

THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today  
(1) was not written for publication in a law journal and  
(2) is not binding precedent of the Board.

Paper No. 18

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

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Ex parte JOHN N. BERG

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Appeal No. 93-3114  
Application 07/825,465<sup>1</sup>

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ON BRIEF

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Before GRON, Administrative Patent Judge,  
McKELVEY, Senior Administrative Patent Judge, and  
WEIMAR, Administrative Patent Judge.

GRON, Administrative Patent Judge.

DECISION ON APPEAL UNDER 35 U.S.C. § 134

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<sup>1</sup> Application for patent filed January 24, 1992.  
According to applicant, this application is a continuation  
of Application 07/534,894, filed June 7, 1990, abandoned.

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This is an appeal from an examiner's rejections of Claims 1-8, all claims pending in this application. Claims 1-8 stand finally rejected under 35 U.S.C. § 102(b) as drawn to a process which purportedly is described by Maas, Synthea (Maas), "The Immune Responses of Mice and Cattle to Fusobacterium Necrophorum," A Dissertation Presented to the Faculty of the Graduate School, University of Missouri-Columbia, Berg, John N, Dissertation Supervisor, pages 1-215, August 1986.<sup>2</sup> Claims 1-8 stand finally rejected under 35 U.S.C. § 102(f) as drawn to a process which John N. Berg did not himself invent. Claims 1-8 also stand finally rejected under 35 U.S.C. § 103 as unpatentable over the combined teachings of Abe et al. (Abe), "Immunization of Mice Against *Fusobacterium necrophorum* Infection by Parenteral or Oral Administration of Vaccine," American Journal of Veterinary Research, Vol. 39, No. 1, pp. 115-118 (January 1978); Nelson, U.S. 4,789,544, patented December 6, 1988; and Adam, U.S. 4,061,751, patented December 6, 1977.

All claims stand or fall together (Appeal Brief, p. 4;

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<sup>2</sup> Appellant does not contest the examiner's holding that Maas is prior art under 35 U.S.C. § 102(b).

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Examiner's Answer, p.3). Representative Claim 1 reads:

1. A method for treating cattle and sheep to prevent foot rot or liver necrosis comprising administering a Fusobacterium necrophorum bacterin, which is a B-propiolactone inactivated Fusobacterium necrophorum isolate, to the animal being treated.

1. Rejections based on Maas

Claim 1 stands rejected under 35 U.S.C. § 102(b) because Maas purportedly describes the claimed process, and under 35 U.S.C. § 102(f) because applicant signed a statement that he actually examined the Maas dissertation prior to the June 7, 1990, the filing date of applicant's parent application.

A. Maas' disclosure

In Chapter III, "The Immune Responses of Mice and Cattle to Fusobacterium Necrophorum," at pages 101-102, bridging paragraph, Maas describes the preparation of vaccines (emphasis added):

Three whole-cell monovalent F. necrophorum vaccines (FN 2101, FN 2382, and FN 3080) were prepared. The bacteria were removed from the surface of plate cultures (BHIBA) with a sterile loop and suspended in sterile 0.1 M PBS at pH 7.1 to a turbidity comparable to a No. 5 tube of a McFarland nephelometer set. Beta-propiolactone (BPL) . . . was added (0.1% v/v). The resulting mixtures were incubated for 4 days at 4 C to kill the bacteria. . . . [T]he vaccines were then warmed at 37 C for 4 hours to eliminate the concentration of (BPL)(Staples, 1981). A low viscosity aluminum hydroxide gel (10% v/v) . . . was added as an

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adjuvant and gentamicin (30 ug/ml) . . . was added  
as a preservative (Oden et al, 1974).

In Chapter IV, "The Immune Response of Cattle to Fusobacterium  
Necrophorum," at page 148, first full paragraph, Maas states:

The purpose of the present study was i) to determine  
if leukotoxin neutralizing activity was present in bovine  
sera after immunization with 2 F. necrophorum vaccine  
preparations or experimental F. necrophorum  
infection  
and ii) to evaluate the effect of these vaccines or  
infection on the peripheral blood lymphocyte  
response.

