

75 Day Report

**75- Day Notification for New Dietary Ingredient (ABPC®)**

**I. Name and Address**

A. Manufacturer

JAPAN APPLIED MICROBIOLOGY RESEARCH INSTITUTE LTD.  
326 Otoguro, Tamaho-cho  
Nakakoma-gun, Yamanashi  
409-3812 JAPAN

B. Distributor

Obiken New York, Inc.  
119 West Broadway  
New York, NY 10013

In Japan, the official name of the manufacturer is Kabushikikaisha Oubiken. The name in English is JAPAN APPLIED MICROBIOLOGY RESEARCH INSTITUTE LTD.

Kabushikikaisha means Company, Limited, Incorporated, or Corporation. The words, Oubiken and Obiken are pronounced the same in Japanese but have different pronunciations in English. In the past, both "ou" and "o" were used interchangeably, but now there is a tendency to use "o" instead of "ou".

In legal documents JAPAN APPLIED MICROBIOLOGY RESEARCH INSTITUTE LTD, or JAMRI, is used. As the name of Oubiken or Obiken has become more familiar to vendors overseas, the manufacturer often uses "Obiken" for business contacts. For example, our affiliate in the U.S. is Obiken New York, Inc.

**II. Name of the New Dietary Ingredient**

Common or Usual Name: Enzyme-treated *Agaricus blazei* Murrill Mycelia

Trade Name: ABPC® (Agaricus Blazei Practical Compound)

75-day Notification Submission (continued)

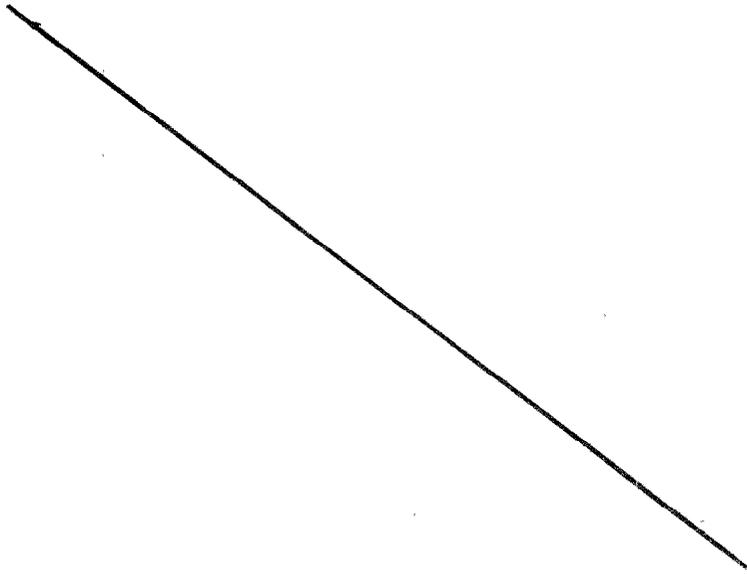
**III. Description of the New Dietary Supplement**

A. Identity

Agaricus Blazei Practical Compound (ABPC<sup>®</sup>) is the Enzyme-treated *Agaricus blazei* Murrill mycelia. ABPC<sup>®</sup> is a freeze-dried mixture of the mycelia from *Agaricus blazei*

