

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opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.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. 62

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

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Ex parte KRISTEN P. BRENNER,  
CLIFFORD C. RANKIN,  
YVETTE R. ROYBAL  
and ALFRED P. DUFOUR

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Appeal No. 98-1012  
Application No. 08/117,342<sup>1</sup>

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Hearing: March 23, 1999

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Before WINTERS, WILLIAM F. SMITH, and LORIN, Administrative Patent Judges.

LORIN, Administrative Patent Judge.

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<sup>1</sup> Application for patent filed September 7, 1993. According to applicants, this application is a continuation of Application 07/793,881, filed November 18, 1991, abandoned.

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### DECISION ON APPEAL

This is a decision on appeal from the examiner's final rejection of claims 2-15, 23-27, which are all of the claims pending in this application. We construe appellants' Amendment Before the Board of Appeals and Interferences of March 25, 1999, as withdrawing claims 24 and 27 from the appeal. Therefore, the appeal with respect to these claims is dismissed. We reverse as to the rejections of claims 2-15, 23, and 25-26.

### Representative Claim

Claim 23 is representative of the subject matter on appeal and reads as follows:

A growth medium for detection of total coliforms and E. coli comprising a broth containing:

a growth-encouraging effective amount of ingredients as means of supporting growth and repair of injured coliforms,

buffers to maintain a Ph (sic) of 6.5 to 8,

at least one agent that suppresses growth of gram positive

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cocci and spore-forming organisms,  
at least one agent to suppress growth of non-coliform gram  
negative bacteria, and  
at least one chromogen and one fluorogen.

#### Background

As the representative claim indicates, the claimed invention is directed to a medium for detecting E. coli and coliform bacteria. The detection of E. coli is accomplished by introducing a chromogen to the medium. When acted on by an enzyme generated by the E. coli, a blue color is produced B a color that other organisms would not generally produce. (Specification, p. 11, lines 8-14.) A fluorogen in the medium

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detects the total coliforms. When enzymes from coliforms act on the fluorogen, the coliforms fluoresce under long wave ultraviolet light, something non-coliforms would not do.

(Specification, p. 11, lines 1-7.) E. coli, which is also a coliform, would exhibit a similar fluorescence.

(Specification, p. 11, lines 11-13.) Aside from the detectors and a buffer, the medium additionally comprises one or more agents that

encourage the growth of E. coli and coliform bacteria;  
suppress the growth of Gram-positive bacteria; and,  
suppress the growth of non-coliform bacteria.

The effect is a suppression of the growth of Gram-positive bacteria and all Gram-negative bacteria except E. coli and non-coliform bacteria, which, while the growth of other bacteria is

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being suppressed, are encouraged to grow. The salient features of the claimed medium is summarized in the following table:

	Bacteria	Bacteria	Bacteria	Bacteria	-
	Gram-	Gram-	Gram-	Gram-	
		Coliform	Coliform	Non-Coliform	
		Other	E. Coli		
<b>CLAIMS recite</b>	<b>suppress</b>	<b>grow</b>	<b>grow</b>	<b>suppress</b>	<b>-</b>

In deciding this appeal to determine the patentability of the claimed invention, we have carefully reviewed the record, including the following actions:

final rejection (paper no. 32, mailed November 17, 1995);  
response to final rejection (paper no. 37, filed April 19, 1996);  
advisory action (paper no. 40, mailed April 26, 1996);  
brief (paper no. 41, filed June 2, 1996);  
examiner=s answer (paper no. 43, mailed July 9, 1996);  
reply brief (paper no. 46, filed July 19, 1996);  
supplemental examiner=s answer (paper no. 47, mailed October 1, 1996);  
second reply brief (paper no. 48, filed October 31, 1996);  
second supplemental examiner=s answer (paper no. 48.5, mailed January 22, 1997);  
third reply brief (paper no. 49, filed March 26, 1997);

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examiner=s answer (paper no. 50, mailed June 20, 1997);  
fourth reply brief (paper no. 51, filed July 16, 1997);  
supplemental examiner=s answer (paper no. 53, mailed October  
16, 1997); and,  
fifth reply brief and declaration under Rule 132 (paper no.  
54, filed November 17, 1997).

The major factor for prolonging the prosecution was to  
clarify the function of Cefsulodin as a non-coliform Gram-  
negative bacteria suppressing agent. This limitation now  
appears only in pending claim<sup>5</sup>.

