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660 Pennsylvania Ave SE Suite 302

Washington DC 20003

Telephone (202) 547-9359

Facsimile. (202) 547-9429

Assistant Commissioner for Patents
Mail Stop Inter-Partes Reexamination
PO Box 1450
Alexandria VA 22313-1450
February 25, 2004

In Re U.S. Patent No. US-6,444,872-B1

Dear Sir or Madam:

Reexamination under 35 U.S.C. §§ 311-318 and 37 CFR §§ 1.902-1.997 is respectfully requested of U.S. Patent No. 6,444,872 (issued on 03 Sept. 2002) to Borje S. Andersson, et al. It is believed that this patent is still within its period of enforceability. Requesters hereby certify that a copy of the request has been served in its entirety on the Patent Owner at the address provided for in § 1.33(c). The name and address of the party served is:

Fulbright & Jaworski LLP
600 Congress Avenue, Suite 2400
Austin, TX 78701

I. Requesters and Real Parties in Interest

The Requesters and the real parties in interest are: American Anti-Vivisection Society

(AAVS), a nonprofit corporation of Pennsylvania; and International Center for Technology Assessment/PatentWatch Project, a 501(c)(3) organization of Washington DC.

II. Certification Regarding Estoppel Provisions of 37 C.F.R. § 1.907

Third Party Requesters and all real parties in interest hereby certify that the estoppel provisions of 37 C.F.R. § 1.907 (2004) do not prohibit *inter partes* reexamination.

III. Claims for which reexamination is requested.

Reexamination is requested of claims 1-23 of the Andersson patent. This request is accompanied by payment of the government filing fee of \$8,800.

IV. Nomenclature for References

The reference hereafter to be referred to as “Ruthe”, is entitled “Experimental Granulocyte Transfusions in the Control of Systematic Candidiasis in the Leukopenic Host”, BLOOD, volume 52, #3, (September 1978), pp. 493-498.

The reference hereafter to be referred to as “Dagle”, is entitled “Atlas of Experimentally-Induced Neoplasia in Beagle Dogs”, and is Dep't of Energy Doc. # PNNL-11358, (G.E. Dagle, et al., eds., October 1996), and prepared for the U.S. Department of Energy under Contract DE-AC06-76RLO 1830 (pages i-viii).

The reference hereafter to be referred to as “Stedman”, is entitled “STEDMAN'S MEDICAL DICTIONARY, (25th Edition, 1990), Baltimore: Williams & Wilkins.

The reference hereafter to be referred to as “Tamburini”, is U.S. Patent No. 5,833,946, (issued 10 November 1998) and available as prior art by virtue of its U.S. filing date of 06 June 1995.

The reference hereafter to be referred to as “Schick”, is entitled “Experimental Lobar Pneumonia in Canine Lung Grafts”, SURGERY, Vol. 75, #3, pp. 348-356 (March 1974).

The reference hereafter to be referred to as “Reynolds”, is entitled “Changes in the Composition of Canine Respiratory Cells Obtained by Bronchial Lavage following Irradiation or

Drug Immunosuppression”, PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE, volume 151, pages 756-761 (1976).

The Venker-van-Haagen reference is from TIJDSCHRIFT VOOR DIERGENEESKUNDE, volume 116, Suppl. 1 (April 1991), page 34S.

The Weber reference is from EXP. HEMATOL., vol 13, pp. 791-795 (1985).

The Michaelson reference is entitled: Radiation Time-Intensity and Pathophysiologic Correlations in Whole and Partial-Body-X-irradiated Beagles, and is part of the “PROCEEDINGS OF A SYMPOSIUM ON DOSE RATE IN MAMMALIAN RADIATION BIOLOGY”, held April-May, 1968, edited by D.G. Brown et al., and published by the US Atomic Energy Commission as CONF-681410.

Springmeyer is "Alveolar Macrophage Kinetics and Function after Interruption of Canine Marrow Function", AM. REV. RESPIR. DIS., (1982), vol. 125, pp 347-351.

Morrison is "Non-Candida Fungal Infections After Bone Marrow Transplantation: Risk Factors and Outcome". AMERICAN JOURNAL OF MEDICINE, vol. 96, pp. 497-503 (June 1994).

Farrell is "Experimental Canine Histoplasmosis with Acute Fatal and Chronic Recovered Courses". AM. J. PATHOLOGY, col. 53, #3, pp. 425-446 (Sept. 1968).

Southard is "Bronchopulmonary Aspergillosis in a Dog", J. AM. VETERINARY MED. ASSOC., vol. 190, #7, pp. 875-877 (April 1987).

Spreadbury is "Invasive Aspergillosis: Clinical and Pathological Features of a New Animal Model". J. MED. AND VET. MYCOLOGY, vol. 27, pp. 5-15 (1989).

A copy of every reference relied upon to support the below-described Substantial New Questions of Patentability is herein enclosed and listed on Form PTO/SB/42.

V. Statement pointing out each substantial new question of patentability based on the cited printed publications, and a detailed explanation for every claim for which reexamination is requested.

Obviousness

Grounds 1. Claims 5, 13-15 and 18 are unpatentable under 35 U.S.C. §103(a) (2003) as being obvious to the person of ordinary skill in the art, in view of Ruthe, Dagle and Stedman.

Ruthe teaches a method for obtaining an alleged canine model for pulmonary fungal infection in an immunocompromised host, which method comprises the steps of:

- (a) obtaining a dog;
- (b) immunocompromising that dog by rendering it leukopenic; and
- (c) infecting said dog with a fungus, namely, *Candida albicans*.

In particular, these features are taught at page 494, second and third full paragraphs, wherein healthy dogs were obtained and rendered leukopenic by an single intravenous injection of cyclophosphamide (50 mg cyclophosphamide/kg body weight). The effect of this cyclophosphamide injection was to render the dog granulocytopenic, with a granulocyte count of less than about 500/mm³ (see page 493, column 1, lines 5-9).

Since the dog of Ruthe clearly has been rendered leukopenic as required by instant claim 13, and since instant claim 13 further limits the “immunocompromised” state required in the claim from which it depends, then the cyclophosphamide treatment of Ruthe falls squarely within the scope of “immunocompromising” recited in claim 5, by the tenets of claim construction.

Furthermore, Stedman teaches that “immunocompromised” is defined as “Denoting an individual whose immunologic mechanism is deficient either because of an immunodeficiency disorder or because it has been rendered so by immunosuppressive agents”. See page 766, column 2. Cyclophosphamide is an “immunosuppressive agent” within the scope of Patentee's disclosure (c.f., col. 19, line 1).

