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UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

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JOSEF PITHA  
Junior Party  
(Patent 4,727,064),

v.

BERND W. MULLER and ULRICH BRAUNS  
Senior Party  
(Application 07/264,726).

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Patent Interference No. 102,413

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Before SCHAFER, TORCZON, and JEFFREY T. SMITH, Administrative  
Patent Judges.

JEFFREY T. SMITH, Administrative Patent Judge.

**FINAL JUDGMENT**

**A. Introduction**

Dr. Joseph Pitha is the Junior Party (Pitha) to the  
interference. Dr. Bernd W. Muller and Dr. Ulrich Brauns are  
the Senior Party (Muller) to the interference. The involved

patent for Pitha is U.S. Patent 4,727,064 ('064) issued February 23, 1988, which is based on application 06/738,749 filed May 29, 1985. Pitha has been accorded the benefit of the filing date of the U.S. application 06/603,839 filed April 25, 1984, which issued as U.S. Patent 4,596,795 on June 24, 1986. The involved application for Muller is U.S. application 07/264,726, filed October 31, 1988. Muller has been accorded the benefit of the filing date of the U.S. application 07/756,498, filed July 3, 1985 and the priority document Fed. Rep. Germany P 3346123.6 which was filed on December 21, 1983.

In the Decision on Motions dated July 24, 1992, the Examiner in Chief (APJ) granted Muller motion 1 which was a motion under 37 C.F.R. § 1.633(a) for judgment on the ground that Pitha claims 6-11 and 13-27 were unpatentable to Pitha under 35 U.S.C. §§ 102, 103 and 112. Pitha has failed to raise the issue decided by the APJ with respect to Muller motion 1, as required by 37 C.F.R. § 1.655(a)(5). Thus, the decision on this motion is no longer an issue in this interference.

**B. The Subject Matter of the Interference**

The subject matter of this interference involves the production of a stabilized amorphous complex of a drug and a mixture of cyclodextrin derivatives. Cyclodextrins are cyclic oligosaccharides built up from six ("), seven (\$) or eight (() glucopyranose units.<sup>1</sup> The non-selective alkylation of cyclodextrin forms a cyclodextrin derivative.<sup>2</sup> The stabilized complexes are said to be useful for the formation of pharmaceuticals which have improved drug dissolution properties and absorption by the body.<sup>3</sup>

Pitha claims 1-28 and Muller claims 1-11 and 22-36 correspond to count 3. Count 3, the sole count in the interference follows:

Count 3

A method of producing a stabilized amorphous complex of a drug and a mixture of cyclodextrins which comprises the steps of:

1. Dissolving an intrinsically amorphous mixture of cyclodextrin derivatives which are water soluble and capable of forming inclusion complexes with drugs in water; and
2. Solubilizing lipophilic drugs into the aqueous media to form a solution and form a solubilized drug/cyclodextrin derivative complex;  
or

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<sup>1</sup> J. Szejtli "Cyclodextrins and Their Inclusion Complexes," Akademiai Kiado, Budapest Hungary 1982, p. 13.

<sup>2</sup> Pitha '064, column 1 lines 11-14.

<sup>3</sup> Pitha '064, column 1 lines 26-36.

the composition of matter made by the method which contains an amorphous complex of cyclodextrin derivatives and a drug.

**C. Count interpretation**

In order for a party to prove conception or actual reduction to practice, the party must show conception or actual reduction to practice of an embodiment within the scope of the count. The count is in an alternative format incorporating by reference certain claims of each party. In this format, a party must show conception or actual reduction to practice of an embodiment falling within at least one of the alternatives of the count.

An embodiment falls within the scope of a count if it meets all the limitations of at least one of the claim alternatives of the count. The physical embodiment relied upon as an actual reduction to practice must include every limitation of the count. Cooper v. Goldfarb, 154 F.3d 1321, 1327, 47 USPQ2d 1896, 1902 (Fed. Cir. 1998). The constructed embodiment or performed process must include the precise elements recited in the count. Eaton v. Evans, 204 F3d 1094, 1097, 53 USPQ2d 1696, 1698 (Fed. Cir. 2000).

In this interference to establish a reduction to practice, Pitha must show (1) solubilization of lipophilic

drug in an aqueous mixture of intrinsically amorphous cyclodextrin derivatives or (2) a composition of matter made by the method which contains amorphous complex of cyclodextrin derivatives and a drug.

### Glossary

The following abbreviations are used in this decision as follows:

PR	=	Pitha record followed by the record page number.
PX	=	Pitha exhibit followed by the exhibit page number.
PB	=	Pitha brief followed by the page number and line number.
PRB	=	Pitha reply brief followed by the page number and line number.
BCD	=	beta-cyclodextrin
HPBCD	=	2-hydroxypropyl-beta-cyclodextrin
PBCD	=	poly-beta-cyclodextrin

### **D. Pitha's Case**

Pitha seeks to show prior conception and reduction to practice before the critical date of December 21, 1983, Muller's earliest priority date (DE3346123.6). Pitha is relying upon the experiments described in the laboratory notebooks of Dr. Lajos Szente, Dr. Teresa Czajkowska and Dr. Ciesielski to show a reduction to practice of an embodiment within the scope of the count. The Pitha exhibits include, *inter alia*, declarations and transcripts of oral testimony

from Dr. Lajos Szente and Dr. Teresa Czajkowska. Pitha's exhibits do not include a declaration or transcript of oral testimony from Dr. Winicjusza Ciesielski.