Claim 5 was initially rejected (final rejection, paper no. 32, p. 4) under 35 U.S.C. ' 103  
over Manafi in view of Edberg and Kradolfer (US Patent No.  
4,263,280). Kradolfer, according to the examiner, applied  
because it

Ateaches that cefsulodin sodium is an antibiotic whose  
action is directed against Gram negative cocci (non-coliform  
Gram negative bacteria), and Gram positive cocci and bacteria.  
Cefsulodin, however, has insignificant action against  
enterobacteria such as E. coli and other gram negative

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coliform bacteria<sup>2</sup> (final rejection, paper no. 32)  
Later, Examiner indicated that Kradolfer

clearly teaches that the antibiotic Cefsulodin is effective in killing only [examiner's emphasis] Gram-negative cocci (non-coliform Gram-negative bacteria) and Gram-positive bacteria, including cocci.<sup>3</sup> (supplemental examiner's answer, paper no. 47, p.1)

Appellants, however, disagreed (second reply brief, paper no. 48, p. 1<sup>2</sup>). They submitted an article<sup>3</sup> disclosing Cefsulodin as suppressing Gram-negative cocci but also the very E. coli the claimed medium sought to grow<sup>4</sup>. The examiner responded by dropping

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<sup>2</sup> The Examiner has not previously indicated that she believed that Kradolfer taught Gram-negative cocci only and no other forms of Gram-negative organisms were affected by cefsulodin. The belief is incorrect. Kradolfer teaches, at column 1, line 22 that cefsulodin is effective against Pseudomonas strains, which are Gram-negative rods, not cocci.<sup>3</sup>

<sup>3</sup> Gertrude H. Jacoby and Kevin D. Young, Cell Cycle-Independent Lysis of Escherichia coli by Cefsulodin, an Inhibitor of Penicillin-Binding Proteins 1a and 1b, Journal of Bacteriology, Jan. 1991, p. 1-5.

<sup>4</sup> The Examiner's assumptions are clearly refuted by the actual teachings in the art, which teaches one of ordinary skill in the art that cefsulodin lyses actively growing E. coli.<sup>3</sup> (second reply brief, paper no. 48, p. 3).

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Kradolfer as a reference in the ' 103 rejections and raising a new rejection under the enablement requirement of 35 U.S.C. ' 112:

ASince Applicants have shown that this particular antibiotic will destroy by lysis the very bacteria which the instant medium is used to detect, the specification is deemed non-enabling. Applicants have not shown how the antibiotic cefsulodin, which lyses coliform bacteria, may be used in a medium for detection of coliform bacteria@ (second supplemental examiner=s answer, paper no. 48.5, p. 2).

Thereafter a debate ensued, with appellants arguing that the data and methodology described in the specification are satisfactory to teach one how to make and use the claimed medium, and the examiner arguing, for example, that there are no claim limitations or discussion in the specification regarding the use of Cefsulodin at a particular concentration such that it will perform as appellants describe; namely, suppressing non-coliform but not coliform bacteria (third reply brief, paper no. 49, p. 2; examiner=s answer, paper no. 50, p. 2; fourth reply brief, paper no. 51, p. 2; supplemental

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examiner=s answer, paper no. 53, p.1).

Finally, appellants (fifth reply brief, paper no. 54) filed a Rule 132 Declaration to support their position that no undue experimentation is required. However, upon the Board=s initial review of the record, it was apparent that the examiner did not have the opportunity to consider the declaration and for this reason, among others, the application was remanded (paper no. 56, mailed May 28, 1998) to the examiner. Given the examiner=s response that the Areply brief of November 17, 1997 has been entered and considered but no further response by the examiner is deemed necessary,@ (paper no. 57, mailed August 3, 1998), we are satisfied that the opportunity to review the declaration has been taken.

#### Grounds of Rejection

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We direct our attention to the new grounds of rejection made in the second supplemental examiner=s answer (paper no. 48.5, mailed January 22, 1997). The references relied on are:

Edberg (Edberg)	4,925,789	May 15, 1990
Matner et al (Matner)	5,073,488	Dec. 17, 1991

Manafi, Kniefel and Bascomb (Manafi); Fluorogenic and Chromogenic Substrates Used in Bacterial Diagnostics, Microbiological Reviews, Vol. 55, No. 3, September 1991, pp. 335-348

The claims under appeal stand rejected as follows:

Claim 5 is rejected under the enablement requirement of 35 U.S.C. ' 112, first paragraph.