Additionally, please note that the instant specification contemplates a wide variety of modes of immunosuppression of the claimed dog, not just the specifically-exemplified combination of X-irradiation and steroids. See, e.g., instant column 18, lines 41-43: “However, other methods of immunosuppression are known in the art and may be employed to immunosuppress animals.” This would fairly suggest that any art-recognized means of achieving immunocompromise of a dog (such as the cyclophosphamide treatment taught by Ruthe), would be within the scope of instant claim 5. Note yet further that the instant specification contemplates achieving immunosuppression by any one of: (a) radiation alone (col. 18, line 45);

(b) chemical immunosuppression alone (col. 18, lines 64-65); and, importantly, (c) combinations of the foregoing (col. 19, lines 16-21). While it is a “preferred embodiment” of the Patent to achieve immunosuppression by irradiation followed by steroid administration, the claims are not to be construed as limited by a preferred embodiment.

Patent Owner's specification is not at all relied upon as a grounds of rejection, but merely as a “dictionary” for the breadth of the terms of the claims.¹

Note that the dog(s) of Ruthe infected with *Candida*, constitute an alleged canine model for *pulmonary* fungal infection (even though the mode of infection was intra venous), because autopsies of such infected, immunocompromised dogs shows lesions in the lung, as well as other organs. See Table 1 at page 495, experiment numbers 2, 4, 5 and 6 on “NT” dogs (*viz.*, dogs not transfused with granulocytes at a later time).

The sole difference between the method described in Ruthe, and the method steps required in instant claim 5, is that Ruthe does not teach the use of Beagle dogs.

Dagle discusses the use of Beagle dogs in research and states that “beagle dogs have been utilized extensively in biomedical research ... [and in] radiation studies”. Dagle further teaches that “reasons for choosing the beagle over other breeds of dogs included their convenient size, good disposition, and low natural incidence of bone tumors”. See page iii, lines 1-9.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made, to have employed Beagle dogs in the Ruthe method, in order for the researcher to garner the conveniences of their “convenient size” and “good disposition”, as taught by Dagle.

To the extent that it may be argued that the dog of Ruthe (as modified in view of Dagle), is not a “model” for “invasive pulmonary fungal infection”, please note that this stipulation appears only in the preamble of claim 5, and does not impart any method steps to the claim. This is not to say that the preamble is being ignored; however, the mere recitation of

¹ Markman v. Westview Instruments, 52 F.3d 967, 979, (Fed. Cir. 1995), 34 U.S.P.Q. 2d 1321, 1329-30 (rev'd en banc), aff'd, 517 U.S. 370 (1996) (stating: “For claim construction purposes, the description may act as a sort of dictionary, which explains the invention and may define terms used in the claims.”)

this term “invasive pulmonary”, without more, does not impart any structure to the claim. For instance, the Federal Circuit has provided guidance as to when to construe preamble language as a claim limitation: in STX, L.L.C. v. Brine Inc.², the court opined that “where a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention, the preamble is not a claim limitation”. In the case of a method claim, the “structure” is in the steps. Claim 5 has three method steps; it is a complete claim in that sense. Thus in the present case the preamble cannot provide added steps.³

Furthermore, claim 5 broadly states a step of “infecting said beagle with a fungus”, in some unspecified manner. It would be impermissible to import a limitation into this claim step from elsewhere; rather, the Examiner should give the term “infecting” its broadest reasonable interpretation consistent with the specification. In the instant case, the Ruthe reference teaches the formations and detection of colonies of *Candida* in the pulmonary tissue of the leukopenic dogs challenged with *Candida* (*vide supra*); thus they are “infected”. Note also that the instant specification does not choose to define “infecting” in any limited fashion.

In any event, the Examiner is respectfully requested to consider the hypothetical scenario where an alleged infringer of instant Patent claim 5 carries out all three of the steps of

2 211 F.3d 588 (Fed. Cir. 2000).

3See also Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc., 289 F.3d 801(Fed. Cir. 2002); 62 U.S.P.Q.2D (BNA) 1781 (2002): (stating "a preamble generally is not limiting when the claim body describes a structurally complete invention such that deletion of the preamble phrase does not affect the structure or steps of the claimed invention." ; c.f. IMS Tech., Inc. v. Haas Automation, Inc., 206 F.3d 1422, 1434, (Fed. Cir. 2000), 54 USPQ2d 1129, 1136-37 (preamble phrase "control apparatus" does not limit claim scope where it merely gives a name to the structurally complete invention). Thus, preamble language merely extolling benefits or features of the claimed invention does not limit the claim scope without clear reliance on those benefits or features as patentably significant; c.f., Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc., 246 F.3d 1368 (Fed. Cir. 2001) (steps of claimed method are performed the same way regardless of whether, as stated in the preamble, a reduction of hematologic toxicity occurs).

obtaining a Beagle dog; immunocompromising that Beagle; and then infecting him with a fungus. It would defy logic to think that such hypothetical alleged infringer would be able to evade a charge of infringement by the Patent Owner of at least claim 5, by virtue of having literally performed those three method steps.

Instant claim 14 specifies that “infecting is performed when the beagle has immunosuppression”.

This claim limitation is met by the reference of Ruthe (as modified in view of Dagle), because Ruthe injects dogs with cyclophosphamide; and then, after five days, the dogs are seen as being granulocytopenic (< 500 granulocytes/mm³ blood); and then on day 5 are challenged with yeast phase *Candida*. See page 494, lines 11-30 of the reference. Since Ruthe performs the *Candida* challenge at a time when the cyclophosphamide is still having an effect (and not when that effect has subsided), then it clearly constitutes a step of “infecting when the dog has immunosuppression”.

Instant claim 15 requires that “infecting is performed when the beagle has a neutrophil count of <about 400 per" microliter.

This claim limitation is met by the reference of Ruthe (as modified in view of Dagle), because Ruthe teaches (at its Figure 1 on page 495) that its “control dogs” actually have a granulocyte count of less than 250/mm³ on days 5, 6, 7, and 8. Stedman teaches (at page 1051, column 1) that by definition “neutrophil” cells are a subset of the class of cells termed “granulocytes”. Thus Ruthe fairly teaches performing infection when the dogs have a “neutrophil count of <about 400 per" microliter [note that a cubic millimeter is a microliter], and such would be recognized by the person having ordinary skill in the art, in view of the definition provided by Stedman.

Instant claim 18 requires “further comprising administering to the beagle a standard cancer therapy”.

This claim limitation is met by the reference of Ruthe (as modified in view of Dagle), because Ruthe injects the dogs with the alkylating agent, cyclophosphamide (vide supra). Note that the instant specification details a huge variety of agents which it considers to be “Cancer

Therapies” (from instant column 8, line 30 through instant column 18, lines 36); cyclophosphamide is specifically recited at instant col. 16, lines 47-53.

Patent Owner's specification is not at all relied upon as a grounds of rejection, but merely as a “dictionary” for the breadth of the terms of the claims.¹

Grounds 2. Claims 5, 13-15 and 18-21 are unpatentable under 35 U.S.C. §103(a) as being obvious to the person of ordinary skill in the art in view of the teaching of Ruthe, Dagle and Stedman, as already applied to claims 5, 13-15 and 18, and further in view of Tamburini.

All of the above-detailed arguments set forth above with respect to claims 5, 13-15 and 18 are hereby realleged and incorporated by reference.