**1. Intrinsically amorphous cyclodextrin derivatives.**

Pitha describes the research he supervised performed by Dr. Lajos Szente which purportedly exhibited the synthesis of intrinsically amorphous cyclodextrin derivatives which are water soluble and capable of forming inclusion complexes with drugs in water. The experiments Sz-8, and Sz-111 are said to describe the synthesis of Poly-beta-cyclodextrin (PBCD) cyclodextrin derivative.<sup>4</sup> PBCD is said to be formed by the condensation of beta-cyclodextrin with epichlorohydrin.<sup>5</sup> Pitha argues the absence of indication of crystals upon purification and the reaction described on Sz-8 is recognized to indicate amorphous-type characteristics.<sup>6</sup> The experiments Sz-20, Sz-28, Sz-35, Sz-42 and Sz-49 are said to describe the synthesis of Hydroxypropyl-beta-cyclodextrin (HPBCD) cyclodextrin derivative.<sup>7</sup> HPBCD is said to be formed by the

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<sup>4</sup> PB page 17, lines 2-7.

<sup>5</sup> PX-38 column 4, lines 44-47.

<sup>6</sup> PB page 15, 14-23.

<sup>7</sup> PB page 15, lines 1-9.

condensation of beta-cyclodextrin with propylene oxide.<sup>8</sup>

Pitha presents Dr. Szente's testimony (PR 172-175) to establish the intrinsically amorphous nature of PBCD and HPBCD.

Pitha describes the research he supervised performed by Dr. W. Ciesielski which purportedly exhibit the synthesis of intrinsically amorphous cyclodextrin derivatives which are water soluble and capable of forming inclusion complexes with drugs in water. The experiments W-11, W-14 and W-44 are said to describe the synthesis of Poly-beta-cyclodextrin (PBCD) cyclodextrin derivative.<sup>9</sup> Pitha argues that the intrinsically amorphous nature of W-14 is shown by the absence of indication of the formation of crystals.<sup>10</sup> Pitha also argues the synthesis described in making of PBCD product W-14 was a condensation reaction of beta-cyclodextrin with epichlorohydrin which results in an intrinsically amorphous product.<sup>11</sup> The experiments W-17, W-22, W-38, W-48 and W-55 are said to describe the synthesis of HPBCD cyclodextrin

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<sup>8</sup> PX-38 column 4, lines 44-47.

<sup>9</sup> PB page 17, lines 2-7.

<sup>10</sup> PB page 16, lines 12-18.

<sup>11</sup> PB page 16, lines 16-20.

derivative.<sup>12</sup> Pitha argues that the intrinsically amorphous nature of W-17 is shown by the product having to be freeze dried.<sup>13</sup> Pitha also argues the synthesis described in the making of HPBCD product W-17 was a synthetic procedure analogous to the procedure described in Gramera patent 3,459,731 (PX-14) which resulted in a viscous liquid.<sup>14</sup> As other examples of intrinsically amorphous PBCD Pitha directs us to laboratory notebook pages W-11 and W-44.<sup>15</sup>

Pitha describes the research he supervised performed by Dr. Teresa Czajkowska which purportedly exhibit the synthesis of intrinsically amorphous cyclodextrin derivatives which are water soluble and capable of forming inclusion complexes with drugs in water. The experiment C-70 is said to describe the synthesis of PBCD cyclodextrin derivative.<sup>16</sup> Pitha argues the absence of indication of crystals, on page C-70, support the conclusion that the product was intrinsically amorphous.<sup>17</sup>

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<sup>12</sup> PB page 15, lines 1-9.

<sup>13</sup> PB page 13, lines 10-16.

<sup>14</sup> PB page 13, line 15 to page 14, line 2.

<sup>15</sup> PB page 17, lines 3-6.

<sup>16</sup> PB page 17, lines 2-7.

<sup>17</sup> PB page 16, 3-5.

Pitha presents Dr. Czajkowska's testimony (PR 352-356) to establish the intrinsically amorphous nature of C-70 PBCD. The experiment C-116 is said to describe the solubilization of testosterone with the product produced from C-70.