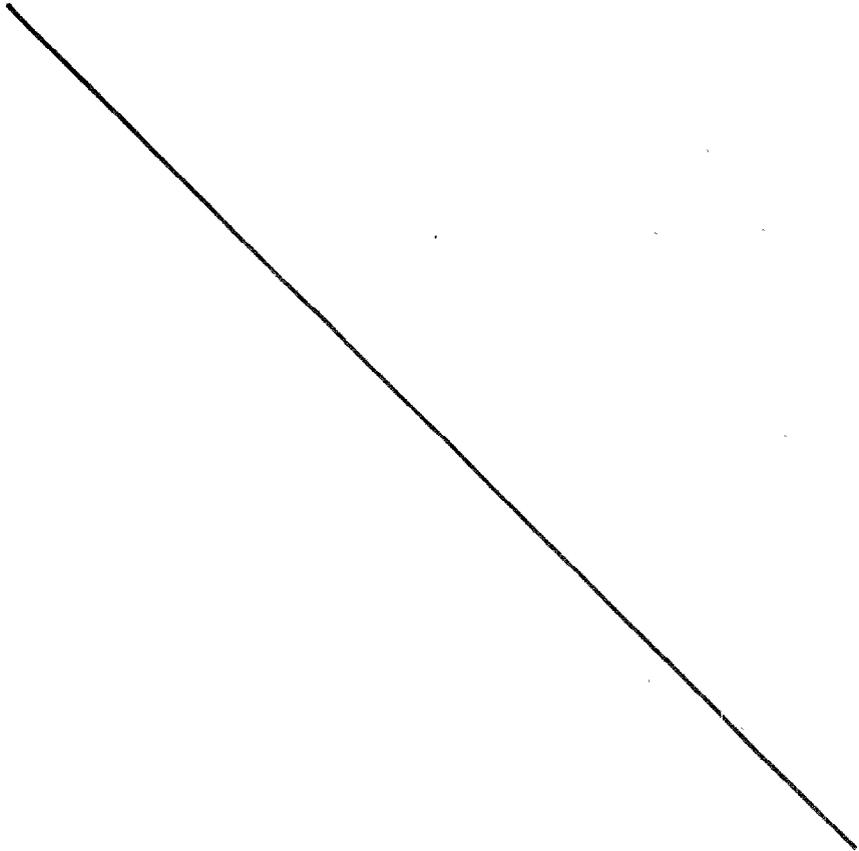
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B. Composition and Specifications for ABPC<sup>®</sup>- FD



75-day Notification Submission for ABPC® (continued)

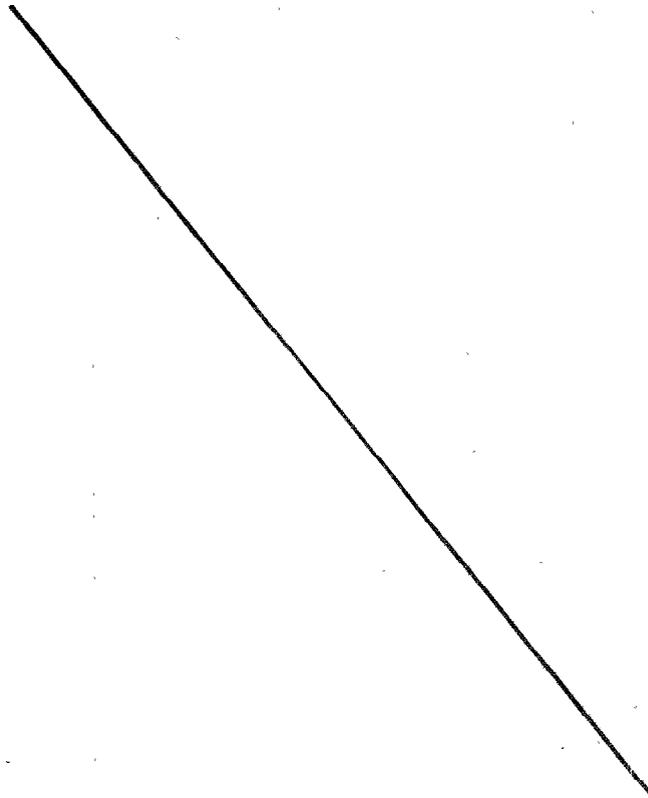
III. Description of the New Dietary Supplement (continued)



75-day Notification Submission for ABPC® (continued)