Neither Ruthe nor Dagle appear to teach a step of “administering ..[an antifungal] agent to” the infected dog, then measuring and comparing symptoms of fungal infection in a dog treated with that agent with the symptoms of a dog not treated with that agent.

Tamburini teaches a method for identifying candidate medicaments which may be useful for preventing or treating infection by *Candida*, which comprises the following steps:

treating test and control groups of immunosuppressed mammals with a potential antifungal medicament, and with vehicle not containing that potential medicament, respectively;

administering to said test and control groups of mammals at least one *Candida* species;

monitoring for a biological response of said test and control groups of mammals to said treating and administering steps; and

comparing said biological response of said test and control groups of mammals over time. See col. 2, lines 40-60 of Tamburini. This reference is taken to fairly suggest, to the person of ordinary skill in art, that candidate antifungal medicaments can be identified by comparing symptoms of a mammal treated by the potential medicament with symptoms of one not so treated.

Thus, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to have administered an antifungal agent to the *Candida*-infected dog of Ruthe (as modified in view of Dagle and Stedman), then measuring and comparing symptoms of

fungal infection in a dog treated with that agent with the symptoms of a dog not treated with that agent, because:

Tamburini teaches that one can identify medicaments which are useful for preventing or treating infection by *Candida*, via the steps of treating test and control groups of immunosuppressed mammals with a potential antifungal medicament, and with vehicle not containing that potential medicament, respectively; administering to said test and control groups of mammals at least one *Candida* species; monitoring for a biological response of said test and control groups of mammals to said treating and administering steps; and comparing said biological response of said test and control groups of mammals over time.

The person of ordinary skill in the art would have expected that the method of the combined references, would result in one type of screening method for potential antifungal agents.

Instant claim 20 further requires that the antifungal agent “comprises a combination of pharmaceutical agents”.

However, please note the following teaching in Tamburini:

Tamburini teaches that the medicaments to be evaluated for antifungal activity, can be formulated to contain one, or more than one, “active ingredient(s)”. See column 5, lines 23-25 and column 5, line 36-37. This indicates that the process of Tamburini contemplates administering a medicament containing a combination of pharmaceutical agents, in order to test them for antifungal activity.

Thus it would have been obvious to have administered a combination of pharmaceutical agents to the alleged dog model of the heretofore combined references, because it is within the scope of Tamburini to do so, in order to test the efficacy of such combination as an antifungal agent.

Grounds 3. Claims 9-12 are unpatentable under 35 U.S.C. § 103(a) as being obvious to the person of ordinary skill in the art in view of the teaching of Ruthe, Dagle, Stedman and Tamburini, as already applied to claims 5, 13-15 and 18-21 , and further in view of Schick.

All of the above-detailed arguments set forth above with respect to claims 5, 13-15

and 18-21 are hereby realleged and incorporated by reference.

Method claims 9-12 specifically require that the canine be given a fungal infection at a pulmonary site (by means of, e.g., a bronchoscope); note that this is *not* required in method claims 5 and 19. The dogs of Ruthe are not initially given a fungal infection at a localized pulmonary site.

However, as noted above, Tamburini screens antifungal agents by providing “immunosuppressed mammals”, generically, and then infecting them with a fungus “via the airways”. See column 2, lines 40-55. Some non-limiting examples of airway administration include the intranasal mode and the intratracheal mode (see col. 7, lines 19-22 of Tamburini).

It would have been obvious to the person having ordinary skill in the art to have utilized the immunosuppressed dog of Ruthe (as modified in view of Dagle), in the airway-challenge process of Tamburini, because Tamburini requires an immunosuppressed mammal, generically, as a “model” against which to test antifungal medicaments, and because Ruthe teaches an alleged “canine model” of spontaneous fungal infections in leukopenic patients, which canine has been rendered immunosuppressed and susceptible to *Candida* infection.

Method claims 9-12 also specifically require that the canine be given a localized fungal infection at a pulmonary site by means of a bronchoscope. This is not taught or suggested by Ruthe or Tamburini.

Schick teaches a process for locally infecting the lungs of immunocompromised dogs with a micro-organism. The microorganism was a bacterium that caused pneumonia in the dogs. The dogs were first immunosuppressed with prednisolone, and then were infected via “transbronchoscopic injection of the inocula via 36 inch 18 gauge polyethylene catheters into the left lower bronchi”. The advantage of this mode of infection was that it induced a pneumonia in the dog that was amenable to therapy, without inducing sepsis. For all of these features, see: page 349, column 1, lines 3-9; page 349, column 2, lines 12-19; and page 354, column 2, first full paragraph. It would appear that the bronchoscope used in the Schick reference would be within the scope of the claimed “pediatric bronchoscope” (giving the latter term its broadest reasonable interpretation), since Schick's bronchoscope was small enough to fit deep down into the pulmonary tree of a dog, and a dog is usually of a size comparable to a human child.

It would have been obvious to the person having ordinary skill in the art to have performed the fungal airway challenge of an immunocompromised Beagle, (i.e., that which is suggested by the combination of Ruthe, Dagle and Tamburini, supra) with a pediatric bronchoscope, because Schick teaches (in an analogous method of inducing infection in an immunocompromised dog) that this mode of infection induces a pneumonia in the dog that was amenable to therapy, without inducing sepsis.

Grounds 4. Claims 6-7 are unpatentable under 35 U.S.C. §103(a) as being obvious to the person of ordinary skill in the art in view of Ruthe, Dagle and Stedman, as already applied to claims 5, 13-15 and 18 above, and further in view of Reynolds.

All of the above-detailed arguments set forth above with respect to claims 5, 13-15 and 18 are hereby realleged and incorporated by reference.

Ruthe does not teach that the state of leukopenia and neutropenia in the dogs was achieved through total-body-irradiation with “X-ray-cobalt irradiation”.

However, Reynolds teaches a method of immunosuppressing Beagle dogs by exposing them to 350 rad (3.5 Grey) of total body irradiation from cobalt-60 radiation sources. This radiation dose produced leukopenia but “without serious toxicity”. By 10-12 days after irradiation, the total white blood count was less than 100 cells/mm³. For these features, see page 756, column 1, last seven lines, through column 2, lines 1-5. A person with ordinary skill in this art would know from Stedman's Dictionary (definition of leukopenia at page 862 and definition of neutropenia at page 1051), that such a Beagle would be both leukopenic and neutropenic. The Reynolds reference furthermore teaches that its irradiation causes both “bone marrow suppression and prompt peripheral blood leukopenia” in the Beagle dog (see page 760, column 2, lines 6-9). The reference also teaches (at page 760, column 1, lines 15-18) that “the ability to mobilize granulocytes to the lung and other sites of acute infection is basic to the host's immunity”.

Note that, as mentioned supra, the Ruthe reference requires a dog that is both leukopenic and neutropenic, in order to induce a fungal infection in a dog. Furthermore, Ruthe teaches that transfusing granulocyte cells into a fungally infected dog significantly reduces the

number of fungal organisms infecting a leukopenic canine host as compared to a nontransfused one (page 497, lines 1-6).