In order to establish the intrinsically amorphous nature of HPBCD and PBCD products are well known in the art and to help establish the intrinsically amorphous property as inherent, Pitha cites exhibits PX-41 published September 1985, PX-54 published February 1986 and MCX-4 published October 1987.<sup>18</sup>

## **2. Solubilized drug/cyclodextrin derivatives complex**

Pitha describes the research he supervised performed by Dr. Lajos Szente and Dr. Teresa Czajkowska which purportedly exhibit the synthesis of solubilized drug/cyclodextrin derivatives complexes. Specifically, Pitha directs us to the experiments appearing in Dr. Szente and Dr. Czajkowska's laboratory notebooks which are said to take the formed cyclodextrin derivatives and lipophilic drugs and solubilize them in aqueous media.

## **3. The Laboratory Notebook of Dr. Lajos Szente**

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<sup>18</sup> PB page 14, lines 8-19 and page 16, lines 17-21.

Exhibit PX-19 is said to be a reproduction of the laboratory notebook of Dr. Lajos Szente (Sz).<sup>19</sup> The exhibit appears to be a bound book with consecutively numbered pages. According to the first page of the notebook (PX-19-001), the entries in the notebook occurred between the dates of May 15, 1981 to December 28, 1981.

In Sz-8 (PR 181, PX-19-16), the experiment took place no later than June 2, 1981, which is the date indicated on the request for analytical services PX-19-16. The reaction product of BCD and epichlorohydrin was said to be formed during the experiment. There was no description of the substance formed. There is no indication that crystals are formed. There is no indication whether the product contained more than one cyclodextrin derivative. The solubility of the substance in water at room temperature is reported to be approximately 20mg/ml.

In Sz-11 (PR 182, PX-19-20), the experiment took place no later than July 2, 1981, which is the date indicated on PX-19-37. The reaction product of BCD and 1,4 butanediol diglycidyl ether was said to be formed during the experiment. The substance formed was described as white and foam like with no

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<sup>19</sup> PB page 9, lines 16-19.

homogenous composition of product. There is no indication whether crystals are formed. There is no indication whether the product contained more than one cyclodextrin derivative. The solubility of the substance in water at room temperature is reported to be 3.60g/100ml. Dr. Szente states the solubility was improperly recorded.<sup>20</sup>

In Sz-20 (PR 173-174 reproduction of PX-19-30), the experiment took place no later than July 2, 1981, which is the date indicated on PX-19-37. The oxymercuration-demercuration of HPBCD also known as 2,6-di-o-allyl- $\beta$ -cyclodextrin was described by the experiment.<sup>21</sup> The substance is described as a light yellow, glass powder like substance. There is no indication whether the product contained more than one cyclodextrin derivative. Dr. Szente states that his attempts to crystallize the product failed which is the reason the phrase "no crystals" is used to describe the product.<sup>22</sup> The solubility of the substance in water at 20°C is reported to be 15.8g/100ml.

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<sup>20</sup> PR page 182, lines 14-15.

<sup>21</sup> The notebook refers to the substance 2,6-di-o-allyl- $\beta$ -cyclodextrin which is another name for hydroxypropyl-beta-cyclodextrin (HPBCD).

<sup>22</sup> PR page 175, paragraph 16.

In Sz-28 (PR 184, PX-19-39), the experiment appears to have taken place no later than August 17, 1981, which is the date that appears on the request for analytical testing (PX-19-40). The oxymercuration-demercuration of hydroxypropyl-beta-cyclodextrin with dioxane was described by the experiment. The substance is described as a very hygroscopic white powder. There is no indication whether crystals were formed. There is no indication whether the product contained more than one cyclodextrin derivative. The solubility of the substance in water at 20°C is reported to be 16g/100ml.

In Sz-32 (PX-19-44), the product produced from Sz-20 was solubilized in water with Vitamin A (retinol) and Vitamin D<sub>3</sub>. The experiment took place no later than July 14, 1981, which is the date indicated on PX-19-45.

In Sz-34 (PR 185, PX-19-46), the products produced from Sz-8, Sz-11 and Sz-20 were individually solubilized in water with beta-ionone. The experiments appear to have taken place on July 19, 1981, which is the date indicated on PX-19-46.

In Sz-36 (PR 185, PX-19-49), the products produced from Sz-8, Sz-11 and Sz-28 were individually solubilized in water with beta-carotene. The experiments appear to have taken place no later than July 29, 1981, which is the date indicated on the subsequently occurring page PX-19-54.

In Sz-40 (PR 187, PX-19-56), the products produced from Sz-11 and Sz-28 were individually solubilized in water with beta-carotene. The experiments appear to have taken place no later than September 1, 1981, which is the date indicated on the subsequently occurring page PX-19-66.

In Sz-41 (PR 187, PX-19-57), the product produced from Sz-28 was solubilized in water with Vitamin D<sub>3</sub>. Dr. Szente states the vitamin D<sub>3</sub> was not decomposed by the solubilization with Sz-28.<sup>23</sup> The experiment apparently took place no later than September 1, 1981, which is the date indicated on the subsequently occurring page PX-19-66.