At page 151, last paragraph, Maas states (emphasis added):

A whole-cell (FN 3080 WC) and a RRE (FN 3080  
RRE) vaccine were prepared for immunization of calves.  
The whole-cell vaccine was prepared as described in  
Chapter III.

See Group III of Table 1. Experimental design of bovine F.  
necrophorum immunological study, page 153. "An experimental  
infection with F. necrophorum isolate FN 3080 was induced in  
the group II, III, and IV calves 7 days after the last  
immunization (Table 1)" (pages 152 & 154, bridging sentence).

The experiments were designed (page 170, last full sentence):

. . . to determine if, after specific immunization  
or infection, leukotoxin neutralizing activity and  
transformed lymphocytes were present which may  
contribute to effective antitoxic and cellular  
immunity to F. necrophorum infections in cattle.

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Maas analyzed the results as follows (page 170, last two lines, through page 171, first full paragraph; emphasis added):

Leukotoxin neutralizing activity in specific bovine antiserum to the leukotoxic substances of F. necrophorum has not been previously reported. In this study, an increased macrophage viability was demonstrated when 2 leukotoxin types were incubated with sera from calves that had been immunized or infected with FN 3080 preparations

(Tables 3 and 4). This viability was significantly greater than that observed with serum from calves that had received only PBS injections.

These data indicate the presence of a specific leukotoxin neutralizing component in the bovine sera. The sera . . . from F. necrophorum-immunized and -infected calves (no. 74, 78 and 76; Table 2) used in this leukotoxin neutralization assay were positive for anti-F. necrophorum antibody with the ELISA screen. The detection of specific antibody and specific leukotoxin neutralizing activity in the same serum samples from calves immunized or infected with F. necrophorum but not in the control serum suggests that specific antitoxin may be generated in the bovine using F. necrophorum vaccines and may, therefore, be an important aspect of protection in vivo.

However, Maas also found that (pages 180-181, bridging paragraph):

Peripheral blood lymphocytes from F. necrophorum-immunized and -experimentally infected calves did not demonstrate uniform specific stimulation when cultured with a ribosome-rich antigen prepared from F. necrophorum. However, these calves did produce anti-F. necrophorum antibody as assessed by the enzyme-

linked immunosorbent assay. The response observed with the lymphocyte transformation is not at clinical variance with the pathological events noted in necrobacillosis infections of the bovine.

B. Applicant's disclosure

Applicant's specification teaches (Spec., p. 3, lines 5-32):

The present invention relates to a process for bacterin preparation in which *B*-propiolactone (BPL) is used to inactivate virulent *F. necrophorum* isolates. Residual BPL may be hydrolyzed and an adjuvant may then be added. The bacterin prepared by this process is useful in the prevention and control of *F. necrophorum* in ruminant animals such as sheep, goats and cattle under normal field conditions.

The present invention also relates to a *B*-propiolactone (BPL) killed bacterin prepared from virulent isolates of *Fusobacterium necrophorum* which is useful as an aid in protecting against diseases caused by *F. necrophorum* in cloven hoofed animals (i.e. cattle, sheep, goats, etc.). Examples of such diseases include Footrot, Liver Abscess, Calf Diphtheria, Interdigital Dermatitis, etc. Previous attempts at preparing efficacious bacterins using *Fusobacterium necrophorum* have been unsuccessful, probably due to the fact that critical antigens necessary for induction of immunity were not preserved by use of inactivation processes which involved heat or formaldehyde. Applicant has found, however, through challenge studies conducted in mice that BPL inactivated, adjuvanted cultures can protect mice against experimental challenge with heterologous isolates of *F. necrophorum*. Field challenge trials conducted in pregnant sheep and feedlot cattle have also shown that the BPL inactivated bacterin of the present invention is effective in reducing both incidence and severity of ovine and bovine Footrot.

The present invention can be practiced with any virulent isolate of *F. necrophorum*. . . .