Claims 2-4, 6-8, 14-15, 23, 25, and 26 are rejected under 35 U.S.C. ' 103 over Manafi in view of Edberg.

Claims 9-13 are rejected under 35 U.S.C. ' 103 over Manafi in view of Edberg and further in view of Matner.

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DISCUSSION

Enablement<sup>2</sup>

The crux of examiner's position is that claim 5 does not recite the concentration at which Cefsulodin suppresses non-coliform bacteria but not coliform bacteria. Furthermore, the specification does not provide the necessary information to determine the appropriate level for achieving that result.

In considering this issue, we note that appellants are not required to disclose every concentration encompassed by the

claims. See In re Angstadt, 537 F.2d 498, 190 USPQ 214 (CCPA 1976). However, there must be sufficient disclosure, either through illustrative examples or terminology to teach those of ordinary skill in the art how to make and use the invention as broadly as it is claimed. See In re Vaeck, 947 F.2d 488, 20

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USPQ2d 1438 (Fed. Cir. 1991). It is the examiner's burden to show that one skilled in the art would have to resort to undue experimentation in order to practice the invention as broadly claimed. Here, no persuasive reason has been given why the specification does not reasonably enable one skilled in the art to practice the invention as broadly as it is claimed and without undue experimentation. See In re Marzocchi, 439 F.2d 220, 169 USPQ 367 (CCPA 1971).

The specification teaches an Example (page 9) which describes a medium formulation where A5 ml of a freshly-prepared 1 mg/ml sterile-filtered solution of Cefsulodin (5 g/ml final concentration) were added per liter of tempered agar medium@ (specification, p. 10, lines 21-23). The other agents and their concentrations in the medium are also clearly explained. Furthermore, the mixing technology that the example and alternatives (see specification, pages 17-22) employ is not an unpredictable art. See In re Fisher, 427 F.2d 833, 166

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USPQ 18 (1970), where the court stated that the scope of enablement varies inversely with the degree of unpredictability of the involved factors. While some experimentation may be required to determine the right concentration in the detecting medium in addition to what is described, we do not consider such experimentation to be undue. As explained in PPG Indus., Inc. v. Guardian Indus. Corp., 75 F.3d 1558, 1564, 37 USPQ2d 1618, 1623 (Fed. Cir. 1996):

In unpredictable art areas, this court has refused to find broad generic claims enabled by specifications that demonstrate the enablement of only one or a few embodiments and do not demonstrate with reasonable specificity how to make and use other potential embodiments across the full scope of the claim. *See, e.g., In re Goodman*, 11 F.3d 1046, 1050-52, 29 USPQ2d 2010, 2013-15 (Fed. Cir. 1993); *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1212-14, 18 USPQ2d 1016, 1026-28 (Fed. Cir.), *cert. denied*, 502 U.S. 856, 112 S.Ct. 169, 116 L.Ed.2d 132 (1991); *In re Vaeck*, 947 F.2d at 496, 20 USPQ2d at 1445. Enablement is lacking in those cases, the court has explained, because the undescribed embodiments cannot be made, based on the disclosure in the specification, without undue experimentation. But the question of undue experimentation is a matter of degree. The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation must not be unduly

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extensive.@ *Atlas Powder Co., v. E.I. DuPont de Nemours & Co.*, 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984). The Patent and Trademark Office Board of Appeals summarized the point well when it stated:

The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

*Ex parte Jackson*, 217 USPQ 804, 807 (1982).

Here the goal is clearly stated B to suppress the growth of non-coliform bacteria in a medium that also encourages the growth of coliform bacteria. While it may take considerable experimentation, it is simply a matter of mixing certain agents in a buffered vehicle, with the necessary chromogen and fluorogen detectors, until an E. coli/coliform detecting medium is obtained that can both encourage coliform growth and suppress Gram-positive and non-coliform bacteria. This is

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plainly demonstrated by the Rule 132 Declaration<sup>5</sup> (fifth reply brief, paper no. 54). Appellants have shown that an appropriate concentration for Cefsulodin in the medium can be determined in about 45 minutes. Through routine experimentation, one can therefore determine the recipe, among all those encompassed by the claims that would possess the disclosed utility. The specification provides adequate guidance to the technician of ordinary skill.