In Sz-42 (PR 187, PX-19-58), the experiment apparently took place no later than September 1, 1981, which is the date indicated on the subsequently occurring page PX-19-66. HPBCD was said to be formed during the experiment. The substance is described as a white solid substance. There is no indication whether crystals were formed. There is no indication whether the product contained more than one cyclodextrin derivative. The solubility of the substance in water at 20°C is reported to be 16g/100ml.

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<sup>23</sup> PR page 187, lines 14-16.

In Sz-111 (PR 189, PX-20-52), the experiment apparently took place no later than February 22, 1982, which is the date indicated on the request for analytical services PX-20-51. The reaction product of BCD and epichlorohydrin was said to be formed during the experiment. The substance was freeze dried to form a white powder substance. There is no indication whether crystals were formed. The solubility of the substance in water at 20°C is reported to be 13-14g/100ml.

**4. The Laboratory Notebook of Dr. Czajkowska.**

Exhibits PX-23 and PX-24 are said to be reproductions of the laboratory notebooks of Dr. Teresa Czajkowska (C).<sup>24</sup> The exhibits both appear to be a bound book with consecutively numbered pages. Exhibit PX-23 contains pages C-1 to C-75. Exhibit PX-23 is said to contain research performed from October 19, 1981 to June 21, 1982.<sup>25</sup> Exhibit PX-24 contains pages C-101 to C-175. Exhibit PX-24 is said to contain research performed from June 21, 1982 to September 17, 1982.<sup>26</sup>

In C-70 (PR 282, PX-23-82), the experiment took place no later than June 9, 1982, which is the date indicated on the

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<sup>24</sup> PB page 9, lines 16-19.

<sup>25</sup> PR page 259, lines 6-7.

<sup>26</sup> PR page 259, lines 8-9.

request for analytical services PX-23-82. The reaction product of BCD and epichlorohydrin was said to be formed during the experiment. There is no description of the substance formed. There is no indication whether crystals were formed. There is no indication whether the product contained more than one cyclodextrin derivative.

In C-116 (PR 282, PX-24-23), the product produced from C-70 was solubilized in water with testosterone. The experiment took place no later than September 9, 1982, which is the date indicated on PX-24-45.

**5. The Laboratory Notebook of Dr. W. Ciesielski.**

Exhibit PX-27 is said to be a reproduction of the laboratory notebook of Dr. Winicjusza Ciesielski (W).<sup>27</sup> The exhibit appears to be a bound book with consecutively numbered pages. According to the first page of PX-27 (PX-27-001) the entries in the notebook occurred between the dates of June 28, 1982 to June 23, 1983.

In W-14 (PR 298, PX-27-23), the reaction product of BCD and epichlorohydrin was said to be formed during the experiment. The experiment apparently took place no later than August 24, 1982, which is the date when sample W-15 was

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<sup>27</sup> PB page 9, lines 16-19.

sent out for testing (PX-26). There is no description of the appearance of the substance formed. There is no indication whether crystals were formed. There is no indication whether the product contained more than one cyclodextrin derivative.

The product W-14 was said to be solubilized in water with various drugs into aqueous media by Dr. Czajkowska.<sup>28</sup> The following is a list of drugs solubilized in water with W-14 and the respective pages from Dr. Czajkowska's laboratory notebook on which they appear:

Testosterone, C-161; Progesterone, C-171; and Estradiol, C-172.<sup>29</sup>

In W-17 (PR 299, PX-27-28), HPBCD was said to be formed by the condensation reaction of beta-cyclodextrin and propylene oxide in aqueous alkali during the experiment. There is no description of the appearance of the substance formed. There is no indication whether crystals were formed. There is no indication whether the product contained more than one cyclodextrin derivative. The experiments appearing on pages W-22, W-38, W-48 and W-55 are said to be reproductions

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<sup>28</sup> PB paragraph bridging pages 18-19.

<sup>29</sup> PR page 285 and 287.

of the experiment W-17.<sup>30</sup> The following is a list of drugs said to have been solubilized in water with W-17 in aqueous media and the respective pages from Dr. Czajkowska's laboratory notebook on which they appear:

Testosterone, C-160; Estradiol, C-162; Progesterone, C-163; Testosterone, C-166; Estradiol, C-173; Progesterone, C-207; Epichlorohydrin, C-170; Retinoic acid, C-174; Complex of insulin and HPBCD, C-231; and Retinoic acid, C-250.<sup>31</sup>

#### **E. DISCUSSION**

As the junior party, Pitha has the burden of proof on the issue of priority. 37 CFR § 1.657(b); Bosies v. Benedict, 27 F.3d 539, 541, 30 USPQ2d 1862, 1863 (Fed. Cir. 1994); "It is well settled that where an interference is between a patent that issued on an application that was copending with an interfering application, the applicable standard of proof is preponderance of the evidence." Bosies, 27 F.3d at 541-42, 30 USPQ2d at 1864. Since the applications were copending, the applicable standard of proof is preponderance of the evidence.

##### **1. Actual Reduction to Practice**

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<sup>30</sup> PR pages 299, 300 and 301.