Therefore it would have been obvious to have provided the irradiated Beagle dog of Reynolds for the combined process suggested by Ruthe taken in view of Dagle and Stedman's, because:

the Ruthe reference requires a dog that is both leukopenic and neutropenic, in order to induce a fungal infection in a dog,

and

Reynolds provides a Beagle dog in a state of being profoundly leukopenic and neutropenic with total white blood count less than 100 cells/mm³, which state is promptly induced.

Furthermore, the person of ordinary skill in this particular art would recognize the additional "advantage" to the practitioner in using dogs in a more profound state of granulocytopenia: namely, that the effect of Ruthe's granulocyte transfusions would be more pronounced; a deeper granulocytopenia more deeply requires a granulocyte transfusion.

Grounds 5. Claims 19 is unpatentable under 35 U.S.C. §103(a) (2003) as being obvious to the person of ordinary skill in the art, in view of Weber and Dagle.

Weber teaches a asserted method for evaluating ketoconazole as an antifungal agent for treating a fungal infection in an immunocompromised host, which comprises the steps of: providing an immunocompromised dog which has been irradiated with 800 rad and then further infected with a fungus of the Candida species; administering ketoconazole to that dog; and measuring the lifespan of that infected dog compared to the lifespan of a similarly immunocompromised dog not treated with ketoconazole. The above features are found in Weber at: page 791, col. 2, last full paragraph, and page 792, column 2, last nine lines; and page 794, col. 1, first three paragraphs. Note that the dog of Weber was immunocompromised to the point of leukopenia and neutropenia (page 794, col. 1, line 3).

Essentially the only difference between the steps taught by Weber and those required in instant claim 19, is that Weber did not provide a beagle variety of dog, but used mongrels instead.

Dagle discusses the use of Beagle dogs in research and states that “beagle dogs have been utilized extensively in biomedical research ... [and in] radiation studies”. Dagle further teaches that “reasons for choosing the beagle over other breeds of dogs included their convenient size, good disposition, and low natural incidence of bone tumors”. See page iii, lines 1-9.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made, to have employed Beagle dogs in the Weber method, in order for the researcher to garner the conveniences of their “convenient size” and “good disposition”, as taught by Dagle.

To the extent that it may be argued that the dog of Weber (as modified in view of Dagle), is not a “model” for “invasive pulmonary fungal infection”, please note that this stipulation appears only in the preamble of claim 19, and does not impart any method steps to the claim. This is not to say that the preamble is being ignored; however, the mere recitation of this term “pulmonary”, without more, does not necessarily impart any structure to the claim. As already noted above, the Federal Circuit has provided guidance as to when to construe preamble language as a claim limitation: in *STX, L.L.C. v. Brine Inc.* (*vide supra*), the court opined that “where a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention, the preamble is not a claim limitation”. In the case of a method claim, the “structure” is in the steps. Claim 19 has three method steps; it is a complete claim in that sense. Thus in the present case the preamble cannot provide added steps. Furthermore, claim 19 broadly requires a step of causing a beagle to be “infected” with a fungus, in some unspecified manner. It would be impermissible to import a limitation into this claim step from elsewhere; rather, the Examiner should give the term “infected” its broadest reasonable interpretation consistent with the specification. In the instant case, the Weber reference teaches the formations and detection of colonies of *Candida* in the tissues of the leukopenic dogs challenged with *Candida*; thus they are “infected”. Note also that the instant specification does not choose to define “infected” in any limited fashion.

Grounds 6. Claims 5, 13-15 and 18-23 are unpatentable under 35 U.S.C. §103(a) (2003) as being obvious to the person of ordinary skill in the art, in view of Tamburini, Ruthe, Dagle and

Michaelson.

Tamburini teaches an asserted method for identifying candidate medicaments which may be useful for preventing or treating infection by *Candida*, which comprises the following steps: immunosuppressing both a test group and a control group of mammals; administering to said test and control groups of mammals at least one *Candida* species, via the airways, to establish a pulmonary *Candida* infection; treating test and control groups of immunosuppressed mammals with a potential antifungal therapeutic medicament, and with vehicle not containing that potential medicament, respectively; monitoring for a biological response of said test and control groups of mammals to said treating and administering steps; and comparing said biological response of said test and control groups of mammals over time. See col. 2, lines 40-60 of Tamburini.

This reference is taken to fairly suggest, to the person of ordinary skill in art, that candidate antifungal therapies can allegedly be identified by comparing symptoms of an infected mammal treated by the potential therapy with symptoms of one not so treated.

The difference between the teachings of Tamburini and instant claim 19 is that Tamburini, although disclosing the use of all “mammals” generically as test subjects, does not disclose the use of beagle dogs as its test mammal.

Ruthe teaches a method for obtaining an alleged canine model for pulmonary fungal infection in an immunocompromised host, which method comprises the steps of: obtaining a dog; (b) immunocompromising that dog by rendering her leukopenic, with intravenous cyclophosphamide; and (c) infecting said dog with a fungus, namely, *Candida albicans*. These features are taught at page 494, second and third full paragraphs.

Note that the dog(s) of Ruthe infected with *Candida*, constitute an alleged canine model for pulmonary fungal infection (even though the mode of infection was intra venous), because autopsies of such infected, immunocompromised dogs shows lesions in the lung, as well as other organs. See Table 1 at page 495, experiment numbers 2, 4, 5 and 6 on “NT” dogs (viz., dogs not transfused with granulocytes at a later time).

Dagle discusses the use of Beagle dogs in research and states that “beagle dogs have

been utilized extensively in biomedical research ... [and in] radiation studies”. Dagle further teaches that “reasons for choosing the beagle over other breeds of dogs included their convenient size, good disposition, and low natural incidence of bone tumors”. See page iii, lines 1-9.

Michaelson teaches that “In respect to functional criteria, the dog is a more suitable subject than most laboratory animals, because more baseline information is available for this species. The longer life span, large body size, ease of clinical evaluation, and adaptability to laboratory conditions make observations on this animal most suitable for extrapolation to man.” See page 7.1, lines 20-25.

It would have been obvious to have utilized beagle dogs as the mammals in the above-described method of Tamburini since Tamburini teaches the use of a mammal, generically, as a “model” of pulmonary Candida infection, because Michaelson teaches that on a relative basis a “dog is a more suitable subject than most laboratory animals”, and because Ruthe teaches dogs for the purpose of being an alleged “model” of pulmonary Candida infection, and because among dog varieties, Dagle shows that beagles are of a size and disposition amenable to laboratory handling.

With respect to claim 20, note that Tamburini teaches that the medicaments to be evaluated for antifungal activity, can be formulated to contain one, or more than one, “active ingredient(s)”. See column 5, lines 23-25 and column 5, line 36-37. This indicates that the process of Tamburini contemplates administering a medicament containing a combination of pharmaceutical agents, and so it would have been well within the level of ordinary skill to administer a combination therapy.