Obviousness

Claims 2-4, 6-15, 23, 25-26 are at least rejected over Manafi in view of Edberg. According to the examiner (second supplemental examiner's answer, paper no. 48.8, pages 3-4), Manafi teaches a medium for the simultaneous detection of coliforms and E. coli (e.g., p. 338, col. 1, lines 22-27). In particular, Manafi teaches:

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<sup>5</sup> Rule 132 declarations that supply facts, such as test data, from an expert in the field are highly probative and are an appropriate mechanism for rebutting an examiner's prima facie case of enablement. See In re Payne, 203 USPQ 245, 256 (CCPA 1979).

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growth promoting agents (e.g., peptone, lactose) (see Table 1);

a buffer and the claimed pH (e.g., p. 337, col. 1, lines 8-12); and,

chromogenic and fluorogenic detecting compounds (p. 336+, starting under Detection of Activity of Individual Enzymes).

Manafi does not teach:

an agent to suppress growth of gram positive cocci & spore-forming organisms; or

an agent to suppress growth of non-coliform gram negative bacteria.

Manafi therefore teaches a medium for detecting E. coli and coliforms as claimed but without the claimed suppressing agents. This can be summarized as follows:

	Bacteria	Bacteria	Bacteria	Bacteria	-
	Gram-	Gram-	Gram-	Gram-	
		Coliform	Coliform	Non-Coliform	
		Other	E. Coli		
<b>MANAFI discloses</b>	<b>-</b>	<b>grow</b>	<b>grow</b>	<b>-</b>	<b>-</b>

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Examiner cites Edberg to overcome Manafi=s deficiencies.

According to the examiner, Edberg teaches Aan assay for the simultaneous detection of E. coli and other coliform bacteria@ (second supplemental examiner=s answer, paper no. 48.8, page 3) with agents to suppress the growth of Gram-positive bacteria,

yeast (which are eukaryotic, not bacteria), and Aagents to suppress bacterial growth other than coliform bacteria (Edberg, col. 5, lines 29-33 through col. 6, lines 58-62)@ (second supplemental examiner=s answer, paper no. 48.8, page 3). Edberg=s suppressing agents are said to prevent interference in the assay due to the other organisms B reducing false positive and false negative incidences and making the assay more accurate and reproducible. In other words, according to the examiner, Edberg suggests inhibiting the growth of any other organism than the particular bacteria

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(e.g., E. coli and total coliform bacteria) that one is seeking to detect. For this reason, the examiner concludes Ait would have been obvious to one with ordinary skill in the art at the time Applicant=s invention was made to include the antibiotics and agents to suppress non-coliform gram negative bacteria of Edberg in Manafi=s culture medium@ (second supplemental examiner=s answer, paper no. 48.8, sentence bridging pages 3-4).

While we agree that Edberg teaches a medium for simultaneous detection of E. coli and total coliforms (e.g., col. 9, lines 16-21 and claim 16), we are not persuaded that Edberg suggests including an agent to suppress the growth of non-coliform bacteria.

The claims clearly require Aat least one agent to suppress growth of non-coliform gram negative bacteria@<sup>3</sup> and the supporting specification defines this agent as an Ainhibitor@ (page 8, line 11; e.g., antibiotic Cefsulodin

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B page 12, line 2). The antibiotics to which the examiner refers, vancomycin and ansiomycin, suppress the growth of Gram-positive bacteria and yeast, respectively (col. 5, lines 29-32, and col. 6, lines 58-62). No agent or inhibitor for suppressing non-coliform Gram-negative bacteria is disclosed.

The mechanism by which Edberg is able to limit microbial competition (col. 7, lines 20-21), and thereby reduce false-negative results, involves using a primary nutrient for the target microbe to be detected (col. 7, lines 65-68). In a medium that supports the growth of *E. coli* and total coliforms, Edberg introduces two nutrient-indicators B specific to the *E. coli* and coliforms and which they use to metabolize and grow (claim 16) and which they attack, resulting in a detectable change in color (col. 8, lines 17-32). Because other microbes, such as non-coliform bacteria, cannot metabolize these nutrient-indicators, they will not grow (col. 8, lines 21-22) and the microbial competition<sup>6</sup> that would have occurred in a medium with a general nutrient is eliminated. Although Edberg, like the claimed medium, suppresses the growth of non-coliform bacteria,

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<sup>6</sup> AThe nutrient-indicator actively participates in the growth of the target microbes by serving as the preferred or primary nutrient source. Y Competition between target microbes and other microbes for the available nutrients in the media is eliminated by the subject invention.@ (column 3, lines 37-51).