<sup>31</sup> PR page 299.

An actual reduction to practice requires proof of the existence of a physical embodiment within the scope of the count. Correge v. Murphy, 705 F.2d 1326, 1329, 217 USPQ 753, 755 (Fed. Cir. 1983). The embodiment relied upon for an actual reduction to practice must include every limitation stated in the count. Schendel v. Curtis, 83 F.3d 1399, 1402, 38 USPQ2d 1743, 1746 (Fed. Cir. 1996). The evidence must also show that the embodiment is suitable for and actually worked for its intended purpose. Scott v. Finney, 34 F.3d 1058, 1061, 32 USPQ2d 1115, 1118 (Fed. Cir. 1994). Testing need not show utility beyond a possibility of failure, but only utility beyond a probability of failure. Scott, 34 F.3d at 1061-62, 32 USPQ2d at 1118. There is no requirement that the embodiment be in a "commercially satisfactory stage of development" to constitute a reduction to practice. Scott, 34 F.3d at 1063, 32 USPQ2d at 1118.

The sole count in this interference follows:

Count 3

A method of producing a stabilized amorphous complex of a drug and a **mixture of cyclodextrins** which comprises the steps of:

1. Dissolving an intrinsically amorphous mixture of cyclodextrin **derivatives** which are water soluble and capable of forming inclusion complexes with drugs in water; and

2. Solubilizing lipophilic drugs into the aqueous media to form a solution and form a solubilized drug/cyclodextrin derivative complex;  
or

the composition of matter made by the method which contains an amorphous complex of cyclodextrin **derivatives** and a drug.

[Emphasis added]

To establish a reduction to practice Pitha must show (1) solubilization of lipophilic drug in an aqueous mixture of intrinsically amorphous cyclodextrin **derivatives** or (2) a composition of matter made by the method which contains an amorphous complex of cyclodextrin **derivatives** and a drug. We have not been directed to evidence on this record which discloses that the term "derivatives" is accorded a definition other than normally prescribed for the term. Thus, we interpret the count as requiring more than one cyclodextrin derivative.

Pitha relies on the research of Dr. Ciesielski, Dr. Czajkowska and Dr. Szente to establish an actual reduction to practice of an embodiment which falls within the scope of the count.

Dr. Pitha testified (PR 1-147) about the activities performed in his laboratory said to establish an actual reduction to practice of an embodiment within the scope of the count. To show the reduction to practice, Dr. Pitha discusses

the research performed by Dr. Ciesielski, Dr. Czajkowska and Dr. Szente, all said to have been carried out under his direction. We find the testimony of Dr. Pitha to be credible only to the extent that the statements by Dr. Pitha have been corroborated by a person with first hand knowledge of the events which have taken place. We do not find the statements of Dr. Pitha credible regarding the research performed by Dr. Ciesielski because we have not been directed to testimony of a person with first hand knowledge of Dr. Ciesielski's activity to corroborate the statements of Dr. Pitha.

**2. The Research of Dr. Winicjusza Ciesielski.**

Pitha seeks to rely on the research appearing in Dr. Winicjusza Ciesielski's laboratory notebooks, PX-27. Dr. Ciesielski did not testify during the testimony phase of the interference.<sup>32</sup> Pitha provides the testimony of Dr. Pitha and the testimony of Dr. Czajkowska (PR-297) as a corroborating witness for the description of the subject matter contained in Dr. Ciesielski's laboratory notebook. Pitha argues that they should be able to rely on the work described in Dr. Ciesielski's laboratory notebook as evidence because Dr. Pitha carefully supervised the work performed in

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<sup>32</sup> PB page 13, footnote 6.

his laboratory and the work is corroborated by the testimony of Dr. Czajkowska:<sup>33</sup>

Dr. W. Ciesielski did not testify during the Testimony Period of the present interference, since he could not be located despite attempts by Dr. Pitha to contact him in Eastern Europe. It is submitted that Pitha is entitled to rely on Dr. W. Ciesielski's laboratory notebook as evidence of the research work he conducted in Dr. Pitha's laboratory, since his work was carefully supervised by Dr. Pitha and was corroborated by the testimony of Dr. Czajkowska. See Holmwood v. Sugavanam, 20 USPQ2d 1712, 1714-1715 (Fed. Cir. 1991).<sup>34</sup>

The facts of Holmwood, are different from the facts of the present case because (1) the witness whose testimony is presented, the supervisor of the laboratory assistants in Holmwood, Dr. Zeck, was not a named inventor; (2) the record made clear that the testing performed was said to be **standard within the industry** and known to the declarant. Holmwood, 20 USPQ2d at 1714. Dr. Czajkowska's testimony is presented to corroborate the testimony of Dr. Pitha regarding the contents of Dr. Ciesielski's laboratory notebook. Pitha has not directed us to testimony by Dr. Czajkowska that states she supervised the work of Dr. Ciesielski or assisted in the performance of the experiments appearing in Dr. Ciesielski's

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<sup>33</sup> PB page 13, footnote 6.