With respect to claim 21, note that Tamburini contemplates the induction of immunosuppression by any one of a variety of myelosuppressive alkylating agents such as cyclophosphamide or 5-fluoro-uracil, which are also known to standard anticancer therapies (see discussion of instant patent *supra*).

With respect to claim 22, note that Tamburini teaches that the set of adverse biological effects to look for when comparing whether a potential medicament is effective, include fever, wasting, loss of cognition, and loss of organ function, which appear to fairly teach or suggest the list of expected symptoms attendant to a pulmonary fungal infection in an

immunocompromised host. See column 4, lines 33-39 of Tamburini. It would have been obvious to have expected that an immunocompromised host having a pulmonary fungal infection would manifest a loss of appetite, depression, and changes in chest x-rays, since Tamburini teaches that the set of adverse biological effects in such an unfortunate animal includes wasting, loss of cognition, and loss of organ function. With respect to claim 23, note that Tamburini teaches that a set of animals to be used as "toxicity controls" should be established, wherein such animals are treated with drugs but are not infected. These "toxicity controls" were weighed daily over the duration of treatment with drugs. See column 13, lines 1-5.

With respect to claim 5, it appears that these steps would be fully met by the proposed combination of references set forth above. With respect to claim 15, note that Ruthe teaches (at its Figure 1 on page 495) immunocompromised dogs having a granulocyte count of less than 250/mm³ on days 5, 6, 7, and 8. With respect to claim 18, see discussion of claim 21 immediately above.

Grounds 7. Claims 1-8, 13-14 and 16-18 are unpatentable under 35 U.S.C. §103(a) as being obvious to the person of ordinary skill in the art in view of Springmeyer, Morrison, Farrell, Southard, Spreadbury and Venker-van-Haagen.

Springmeyer teaches a Beagle dog which is rendered profoundly immunocompromised through total body irradiation (TBI). This Beagle was given a dose of 9.0-9.5 Grey of TBI from Co-60 sources, and thus was rendered pancytopenic for a 1 to 2 week period. (See page 347, col. 2, lines 4-27).

The reference describes this dog as being a "model of marrow transplantation for pulmonary studies"; that is, in the view of its authors this dog is a "model" for human patients who receive bone marrow transplantation (BMT) who develop opportunistic pulmonary infection (see page 347, col. 1, lines 26-38). The reference also describes the dog as being an "animal model for studying alterations in the lung associated with marrow transplantation"; that is, in the view of its author the lungs of the irradiated dog are a "model" for the lung of human BMT patients (see page 351, col. 1, lines 20-23).

Other features of this dog is that the number of protective alveolar macrophage cells

in the lungs of the irradiated dog are reduced by 50%, by virtue of him having been irradiated. This is measured via bronchoalveolar lavage of the lungs of the dog (see page 350, sentence bridging col. 1 and col. 2). The reference notes that a decline in the number of alveolar macrophages is a factor that increases the susceptibility of hosts to opportunistic infections (page 351, col. 1, lines 5-9).

This dog differs from instant claim 1 in that he is not disclosed to have an opportunistic invasive pulmonary fungal infection.

Morrison teaches that in humans who have undergone BMT, invasive fungal infections by opportunistic species are a major cause of morbidity (see page 497, 1st two full paragraphs). These fungal species include *Aspergillus* and *Histoplasma* (see page 498, Table II). 95% of these invasive infections involve the respiratory tract (page 499, col.2 , lines 7-9). Morrison concludes that there is only sparse clinical data comparing the efficacy of various fungal agents for fungi less common than *Aspergillus*, and moreover newer triazole antifungal agents do not appear to have been studied at all against invasive pulmonary fungal infections (page 502, col. 2, last paragraph). Thus this reference suggests a need in the art to test newer antifungal agents against fungi which cause invasive pulmonary fungal infections.

Farrell teaches the establishment of an experimental invasive pulmonary fungal infection in a dog, which dog has been immunocompromised by daily administration of 100 mg of cortisone acetate for 16 days (see page 425, lines 12-16 and page 426, lines 1-7). On the fourth day following the immunocompromise, infection was performed by intra-tracheally inoculating the dog to fungal growth (of *Histoplasma*). Acute pulmonary fungal disease developed in the dogs (page 427, last 3 lines), and such inoculated, immunocompromised dogs died 18-24 days after infection (page 428, lines 4-7). The disease can be considered to have been "invasive" since, after the initial airway inoculation by fungus, actual fungal culture was detected in blood upon autopsy; it appears that fungus traveling into the lung and then through the lung into the blood, would constitute an "invasive" disease by any standard, since the body was invaded. In any event, since the dogs died due to the fact that their bodies were overwhelmed with pulmonary histoplasmosis, provides another reason why their infection can be considered "invasive".

The Venker-van-Haagen reference teaches that the use of immunosuppressive

treatments on dogs (and immunodeficiency of dogs in general) increases the susceptibility of dogs to succumb to *Aspergillus* infection. See page 34S, lines 24-30. Southard is relied upon to show that even a dog which has *not* been experimentally immunocompromised can develop invasive pulmonary aspergillosis. In this case, a dog developed both the colonizing and invasive forms of pulmonary aspergillosis (see page 877, col. 1, 2nd full paragraph). Thus the Southard and Venker-van-Haagen references are evidence of a reasonable expectation of success for any experimental infection of an immunocompromised dog with *Aspergillus* via the airways.

Spreadbury teaches an alleged animal "model" for invasive aspergillosis, comprising an immunocompromised rabbit which has been inoculated intratracheally with *Aspergillus fumigatus*. The animal was immunosuppressed and then infected by being injected with 1 mL of an inoculum of *A. fumigatus*, through a catheter in the animal's trachea, (pg. 6, lines 5-28), and thus given an invasive pulmonary aspergillosis infection. The purpose of this "model" is to provide an opportunity to make quantitative comparisons in the efficacy of antifungal agents for invasive aspergillosis (see pg. 14, last full paragraph).

Thus, in order to provide an opportunity to compare the efficacy of antifungal agents against invasive aspergillosis in the very specific case of *BMT (bone marrow transplantation) patients*, the following would have been obvious to any person having ordinary skill in the art area of invasive pulmonary fungal infections who believes in the use of animals as "models".

It would have been obvious (to those persons of ordinary skill in the art who consider animals as appropriate models for humans) to have taken the profoundly immunocompromised Beagle dog of Springmeyer, and to have infected his lungs with an inoculum of *Aspergillus*, as taught by Spreadbury:

because Morrison teaches that in human BMT patients, invasive pulmonary aspergillosis is a major cause of morbidity; and moreover newer triazole antifungal agents do not appear to have been studied at all against invasive pulmonary fungal infections; and

because Springmeyer states that its Beagle dog already is an "animal model for studying alterations in the lung associated with marrow transplantation"; and

because Farrell teaches that an analogous experimental invasive pulmonary fungal infection can be established in an immunocompromised dog; and

because Spreadbury teaches that what are called "animal models" of invasive aspergillosis provide the opportunity to test the efficacy of various antifungal agents. The expected result of this infection of Springmeyer's Beagle dog with the intratracheal *Aspergillus* inoculum of Spreadbury, would have been that it would develop and present symptoms of invasive pulmonary aspergillosis, as shown by Southard to occur in even a normal, nonimpaired dog and such condition would be expected to be exacerbated in any immunosuppressed dog, as shown by Venker-van-Haagen. Expected results are evidence of obviousness; see In re Skoner,⁴ While the prior art also generally teach the use of small animals as testing "models" for invasive aspergillosis in the immunocompromised host, none of these animals would be considered "models" for bone marrow transplantation hosts as beagles are alleged to be. This, then, is the motivation for making the proposed combination of references.