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Applicant prepared his test vaccines in a manner which appears to be identical or substantially the same as the vaccine preparation method described at pages 101-102 of Maas; i.e. the fermented cultures are cooled to a temperature of about 4 to 7° C (Spec., p. 5, lines 3-6), the cooled cultures are inactivated with BPL (0.11% v/v)(Spec. p. 5, lines 6-9), the culture is maintained at about 4 to 7° C during the inactivation stage (Spec., p. 5, lines 13-15), the BPL-containing culture is heated to about 36 to 38° C for 3 to 5 hours to remove or inactivate BPL (Spec., p. 5, lines 15-22), preservatives such as gentamicin (30 micrograms/ml) are preferably added (Spec., p. 5, lines 23-28), and adjuvants such as 10% aluminum hydroxide gel are particularly preferred (Spec., p. 5, lines 29-34). While Maas vaccinated test calves, applicant vaccinated adult cattle.

In Example 1 (Spec., pp. 6-9), applicant reports that 3.3% of control cattle developed cases of acute foot rot when challenged. However, 1.4% of the vaccinated cattle developed cases of acute foot rot (Spec., p. 8, lines 11-19). According to applicant, "[a] 64.1% reduction in clinical index was observed among vaccinated cattle" (Spec., p. 8, lines 24-25). Example 1 is the only reported example of immunization trials

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on cattle. On that basis, applicant found that (Spec., p. 8, lines 26-31):

. . . vaccination resulted in a statistically significant reduction in incidence of acute foot rot in feedlot cattle and also showed signs of reducing severity of disease. Results show that the BPL inactivated F. necrophorum bacterin is efficacious against foot rot in cattle under normal field conditions.

C. Claim interpretation

Consistent with the specification and its exemplified success, we hold that applicant's claimed "method for treating cattle . . . to prevent foot rot or liver necrosis comprising administering . . . a B-propiolactone inactivated Fusobacterium necrophorum isolate" broadly reads on vaccinating cattle with a B-propiolactone inactivated Fusobacterium necrophorum isolate, with or without adjuvant, to significantly reduce the incidence of and control foot rot or liver necrosis in cattle. Claim language is to be given its broadest reasonable interpretation consistent with the description of the invention in the specification. In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989).

D. Findings

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We find that Maas reasonably appears to describe the process applicant claims. Accordingly, we affirm the examiner's rejections of Claims 1-8 under 35 U.S.C. § 102(b) over Maas and under 35 U.S.C. § 102(f) because applicant indicated by his signing of the Maas dissertation that he had "examined a dissertation entitled THE IMMUNE RESPONSES OF MICE AND CATTLE TO FUSOBACTERIUM NECROPHORUM presented by Synthea Maas" prior to the June 7, 1990 filing date of his parent application and that "it is worthy of acceptance" (Maas, the signature and acceptance page). While applicant appears to believe that Maas' dissertation describes subject matter outside the scope of the process presently being claimed on appeal, we surmise that he is reading limitations of the specification into the claims, which is improper. In re Prater, 415 F.2d 1393, 1404, 162 USPQ 541, 550 (CCPA 1969).

2. Rejection in view of Abe, Nelson, and Adam

Claims 1-8 stand rejected under 35 U.S.C. § 103 as unpatentable in view of the teachings of Abe, Nelson and Adam.

We affirm.

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Abe describes methods for immunizing mice against Fusobacterium necrophorum. In one method affording protection against the bacterium to a degree of 54.1 to 77.5%, a vaccine formulated from formaldehyde (0.4%)-inactivated Fusobacterium necrophorum cells and an aluminum hydroxide adjuvant was administered to mice by intraperitoneal (IP) injection (Abe, p. 115, Summary (col. 1) and Materials and Methods, Vaccine Preparation (col. 2); and pp. 116-117, bridging paragraph). Abe found that vaccine toxicity is a major factor in preparing Fusobacterium necrophorum vaccines (Abe, pp. 117-118, Discussion) and proffered an improvement on procedures which had previously utilized alum-precipitated toxoids of F. necrophorum to reduce the incidence of hepatic abscesses in cattle in light of this major factor (Abe, p. 115, col. 1, last full sentence).