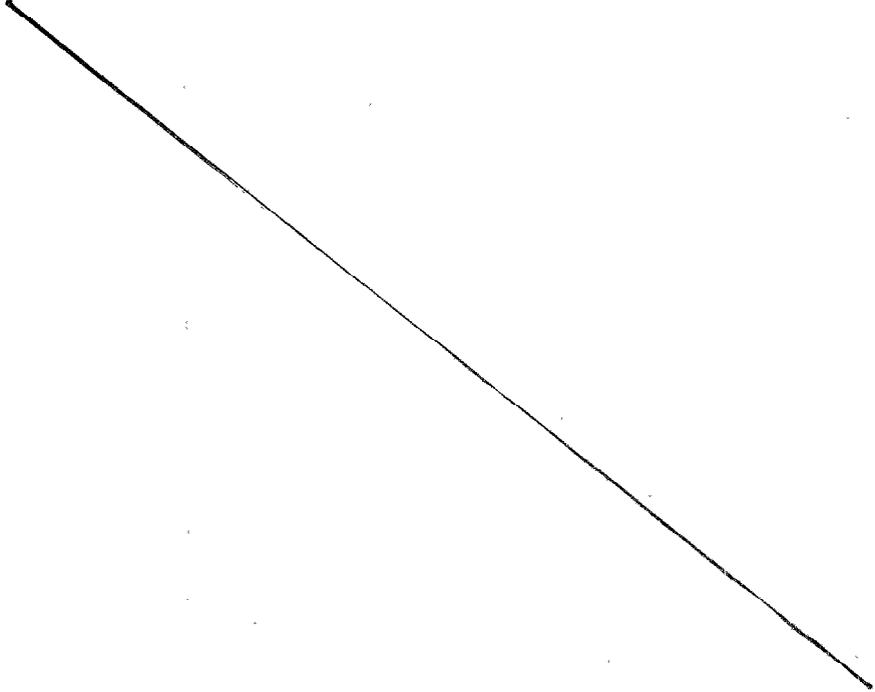
III. Description of the New Dietary Supplement (continued)

C. Molecular Weight Distribution of  $\beta$ -glucans



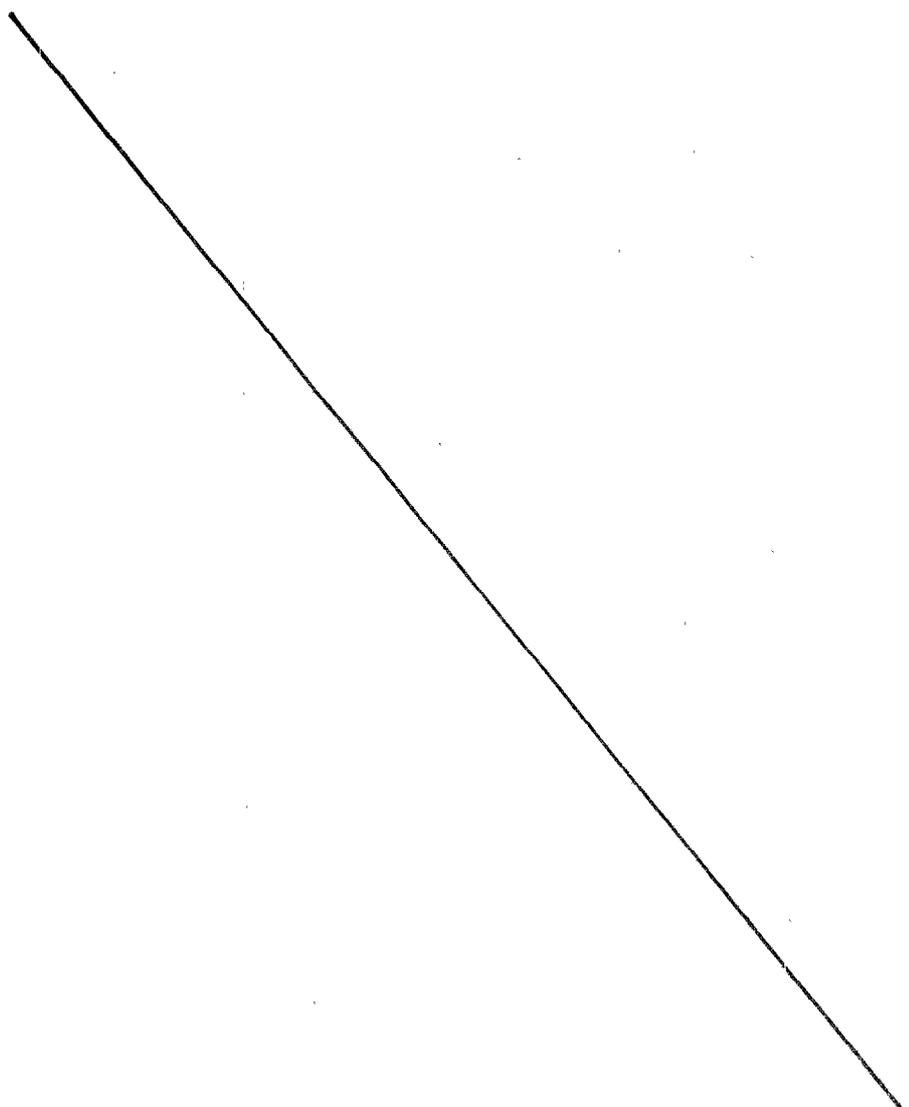
75-day Notification Submission for ABPC® (continued)

