held not to be directed to a medical treatment. He reasons that the Tennessee Eastman case indicates that in the absence of a therapeutic effect, the Applicant's method should not be considered a medical method.

We understand from the application that antibodies labeled with radioisotopes are injected into a body for the purpose of attaching themselves to antigens that are known to exist at a tumor site. At the discretion of the physician, the radioactive material injected may light up a tumor for detection by means of a photoscanning device, or, may react on the suspected tumor to reduce its size. Mr. Watson says the rejected claims present only a detection method whereas the claims cancelled by amendment B, such as original claim 69, are directed to therapy.

The Applicant discusses Burton-Parsons, supra, and its conclusion that the purpose of the conductive cream was "primarily and mainly for the taking of electrocardiograms in routine examinations, not necessarily or mainly in connection with treatment of disease".

Dr. Saxe thinks the rejected claims are directed to diagnostic methods and do not relate any treatment of a patient. He explains the antibody of the invention has two features, one, it binds to a specific antigen, two, it carries a special targeting vehicle, namely, a radioisotope. Such antigens, he continues, are known to be located on the surface of tumors in the body. The injected antibody circulates through the body, and on finding an antigen, binds thereto. The signal from the radioisotope

enables location by an exterior scanner. He considers the small amount of gamma radiation from the imaging isotopes has no therapeutic effect, and that if isotopes of iodine are used, their dosage would be small, thus providing only incidental beta radiation with negligible therapeutic action. The Applicant's method, he relates, is done as a prelude to treatment such as surgery. He says the method locates tumors that cannot be located by X-ray or Cat-Scans, for example those masked by organs, or, in the case where metastisis occurs, the method permits identification of the small tumors that have spread from the main tumor. He notes this is something that was not possible before the advent of nuclear medicine. He adds that, if the antibody finds no antigen, it is excreted and no imaging occurs.

When iodine 131 is used as a label for imaging body portions other than the thyroid, Dr. Saxe explains that something is added to the body to prevent takeup by the thyroid of iodine 131. A solution for this purpose is identified in the application as Lugol's solution. He notes the determination of the particular amount of each labeling agent is done by nuclear medicine physicians in clinical tests of various diagnostic agents. In this way, they classify the stability of the antibody, the stability of the label to stay on the antigen surface and not on other areas, the rate of disposal of the label by the human body so that proper imaging occurs, and the selective take up of the antibody during circulation and the effect of the label on tissue. He says the labeled antibodies are then usually administered by the surgical oncology or nuclear medicine departments of a hospital, since diagnosis and therapy may be involved.

Mr. Watson refers to the Commissioner's Decision on H. Brilliant's application number 880,719 published April 16, 1974 in the Patent Office Record. He notes the subject matter involved diagnostic techniques, and was accepted by the Commissioner (Patent 944,693 issued on April 2, 1974 to Brilliant). He likens the Applicant's method to that of the above application which was found to be controllable and reproducible. Dr. Saxe

points out in the Applicant's case that clinical trials establish the type and amount of the radiolabeled antibody that should be administered, based on the type of tumor. In this manner, Dr. Saxe says in his affidavit that the Applicant's results are controllable and reproducible, and that the non-invasive nature of the Applicant's method produces only diagnostic information.

Mr. Watson refers to the following Canadian patents, from the viewpoint they protect diagnostic methods. Patent 944,693 (to Brilliant, above) relates to applying fluorescent dyes on teeth, and Patent 1,087,981 relates to applying colored dyes on teeth, both to make visible any disease causing matter. Patent 1,071,102 relates a method for introducing polymeric coated particles having a radioactive ion exchange core into an animal's circulatory system and after sacrifice determining the location of the particles. Patent 1,075,154 describes a method of detecting tumors by applying a heat sensitive liquid to the skin, heating the area, and observing for color changes. Patent 1,075,601 presents a method of determining size and location of myocardial infarction by injecting into the blood stream a radiolabeled antibody and measuring emissions at the tissues where uptake occurs. Patent 1,171,952 relates to tumor detection using ultrasonic images to detect concentrations of circulated microbubbles in a suspected tumor area. Mr. Watson feels that where there is no therapeutic effect, an applicant is entitled to a patent.

The examiner considers that Applicant's method of injecting a patient with a substance having a radioactive material is part of an overall treatment performed under medical supervision. He reasons that a nuclear medicine physician by using the Applicant's method is engaged in a medical treatment of a patient and that only part of the regimen is to find where a tumor is, the remaining part being to prescribe the amount and type of radioisotope to be carried by the antibody once localization is determined. He refers to Imperial Chemical Industries Ltd. v. Commissioner of Patents C.P.R. (1967) Vol. 51 102 at 107, hereinafter ICI 1967, as follows:

> "Halothane" is not a medical drug or agent that cures per se, but instead is a medical drug or agent used in medicine in the treatment of patients and is an integral part of surgical therapy of disease, a part of a therapeutic regime.

He notes that halothane as an anaesthetic is not a diagnostic agent but as used is part of a medical treatment in that it produces insensitivity during treatment. For this reason, he regards the passage above as indicative that the Applicant's method forms part of the overall treatment of a patient.

We recall that Dr. Saxe discussed the significance of imaging dosages in the diagnostic steps in obtaining an identification of radiolabeled antibodies lodged in parts of a human body. He stresses that such dosages are known in advance by established testing to ensure that they behave in a predictable manner. From such available information his view is that no beneficial therapeutic results would be obtained. In this way, he points out, the imaging dose is designed to provide only a measurable signal in a diagnostic procedure. He argues that the term non medical treatment in the Applicant's claims points to the fact that an imaging dosage is all that is being defined.

Dr. Saxe says that the Applicant's method is clearly on the side of diagnosis, even though the diagnostic substance is an injectable. He suggests that to conclude that merely because something is injected into a patient's body and that therefore a therapeutic treatment results, is to blur the reasoning that should be brought to bear on the Applicant's case. He points out that the rejected claims are directed only to finding locations of tumors.

We believe that the Supreme court in the Tennessee Eastman case emphasized, by quoting from the Schering case, that patents for medical treatment in the strict sense must be excluded under the Patent Act.

In determining whether or not the Applicant's method is a diagnostic method and therefore patentable, we are unable to find, in reviewing the claims as they pertain to a non medical treatment using pharmacologically inert

substances within the context of the application, that they are directed to more than a diagnostic treatment.

In summary, we think the rejected claims may well be directed to a diagnostic treatment. We recommend therefore that the refusal of the claims be withdrawn for being directed to non patentable subject matter in view of Section 2 of the Patent Act.

M.G. Brown
Acting Chairman
Patent Appeal Board

S.D. Kot
Member

I have reviewed the findings and the recommendation of the Patent Appeal Board. Accordingly, I withdraw the refusal to grant a patent containing the claims of this application, and I remand the application for prosecution consistent with the recommendation.

J.H.A. Gariépy
Commissioner of Patents

dated at Hull, Quebec
this 13 day of May 1988