Nelson teaches (Nelson, col. 2, lines 45-50; emphasis added):

Gram-negative bacterial cells devoid of o-carbohydrate side-chains can be inactivated by boiling or treatment with anti-bacterial agents such as formaldehyde (0.2 percent v/v), beta-

propiolactone [sic], or antibiotics. The preferred method to inactivate the cells is with formaldehyde.

The record establishes and accordingly we find that

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Fusobacterium necrophorum cells are gram-negative bacterial cells (Spec., p. 1, lines 8-14; Maas, Chapter I, Introduction, p. 2, first paragraph).

Adams teaches that Fusobacterium necrophorum is responsible for foot rot and liver abscesses and other lesions in ruminant animals (Adams, col. 1, lines 34-51). Adams utilized mice as models for determining the activity of compounds against Fusobacterium necrophorum infection in ruminant animals (Adams, col. 8, Example 2).

We conclude that persons having ordinary skill in the art in view of the combined prior art teachings reasonably would have been led to expect success in treating cattle with B-propiolactone-inactivated Fusobacterium necrophorum bacterin to prevent or control foot rot or liver necrosis. We agree with the examiner's view that a reasonable expectation of success is required and not absolute predictability to sustain a rejection for unpatentability under 35 U.S.C. § 103.

Compare In re O'Farrell, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988).

While appellant's view that persons having ordinary skill in the art would not have been led by the combined prior art

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teaching to use *B*-propiolactone-inactivated Fusobacterium necrophorum bacterin over the use of formaldehyde, heat, and antibiotics deserves and has been granted considerable weight, i.e., the prior art certainly prefers to use formaldehyde to inactivate gram-negative bacteria, we find the evidence as a whole insufficient to support patentability for the full scope of the subject matter claimed.

Having carefully considered the decision rendered and supporting opinion in In re Baird, 16 F.3d 951, 8 USPQ2d 1550 (Fed. Cir. 1994) in light of the evidence presented in that case, it is our view that the evidence in this case warrants a different result. Here, unlike the case in Baird, the prior art expressly states that *B*-propiolactone may be used to inactivate gram-negative bacteria and that Fusobacterium necrophorum is a gram-negative bacterium. Thus, at the time this application was filed, the claimed process would have been prima facie obvious to persons having ordinary skill in the art for the specific utility indicated in applicant's specification. Here, the prior art does not indicate why formaldehyde was preferred. We will not hazard a guess. Moreover, here applicant has not compared the activity of *B*-

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propiolactone-inactivated F. necrophorum to formaldehyde-inactivated F. necrophorum. Absent objective evidence of record establishing that *B*-propiolactone-inactivated F. necrophorum is unexpectedly superior to formaldehyde-inactivated F. necrophorum "for treating cattle and sheep to prevent foot rot or liver necrosis" (Claim 1), we are obliged to affirm the examiner's rejection of the claimed subject matter under 35 U.S.C. § 103. Finally, we note the statement on page 3, lines 23-26, of the specification that:

Applicant has found, however, through challenge studies conducted in mice that BPL inactivated, adjuvanted cultures can protect mice against experimental challenge with heterologous isolates of F. necrophorum.

With the above statement noted, we also note that the process of Claim 1 on appeal does not require inclusion of an adjuvant.

### 3. Conclusion

We affirm the examiner's final rejection of Claims 1-8 under 35 U.S.C. § 102(b).

We affirm the examiner's final rejection of Claims 1-8 under 35 U.S.C. § 102(f).

We affirm the examiner's final rejection of Claims 1-8 under 35 U.S.C. § 103.

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No time period for taking any subsequent action  
in connection with this appeal may be extended under  
37 CFR § 1.136(a).

AFFIRMED

	Teddy S. Gron	)	
	Administrative Patent Judge	)	
		)	
		)	
		)	
	Fred E. McKelvey, Senior	)	BOARD OF
PATENT	Administrative Patent Judge	)	APPEALS AND
		)	INTERFERENCES
		)	
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