III. Description of the New Dietary Supplement (continued)



75-day Notification Submission for ABPC® (continued)

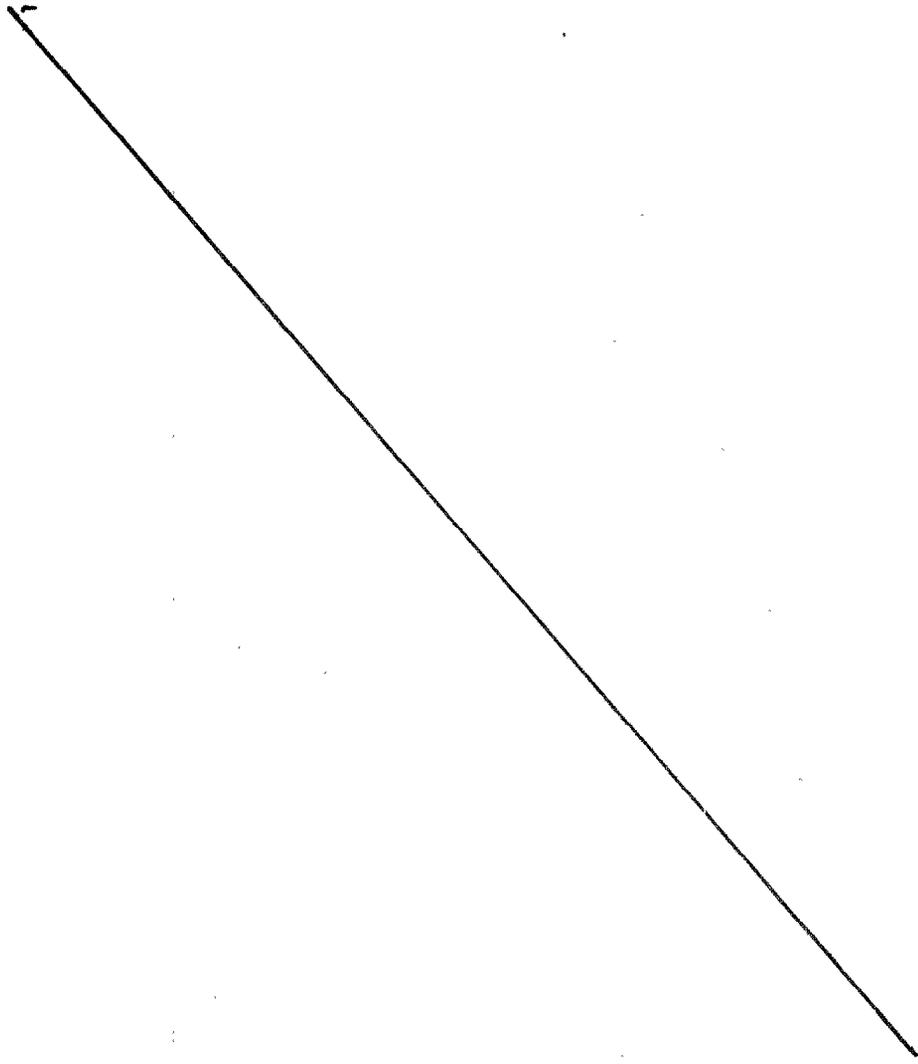
III. Description of the New Dietary Supplement (continued)