It is noted that a fair number of references have been used to prove obviousness against certain of the claims. It would be error to focus on the number of references. Reliance on a large number of references in a rejection does not of itself weigh against the combination thereof: see In re Gorman⁵ (in Gorman, the Court affirmed a rejection of a detailed claim based on thirteen prior art references). In fact, the number of references that may be combined is theoretically infinite: see Ex parte Fine⁶.

Lack of Statutory Subject Matter

Grounds 8. Claims 1-4 lack statutory subject matter under 35 U.S.C. §101 in view of evidence that the person of ordinary skill in the art would reasonably doubt that the claimed "beagle dog", as a whole, is a "machine", "manufacture", or "composition of matter". The evidence is in the form of the following prior art printed publications: the Leesti reference, and the Nadon reference.

The Leesti reference⁷ pertains to the question of whether or not non-human mammals

⁴In re Skoner, 517 F.2d 947, 950 (C.C.P.A. 1975), 186 U.S.P.Q. 80, 82 (1975).

⁵In re Gorman, 933 F.2d 982, 986 (Fed. Cir. 1991), 18 U.S.P.Q.2d 1885, 1888 (1991).

⁶Ex parte Fine, 1927 Dec. Comm'r Pats. 84, 86 (1927).

⁷The Leesti reference is a decision of the Commissioner of Patents of Canada,

are directed to patentable subject matter, and in this context patentable subject matter is defined as: "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." See page 3, lines 9-16 of Leesti (using page numbering from printed document itself). The Leesti reference is reasonably pertinent to the subject matter which Patentee claims, which is also directed to a type of nonhuman mammal; thus Leesti is *pertinent* prior art.

The relevant teaching of Leesti is as follows: "However I cannot extend the meaning of 'manufacture' or 'composition of matter' to include a non-human mammal. On the plain and ordinary meaning of the words ...I do not find that a non-human mammal ...falls within the definition of" 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. See page 7, lines 10-18.

The person having ordinary skill in the art, in view of the Leesti reference, would have reasonable doubt that the subject matter of instant claim 1-4, *as a whole*, constitutes statutory subject matter under 35 U.S.C. §101, because Leesti teaches that a non-human mammal does not fall within the definition of machine, manufacture, or composition of matter based upon the plain and ordinary meaning of the words, and because the claimed Beagle is a nonhuman mammal.

Similarly, the Nadon reference⁸ also pertains to the question of whether or not non-human mammals are directed to patentable subject matter, and in this context patentable subject matter is defined as: "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." That is the language used in the Canadian Patent Act⁹, and is essentially identical to the words of 35 U.S.C. §101 (2003).

available at http://patents1.ic.gc.ca/details_comdec?comdec_number=1203&n=0&p=0&t=0&l=E or <http://tinyurl.com/2fuch> , both last accessed 2-18-2004. Date made public: 04 August 1995.

⁸Harv. Coll. v. Canada (Comm'r of Patents), [1998] 3 F.C. 510. (Can.), Fed. Court of Can. Trial Div., Nadon, Judge. Date made public: April 21, 1998.
⁹R.S.C. 1985, §2 (2003)(Can.)

The following are direct quotes from the Nadon publication:

"A complex life form does not fit within the current parameters of the Patent Act without stretching the meaning of the words to the breaking point."

"On even the broadest interpretation I cannot find that a mouse is 'raw material' which was given new qualities from the inventor."

"... [S]uch a mouse 'cannot really be said, other than on the most metaphorical level, to have been produced from raw materials or to be a combination of two or more substances united by chemical or mechanical means' ". See page 110, lines 26-28; page 112, lines 34-40; and page 114, last two lines, through page 115, 1st line.

The person having ordinary skill in the art, in view of the Nadon reference, would have reasonable doubt that the subject matter of instant claim 1-4, *as a whole*, constitutes statutory subject matter under 35 U.S.C. §101, because Nadon teaches that a complex life form does not fall within the definition of machine, manufacture, or composition of matter based upon the plain and ordinary meaning of the words, and because the claimed Beagle is a complex life form.

Furthermore, there is evidence already of record further establishing that the claimed Beagle dogs are complex life forms and thus not mere manufactures or any inventor's composition of matter. This evidence is found in Patentee's admission at Table I of the Patent. There, Patentees admit that the following two dogs, within the scope of the claims, had "**severe depression**" (2991152 and 2917289). Further admissions are the following: six dogs were characterized as being "**depressed**" (2856721, 2869349, 2705583, 2867192, 2909944, and 2905183); one dog was characterized as being "**moderately depressed**" (2940141); and one dog was characterized as being "**slightly depressed**" (2911892).

Since the examiner is charged with evaluating whether the claims, *as a whole*, constitute patentable subject matter, he/she should look to the record to see what is the character of the claimed dogs. These dogs admittedly suffer from "depression", a mental condition of sentient, self-aware beings; no article of manufacture (e.g., a toaster) or mere inventor's composition of matter (e.g., a vitamin pill) can be characterized as such.

Remarks Pertaining to Scope of Reexamination

It is noted that the following is found in MPEP 2258, relating to the "scope of reexamination":

"Rejections will not be based on matters other than patents or printed publications, such as public use or sale, inventorship, 35 U.S.C. 101, fraud, etc. In this regard, see In re Lanham, 1 USPQ2d 1877 (Comm'r Pat. 1986), and Stewart Systems v. Comm'r of Patents and Trademarks, 1 USPQ2d 1879 (E.D. Va. 1986). A rejection on prior public use or sale, insufficiency of disclosure, etc., cannot be made even if it relies on a prior patent or printed publication. Prior patents or printed publications must be applied under an appropriate portion of 35 U.S.C. 102 and/or 103 when making a rejection."

However, the decisions said to underlie this MPEP section can easily be distinguished from the case at hand. In the case of Stewart Systems, the matter upon which a reexamination could not proceed, was the matter of "fraud". This matter could not be dealt with in a reexamination proceeding since it is not based upon prior art printed publications; moreover the USPTO is not suited to consider issues of fraud during reexamination. The Patent and Trademark Office does not conduct evidentiary hearings in connection with the proceedings, and would not be able to observe the demeanor of witnesses or hear testimony in determining whether fraud had occurred. None of these considerations are present in the case at hand. The Director is not being asked to review a charge of "fraud", but, rather, to review a Substantial New Question of Patentability based solely upon evidence presented in the form of prior art printed publications, and nothing else. No hearing or testimony is required to determine what the prior art printed publications of record mean. Similarly the case of Lanham (noted in MPEP 2258 *supra*) can be easily distinguished, since that case, too, concerned an issue of "fraud" being raised in a reexamination proceeding. Since the "fraud" issue which was raised in Lanham, was not based upon "prior art consisting of patent or printed publication", it was clearly outside of the proper scope. No issues of fraud or inequitable conduct are raised or are going to be raised in this present *inter partes* reexamination request.