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it is accomplished in the absence of any nutrients or agents B in contradistinction to the claimed invention where the presence of the agent or inhibitor is required. Edberg can be summarized as follows:

	Bacteria	Bacteria	Bacteria	Bacteria	Yeast
	Gram-Positive	Gram-	Gram-	Gram-	
		Coliform	Coliform	Non-Coliform	
		Other	E. Coli		
<b>EDBERG</b>	<b>suppress</b>	<b>grow</b>	<b>grow</b>	<b>-</b>	<b>suppres</b>

The examiner appears to agree that Edberg does not disclose agents for suppressing non-coliform bacteria. Nevertheless, according to the examiner,

AY Edberg clearly states >to select E. coli from other gram negative bacteria, the following ingredients are usedY=. Although antibiotics per se are not used, the combination of ingredients clearly has an antibiotic effect with respect to non-coliform gram negative bacteria@ (supplemental examiner=s answer, paper no. 53, p. 2, lines 15-16).

The examiner is referring to column 5, starting at line 34.

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That passage is directed to the second step of a two-step process for detecting E. coli in a sample: 1) Gram-negative bacteria is segregated from other microbes through the use of yeast-killing ansiomycin and Gram-positive bacteria-killing vancomycin, and 2) E. coli is selected from the remaining Gram-negative bacteria by adjusting the medium to supply a nutrient-indicator specific to the E. coli. The result of practicing this example is a medium that encourages the growth of E. coli at the expense of all other

microbes, including other Gram-negative bacteria: coliforms and non-coliforms. Since this would defeat the purpose of the claimed medium B to detect both E. coli and coliforms, the prima facie case is undermined by this disclosure.

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To the extent that the examiner is relying on the disclosure as a suggestion to include a non-coliform suppressing agent, we come to the opposite conclusion. Edberg (column 3, lines 45-48) teaches restricting the nutrients such that the media is so specific that the invention does not have to be sterilized before use. This would suggest adjusting the nutrients alone without a suppressing agent; the addition of such an agent would be superfluous. In this regard Edberg teaches away from employing the claimed suppressing agent.

With respect to any potential antibiotic effect on non-coliforms from Edberg's lack of nutrients, this is immaterial

because it is neither a teaching nor a suggestion of the

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claimed mechanism for doing so.

We are not persuaded that Edberg, which teaches a medium with agents that suppress yeast and Gram-positive bacteria and include nutrient-indicators that preferentially metabolize and grow those organisms one seeks to detect, overcomes the deficiencies of Manafi; namely Manafi's lack of an agent to suppress the growth of Gram-negative non-coliform bacteria. Since this is a required element of the claimed medium, a prima facie case has not been established.

For the reasons stated, the rejection involving Manafi is likewise reversed.

We note that claims 4 and 5 appear to be substantial duplicates of claims 26 and 27. Further disposition of this

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application should include an objection under 37 CFR 1.75 Aas  
being substantial duplicates of allowed claims@ MPEP  
706.03(k), 6<sup>th</sup> Ed., Rev. 3, July 1997.

In conclusion;

The rejection of claim 5 under the enablement requirement  
of 35 U.S.C. ' 112, first paragraph, is reversed;

The rejections of claims 2-4, 6-15, 23, 25-26 under 35  
U.S.C. ' 103 are reversed; and,

The appeal with respect to claims 24 and 27 is dismissed.

REVERSED

SHERMAN D. WINTERS	)	
Administrative Patent Judge	)	
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	)	
	)	BOARD OF PATENT
WILLIAM F. SMITH	)	APPEALS
Administrative Patent Judge	)	AND

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) INTERFERENCES

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<sup>1</sup> 5. A medium of claim 4 wherein the cephalosporin used to suppress growth of non-coliform bacteria is Cefsulodin.

<sup>2</sup> The rejection has been applied against claim 5. It should have also applied to claims 4 and 23, on which claim 5 depends. They also broadly include Cefsulodin as a suppressing agent without mentioning a specific concentration and therefore should have raised the same concern.

<sup>3</sup> Note also that dependent claims 4, 5, 26 and 27 further limit the agent used to suppress growth of non-coliform gram negative bacteria to a particular antibiotic.