<sup>34</sup> PB page 13, footnote 6.

laboratory notebook. Pitha has not directed us to evidence which indicates that the testing performed by Dr. Ciesielski was standard within the industry. Furthermore, we hold the statements by the person who performed the experiments in this case is critical because the identification of the properties of the reaction product is required. Pages W-14 and W-17 of Dr. Ciesielski's laboratory notebook do not indicate the amorphous nature of the products produced or that these products contain more than one cyclodextrin derivative.<sup>35</sup>

Pitha has not directed us to evidence which establishes that it is known in the industry that cyclodextrin derivatives are always intrinsically amorphous. To the contrary, Szejtli patent 4,542,211 describes amorphous and crystalline products result from the methylation of cyclodextrin.<sup>36</sup>

Pitha argues that previous decisions in this interference follow the principle "that it is the inventor's recognition of the subject matter that controls, not the language used to describe the invention."<sup>37</sup> Pitha has not directed us to evidence which indicates that Dr. Pitha or Dr. Czajkowska had

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<sup>35</sup> PX-27 pages 23 and 28.

<sup>36</sup> Szejtli 4,542,211, column 3, lines 9-24.

<sup>37</sup> PB page 14, footnote 7.

personal knowledge of the properties products produced in experiments W-14 and W-17 at the time of their production.

Pitha argues the literature confirms the intrinsically amorphous nature of HPBCD and PBCD. Specifically, Pitha cites exhibits PX-41 published September 1985, PX-54 published February 1986 and MCX-4 published October 1987.<sup>38</sup> These exhibits were all published after April 25, 1984, which is after the accorded benefit date of Pitha. Consequently, the articles are not available to establish Pitha's appreciation of the properties of HPBCD and PBCD as of the time the experiments were performed.

For the above reasons, and because proof of the existence of a physical embodiment within the scope of the count has not been shown, we cannot rely on the experimental evidentiary data which includes the products described in Dr. Ciesielski's laboratory notebook, PX-27, as evidence of an actual reduction to practice. This includes Dr. Czajkowska experiments C-160, C-161, C-162, C-166, C-170, C-171, C-172, C-173, C-174, C-207, C-231, C-250, C-252, C-253, C-254, C-256, C-258, C-259, C-260,

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<sup>38</sup> PB page 14, lines 8-19, page 15, lines 23-25 and page 16, lines 17-21.

C-261, C-262 and C-267 which employ as an ingredient W-14 or W-17.<sup>39</sup>

### **3. The Research of Dr. Czajkowska**

PX-23 and PX-24 are reproductions of the laboratory notebooks of Dr. Teresa Czajkowska. According to the first page of PX-23 (PX-23-001) and PX-24 (PX-24-001), the entries in the notebooks occurred between the dates of October 19, 1981 to September 17, 1982. These experiments all occurred no later than December 21, 1983, Muller's accorded benefit date.

#### **a. The product C-70 and products including C-70**

In C-70 (PR 282, PX-23-82), the experiment took place no later than June 9, 1982, which is the date indicated on the request for analytical services PX-23-82. The reaction product of BCD and epichlorohydrin was said to be formed during the experiment. There is no description of the substance formed or an indication that the product contained more than one cyclodextrin derivative. There is no indication whether crystals were formed.

In C-116 (PR 282, PX-24-23), the product produced from C-70 (PBCD) was said to have been solubilized in water with

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<sup>39</sup> PR page 299, lines 1-17.

testosterone. The experiment took place no later than September 9, 1982, which is the date indicated on PX-24-45.

The count requires an intrinsically amorphous mixture of cyclodextrin derivatives which are water soluble and capable of forming inclusion complexes with drugs in water. The product C-70 was not described in terms of its amorphous nature. Pitha did not direct us to testimony which establishes (1) the amorphous properties of this product or (2) that the product contained more than one cyclodextrin derivative. In fact, page C-70, PX-23-82, does not describe the substance formed. For the above reasons, and because proof of the existence of a physical embodiment within the scope of the count has not been shown, we cannot rely on the experimental evidentiary data described on page C-70 to establish an actual reduction to practice of an embodiment within the scope of the count.

#### **4. The Research of Dr. Lajos Szente.**

PX-19 is a reproduction of the laboratory notebook of Dr. Lajos Szente. According to the first page of the notebook (PX-19-001), the entries in the notebook occurred between the dates of May 15, 1981 to December 28, 1981. These experiments all occurred no later than December 21, 1983, Muller's accorded benefit date.

**a. The product Sz-8 and products including Sz-8**

In Sz-8 (PR 181, PX-19-16), the experiment took place no later than June 2, 1981, which is the date indicated on the request for analytical services PX-19-15. The reaction product of BCD and epichlorohydrin was said to be formed during the experiment. There was no description of the substance formed. There is no indication whether crystals were formed. There is no indication whether the product of Sz-8 contained more than one cyclodextrin derivative. The solubility of the substance in water at room temperature is reported to be approximately 20mg/ml. Pitha does not direct us to testimony which establishes the amorphous properties for this substance.