Furthermore, Stewart Systems, goes beyond merely excluding "fraud" issues from the scope of reexamination; it positively *includes* issues of "double patenting". Although sometimes confused with §§ 102 and 103 of the Patent Act, double patenting is firmly rooted in §101 of the Patent Act. According to In re Lonardo,¹⁰ " 'Same invention' double patenting is based upon 35 U.S.C. § 101 (1994), which states that an inventor may obtain 'a patent' for an invention."

The reason given (in Stewart) as to why an issue under Section 101 (namely, double patenting) *can* be entertained in a Reexamination, was the following: "Double patenting is necessarily based on a U.S. patent". Thus, it is the *type* of evidence presented, and not how that evidence is used, which is what controls what issues may be within the scope of a reexamination. MPEP section 2258 is not fully supported by the case law said to underlie it.

In any event the position of MPEP 2258 (that Section 101 issues are allegedly outside the "scope of reexamination") is not reflected in the statute itself, nor even in any duly promulgated rule. While 37 C.F.R. §1.906(a) (2004) recites that "[c]laims in an inter partes reexamination proceeding will be examined on the basis of patents or printed publications", this does not preclude treatment of an issue under 35 U.S.C. §101 that is based upon printed publications. The Examiner may safely admit this grounds of rejection into Reexamination proceedings without fear of contravening any rule or law.

Compliance with §101 May Depend Upon Underlying Facts

Please see the decision of the Board of Patent Appeals and Interferences entitled Ex parte Bhide et al.,¹¹ Bhide appears to conclude that certain printed publications could be used to show the "sufficiency or insufficiency [under 101] of applicants' specification because each was published prior to the date applicants". The prior art printed publications of record in that case actually called into question whether the claims had patentable "utility" under 35 U.S.C. 101.

This would appear to indicate that sufficiency of a claim under Section 101 *depends upon which printed publications are on the record*.¹²

¹⁰ 119 F.3d 960 (Fed. Cir. 1997), 43 U.S.P.Q.2d (B.N.A.) 1262 (1997).

¹¹ 42 U.S.P.Q.2d 1441 (Bd. Pat. App. & Int. 1996) (decision entered 31 January 1996, which has been designated as "binding precedent").

¹²It is understood that Section 101 has several distinct prongs, including

Even more on point, the Federal Circuit in 1992 noted that "Whether a claim is directed to statutory subject matter is a question of law." However, they also recognized the fact that it may also be an evidentiary question, remarking that "[D]etermination of this question may require findings of underlying facts specific to the particular subject matter and its mode of claiming ...". See Arrhythmia Research Technology v Corazonix Corp.¹³.

Requesters are simply calling into question whether some of the Patent claims are of patentable "subject matter", again based upon evidence presented in the form of prior art printed publications.

Legislative Intent of Reexamination Statute Circumscribes Scope Only in Terms of Type of Evidence Proffered

The legislative intent behind Reexamination Statutes also supports Requesters:

"The legislative history indicates that considerations such as cost and availability of evidence were among the criteria Congress considered in determining the scope of reexamination. ... [T]he purpose in restricting reexamination to printed documents 'was to provide a cheaper and less time-consuming alternative way to challenge patent validity on certain issues'. A patent is clearly the type of evidence that Congress intended the PTO to consider during reexamination, and the cost of examination is not significantly increased by having the PTO consider the ground of double patenting, as it involves issues of claim identity and obviousness, well within the PTO's everyday expertise." See In re Lonardo, *vide supra*.

Based on the legislative intent, a printed publication, like a patent, is clearly the type of evidence that Congress intended the PTO to consider during reexamination (as long as it is

utility, statutory subject matter, and the prohibition against double patenting; Requester has not confused these prongs. However, it is only logical to conclude that if reexamination can proceed to decide one prong or another of §101 (as in Lonardo and Stewart, *supra*), then that would appear to indicate that there is no statutory reason why reexamination cannot decide any prong of §101, as long as the evidence proffered during the reexamination proceeding is limited to prior art consisting of patents and printed publications.

¹³Arrhythmia Research Technology v. Corazonix Corp., 958 F.2d 1053 (Fed. Cir. 1992), 22 U.S.P.Q.2d (B.N.A.) 1033 (1992).

prior art relative to the claim in question), by the plain language of the statute. Furthermore, it is well within the "PTO's everyday expertise" to determine whether a claim is statutory subject matter. It is respectfully submitted that any Primary Examiner, when presented with a claim directed to a law of nature or to an abstract mathematical formula, has the expertise to decide whether such claim is statutory subject matter. A plethora of decisions of the BPAI exist which have grappled with questions of whether claims satisfy Section 101 of the Patent Act. On the contrary, the MPEP explicitly forbids examiners from ever entertaining questions of fraud, c.f. M.P.E.P. 2010, so understandably issues of fraud are always outside of "PTO's everyday expertise".

There is no prior art evidence of record indicating that a "beagle dog" positively is a "manufacture" or "composition of matter". Neither the Leesti reference nor the Nadon reference¹⁴ were made "of record" by the Examiner when the subject Patent was issued, and there is no reason to believe that the Examiner had considered either reference. This Request gives the Examiner, for the first time, a chance to benefit from the evidence set forth in those references. The Examiner may then proffer evidence of his/her own.

Printed Court Decisions Are Evidence

It may appear incongruous to view printed publications comprising Court decisions as constituting "prior art". It is the respectful view of Requesters that this is simply not the case.

¹⁴Although the Nadon reference did not come down from a U.S. Court, nonetheless the MPEP explicitly authorizes Examiners to consider results of foreign courts when deciding whether to grant reexamination requests. See MPEP 2242, section entitled "POLICY IN SPECIFIC SITUATIONS", part D. This section indicates that: "if a foreign patent office or a foreign court has used the same or substantially identical prior art to reject or invalidate the same or similar claims, this would be considered as being **controlling** in making the determination." In the present case, both a foreign patent office and a foreign court (Canada in both cases) have used the same documents as are being applied herewith in order to invalidate similar claims, so this should be considered controlling in making the determination.

Requesters' agent has performed a cursory search of the USPTO patent database, and has verified at least 64 issued US patents¹⁵ which have, in their listing of prior art on the face of the patent, one or more legal decisions such as BPAI decisions, CCPA decisions, and European Patent Office decisions. Patent Examiners often are faced with Court decisions and Board decisions as evidence "on the record", and they know what to do with those decisions in making patentability determinations under Sections 101, 102, 103 and 112. The instant Request is no different. The evidence is presented in a properly limited fashion (i.e., in the form of a prior printed publication), and that is all which is required by 35 U.S.C. §§311-313.