In Sz-34 (PR 185, PX-19-46), the product produced from Sz-8 was solubilized in water with beta-ionone. The experiment took place on July 19, 1981, which is the date indicated on PX-19-46.

In Sz-36 (PR 185, PX-19-49), the product produced from Sz-8 was solubilized in water with beta-carotene. The experiment took place no later than July 29, 1981, which is the date indicated on the subsequently occurring page PX-19-54.

Pitha directed us to pages Sz-34 and Sz-36 to establish that a portion of the product from Sz-8 was solubilized in water with a drug. We have not been directed to evidence which establishes a description of Sz-8 product or that the Sz-8 product contained cyclodextrin derivatives. Thus, the products Sz-34 and Sz-36, both of which incorporate Sz-8, do not describe an embodiment which falls within the scope of the count.

**b. The product Sz-11 and products including Sz-11**

In Sz-11 (PR 182, PX-19-20), the experiment took place no later than July 2, 1981, which is the date indicated on the subsequently occurring page PX-19-38. The reaction product of BCD and 1,4 butanediol diglycidyl ether was said to be formed during the experiment. The substance formed was described as white and foam like with no homogenous composition of product. There is no indication whether crystals were formed. There was no indication whether the product of Sz-11 contained more than one cyclodextrin derivative. The solubility of the substance in water at room temperature is reported to be 3.60g/100ml. Dr. Szente states the solubility was improperly recorded.<sup>40</sup>

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<sup>40</sup> PR page 182, lines 14-15.

In Sz-34 (PR 185, PX-19-46), the product produced from Sz-11 was solubilized in water with beta-ionone. The experiment took place on July 19, 1981, which is the date indicated on PX-19-46.

In Sz-36 (PR 186, PX-19-49), the product produced from Sz-11 was solubilized in water with beta-carotene. The experiment took place no later than July 29, 1981, which is the date indicated on the subsequently occurring page PX-19-54.

In Sz-40 (PR 187, PX-19-56), the product produced from Sz-11 was solubilized in water with beta-carotene. The experiment took place no later than September 1, 1981, which is the date indicated on the subsequently occurring page PX-19-66.

The product Sz-11 is described as white, foam like and no homogenous composition of product. There is no indication that crystals are formed. There is no indication whether the product of Sz-11 contained cyclodextrin derivatives. The solubility of the substance in water was reported. Pitha directed us to pages Sz-32, Sz-36 and Sz-40 which establishes that a portion of the product from Sz-11 was solubilized in water with a drug. Dr. Szente's declaration states the product of Sz-11 was amorphous and solubilized in water with

various drugs.<sup>41</sup> We have not been directed to evidence which establishes that the product Sz-11 contained cyclodextrin derivatives as required by the count. Thus, the products Sz-32, Sz-36 and Sz-40, all of which incorporate Sz-11, fail to describe an embodiment which falls within the scope of the count.

**c. The product Sz-20 and products including Sz-20**

In Sz-20 (PR 173-174 reproduction of PX-19-30), the experiment took place no later than July 2, 1981, which is the date indicated on the subsequently occurring page PX-19-37. The oxymercuration-demercuration of hydroxypropyl-beta-cyclodextrin was described by the experiment. The substance is described as a light yellow, glass powder like substance with no crystals. There is no indication whether the product of Sz-28 contained more than one cyclodextrin derivative. The solubility of the substance in water at 20°C is reported to be 15.8 g/100ml.

In SZ-32 (PX-19-44), the product produced from Sz-20 was solubilized in water with Vitamin A (retinol) and Vitamin D<sub>3</sub>. The experiment took place no later than July 14, 1981, which is the date indicated on the next occurring page PX-19-45.

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<sup>41</sup> PR page 182, lines 9-14, page 185, lines 4-10, page 185 line 19 to page 186 line 6, and page 187, lines 4-9.

In Sz-34 (PR 185, PX-19-46), the product produced from Sz-20 was solubilized in water with beta-ionone. The experiment took place on July 19, 1981, which is the date indicated on PX-19-46.

The product Sz-20 is described as a light yellow, glass powder like substance with no crystals. The solubility of the substance in water at 20°C is reported to be 15.8 g/100ml. Pitha directed us to pages Sz-32 and Sz-34 which establishes that a portion of the product from Sz-20 was solubilized in water with a drug. Dr. Szente's declaration states the product of Sz-20 was amorphous and solubilized in water with various drugs.<sup>42</sup> We have not been directed to evidence which establishes that the product Sz-20 contained cyclodextrin derivatives as required by the count. The products Sz-32 and Sz-34, both of which incorporate Sz-20, fail to describe an embodiment which falls within the scope of the count.