Binding Precedents Distinguishable

Requesters note two precedential decisions, Diamond v. Chakrabarty¹⁶ (Sup. Ct.) and Ex parte Allen¹⁷ (B.P.A.I.).

In Chakrabarty the Supreme Court concluded (from the Committee Reports accompanying the Patent Act of 1952¹⁸) that Congress intended statutory subject matter to "include anything under the sun that is made by man." However, that decision is distinguishable since there are new material facts now which were not present in that case. Firstly, Chakrabarty revolved around whether a bacterium (in which oil-degrading plasmids were rearranged) was statutory subject matter; it did not concern a Beagle dog or any other higher life form. The patentability of any animal was never raised in argument nor discussed in the opinion of the Chakrabarty Court. Questions which merely lurk in the record, neither brought to the attention of the court nor ruled upon, should not be considered as having been "decided". Any holding that is only implicit or assumed in the decision, but not announced, is not the same as deciding whether a "Man's best friend" is a mere article of manufacture or chemical composition.

¹⁵Requesters' Agent would be happy to supply a copy of the face of each of those 64 patents, upon request. One may independently verify this by searching the USPTO internet patent database with search terms such as "OREF/parte or OREF/uspq".

¹⁶Diamond, Commissioner of Patents and Trademarks v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (Sup. Ct., 1980).

¹⁷ 2 U.S.P.Q.2d 1425 (P.T.O. B.P.A.I. 1987).

¹⁸S. Rep. No. 1979, 82d Cong., 2d Sess., 5 (1952).

Secondly the quote from the Committee Report (*supra*) refers to "anything"; the word "anything" is a contraction of "any thing". A Beagle dog is never just a "thing", and so this quote is inapplicable to the facts. Thirdly, it is also noted that the 1952 Senate Committee Report is entirely silent on the term "composition of matter". (Inspection would reveal this to be so.) In the face of silence in the legislative history as to the breadth of "composition of matter", one ought to be reluctant to interpret it broadly. See Dewsnup v. Timm¹⁹.

In Ex parte Allen,²⁰ an oyster in which chromosomal polyploidy was induced, was held to constitute statutory subject matter. However, the facts here are distinguishable for at least the following reasons: Allen concerned an oyster, while the present case concerns a dog, an animal with a large brain, feelings, sentience, self-awareness and intelligence. It is respectfully submitted that these are material differences that cannot be ignored. Also, Allen's oyster was manipulated in a systemic, genome-wide, permanent way while Beagle is merely treated to damage him in some way; such damage can even be temporary (animals within the scope of the claim can actually recover on occasion). The Rule of Allen is presumably that "subject matter made by man" is statutory under 35 U.S.C. §101. However, Patentee did not "make" a Beagle: they **procured** him. Later, they treated him. The Beagle, when a newborn puppy, presumably was "made" in the natural fashion, by nonhuman forces.

If any precedential decision covers the facts at hand more closely, it is American Fruit Growers, Inc. v. Brogdex Co.²¹. There, the Supreme Court, in deciding whether an orange with a rind coated with preservative was statutory subject matter, essentially held that *not everything touched by man rises to the level of manufacture*. "Addition of borax to the rind of natural fruit does not produce from the raw material an article for use which possesses a new or distinctive form, quality, or property. The added substance only protects the natural article against deterioration by inhibiting development of extraneous spores upon the rind. There is no change in the name, appearance, or general character of the fruit. It remains a fresh orange, fit only for the same beneficial uses as theretofore." See Brogdex at 12.

In like manner, a Beagle inoculated with fungi is not statutory subject matter, since he

¹⁹Dewsnup v. Timm, 502 U.S. 410 (1992).

²⁰Ex Parte Allen, 2 U.S.P.Q.2d 1425 (PTO B.P.A.I. 1987)

²¹283 U.S. 1, 8 U.S.P.Q. 131 (1931).

remains a product of nature; the fungal treatment does not change any of his essential characteristics. He was a dog to start with; and remains a dog with no new essential characteristics (the untreated dog was susceptible to infection; and the treated dog has manifest susceptibility to infection). Unlike the Allen oyster where the "new" oyster had an essential characteristic that the "old" oyster did not (inherent sterility), this Beagle remains a dog, a nonmanufacture; a non-composition of matter.

Brogdex is not some isolated decision. The Court of Customs and Patent Appeals (the predecessor court to the Federal Circuit, which court sat in banc for every case) twice held that not everything touched by man is a manufacture. In re McKee²² concerned an animal carcass treated in a creative way. Still, they held that a "carcass is not a 'manufacture' as the term is employed in Sec. 4886 R. S. and as defined in the Century Dictionary. The addition of branding marks beneath the fell does not produce from the raw material (carcass) an article for use which possesses a new or distinctive form, quality or property." Similarly In re Ewald²³ held that a pear, cored in a particularly inventive way, was not statutory subject matter: "A cored half pear is merely a half pear with the inedible portion thereof removed. It, obviously, is not a new and different article, having a new name, character, or use."

A sick dog is still a dog.

Although it may appear to some that Requesters are going over the ground well-trod in Chakrabarty, please note that Requesters are not proposing that a Beagle dog is not patentable solely because he is alive; rather, Requesters respectfully submit that he is a complex life form, a friend to millions, and never fit to be categorized as mere manufacture or inventor's composition of matter.

International Preliminary Examination Report Confirms Reasonableness of Request

It is the view of Requesters that the opinion of the EPO examiner made during International Preliminary Examination confirms the reasonableness of the arguments made herein.

²²In re McKee, 75 F.2d 991 (C.C.P.A. 1935) .

Preliminary Examination of PCT Publication WO/00/22895 was conducted in 2001. This Publication is the equivalent to the patent for which Requesters are requesting reexamination. On 05 November 2001, the Examiner (G. Hillenbrand) from the European Patent Office issued an opinion stating: "the ISEA is not able to see an inventive activity in the selection of a further animal, like a beagle dog, for the design of a further model system of invasive pulmonary aspergillosis ...". In European patent parlance, lack of "inventive activity" equates to a determination that the claims are obvious. Examiner Hillebrand also noted that there is a "question of whether the claimed treatment of beagle dogs is contrary to public order or morality". In US patent law, issues of public order or morality are handled under 35 USC 101, so essentially the EPO examiner is confirming (or at least raising the question) of whether the claims satisfy 35 USC 101.

For all of the foregoing reasons, Reexamination of all the claims of the above-captioned Patent is respectfully requested.

Very respectfully submitted,
Peter T. DiMauro, Ph.D.

Agent for real parties in interest
Reg. Pat. Agent # 47,323
PatentWatch Project/International Center for Technology Assessment
660 Pennsylvania Ave SE, Suite 302
Washington DC 20003
202-547-9359, extension 19 (phone)
202-547-9429 (FAX)

²³In re Ewald, 129 F.2d 340 (C.C.P.A. 1942).