**d. The product Sz-28 and products including Sz-28**

In Sz-28 (PR 184, PX-19-39), the experiment took place no later than July 6, 1981, which is the date indicated on the subsequently occurring page PX-19-41. The oxymercuration-demercuration of HPBCD with dioxane was described by the

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<sup>42</sup> PR page 172, line 19 to page 176 line 19, page 184 lines 15-17, and page 185, lines 4-12.

experiment. The substance is described as a very hygroscopic white powder. There is no indication whether crystals were formed. There is no indication whether the product of Sz-28 contained more than one cyclodextrin derivative. The solubility of the substance in water at 20°C is reported to be 16g/100ml.

In Sz-36 (PR 186, PX-19-49), the product produced from Sz-28 was solubilized in water with beta-carotene. The experiment took place no later than July 29, 1981, which is the date indicated on the subsequently occurring page PX-19-54.

In Sz-40 (PR 187, PX-19-56), the product produced from Sz-28 was solubilized in water with beta-carotene. The experiment took place no later than September 1, 1981, which is the date indicated on the subsequently occurring page PX-19-66.

In Sz-41 (PR 187, PX-19-57), the product produced from Sz-28 was solubilized in water with Vitamin D<sub>3</sub>. The experiment took place no later than September 1, 1981, which is the date indicated on the subsequently occurring page PX-19-66.

The product Sz-28 has been described as a white powder and very hygroscopic. The solubility of the Sz-28 substance

in water at 20°C is reported to be 16g/100ml. There is no indication whether the product of Sz-28 contained cyclodextrin derivatives. Pitha directed us to pages Sz-36, Sz-40 and Sz-41 which establishes that a portion of the product from Sz-28 was solubilized in water with a drug. Dr. Szente's declaration states the product of Sz-28 was amorphous and solubilized in water with various drugs.<sup>43</sup> We have not been directed to evidence which establishes that the product Sz-28 contained cyclodextrin derivatives as required by the count. The products Sz-36, Sz-40 and Sz-41, all of which incorporate Sz-28, do not describe an embodiment which falls within the scope of the count.

**e. The product Sz-42**

In Sz-42 (PR 187, PX-19-58), the experiment took place no later than September 1, 1981, which is the date indicated on the subsequently occurring page PX-19-66. HPBCD was said to be formed during the experiment. The substance is described as white solid substance. There is no indication whether crystals were formed. The solubility of the substance in water at 20°C is reported to be 16g/100ml.

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<sup>43</sup> PR page 184, lines 4-15, page 185 line 19 to page 186 line 10, and page 187, lines 4-15.

Pitha has not directed us to evidence which establishes that the product from Sz-42 comprised cyclodextrin derivatives or was solubilized in water with a drug. Thus, this experiment alone fails to meet all the requirements of the count.

**f. The product Sz-111**

In Sz-111 (PR 189, PX-20-52), the experiment took place no later than February 22, 1982, which is the date indicated on the request for analytical services PX-20-51. The reaction product of BCD and epichlorohydrin was said to be formed during the experiment. The substance was freeze dried to form a white powder substance. There is no indication whether crystals were formed. The solubility of the substance in water at 20°C is reported to be 13-14 g/100ml.

Pitha has not directed us to evidence which establishes that the product from Sz-111 comprised cyclodextrin derivatives or was solubilized in water with a drug. Dr. Szente's declaration states the product of Sz-111 was amorphous and a good solubilizer of lipophilic drugs.<sup>44</sup> However, we have not been directed to evidence which exhibits (1) Sz-111 contained cyclodextrin derivatives or (2) the

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<sup>44</sup> PR page 177, lines 2-11.

solubilization of drugs with the Sz-111 product. Thus, the Sz-111 product alone fails to describe an embodiment within the scope of the count.

Upon review of Pitha's brief, Dr. Pitha's declaration, Dr. Szente's declaration, testimony and laboratory notebook, we have determined that Pitha has not established a *prima facie* reduction to practice of an embodiment falling within the scope of the count. The products Sz-11, Sz-20 and Sz-28, appearing in Dr. Szente's laboratory notebook, have been described as forming a cyclodextrin derivative. We have not been directed to evidence which exhibits that these products comprise cyclodextrin derivatives. Consequently, pages Sz-32, Sz-34, Sz-36, Sz-40 and Sz-41, which describe the solubilization of a drug with the product from Sz-11, Sz-20 or Sz-28, all fail to disclose the process for producing products which meet all of the limitations of the count.

ORDER

Upon consideration of the record of this interference, it  
is-

ORDERED that judgment on priority as to Count 3 is  
awarded against junior party PITHA;

FURTHER ORDERED that junior party PITHA is not entitled  
to a patent containing claims 1-28, which correspond to Count  
3;

FURTHER ORDERED that, based on the record before us,  
senior party MULLER is entitled to a patent containing claims  
1-11 and 22-36 which correspond to Count 3;

RICHARD E. SCHAFER  
Administrative Patent Judge

RICHARD TORCZON  
Administrative Patent Judge

JEFFREY T. SMITH  
Administrative Patent Judge

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