75-day Notification Submission for ABPC® (continued)

III. Description of the New Dietary Supplement (continued)

D. Manufacturing Process [CONFIDENTIAL]



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75-day Notification Submission for ABPC® (continued)

III. Description of the New Dietary Supplement (continued)

E. Level of Use

1-2 g/day (1-2 packets of granules or 4-8 tablets)

The commercial product is sold in a box containing 90 packets of ABPC®. Each packet contains 1.0 g of ABPC® granules. Tablets of ABPC® is sold with 240 tablets, each tablet contains 0.25 g ABPC®.

F. Conditions of Use

Daily use for lifetime except pregnant women, lactating women, or infant should not take this product.

IV. **History of Use**

A. Prior Use

An American mycologist, W. A. Murrill first identified this mushroom on the lawn of a Mr. R. W. Blaze in Gainesville, Florida [Murrill 1945, Appendix 9]. Dr. Paul Stamets provided the first description in USA about the history of *Agaricus blazei* Murrill in his book, titled "Growing Gourmet and Medicinal Mushrooms" third edition published in 2000 [Stamets 2000, Appendix 10]. He stated that it was known locally in Brazil and introduced to Japanese coffee growers in Brazil. Japanese mycologists pioneered its cultivation and currently, China, Brazil and Japan have established cultivation centers for this mushroom. The primary market for *Agaricus blazei* is Japan, where it is called Himematsutake and has an excellent reputation as one of the most expensive of all edible medicinal mushrooms. Dr. Stamets stated that commercial cultivation in the United States has just recently begun. Other common names include Royal Sun Agaricus, Himematsutake, Kawariharatake, Cogmelo de Deus (mushroom of God), Murrill's Agaricus or ABM, King Agaricus, and Almond Portobello.

Dr. I. Iwade, former professor of Mie University in Japan, introduced *Agaricus blazei* in Japan in 1985 [Iwade 1985, Appendix 3]. In the summer of 1965, Dr. Iwade received samples of the wild strain from a friend in Brazil and succeeded in standardizing a cultivation method to meet climate and other conditions in Japan. He has confirmed that this strain is same as *Agaricus blazei* Murrill. The scientific name in Japanese is "Karariharatake", and the common name in Japanese is

75-day Notification Submission for ABPC® (continued)IV. History of Use (continued)

“Himematsutake.” It has a wide range of applications in food and as a medicinal mushroom.

Historically Japanese and Chinese have been eating various kinds of mushrooms. *Agaricus blazei* Murrill is one of many mushrooms currently consumed in Japan and China. Although there are no precise statistics in Japan about the quantity consumed by each person, the Japanese have consumed a wide variety of mushrooms for over 1,000-1,500 years. As ingredients of food, it is estimated that the Japanese eat about 5-100 grams of mushrooms per meal 5-30 times a month.

JAMRI has used the results of searches for *Agaricus blazei* Murrill in the CAB, BIOSIS and AGRICOLA databases as the source of relevant articles referenced in this section.

B. Fruiting Body vs. Mycelia

Mushrooms have been consumed by many cultures for centuries for nutritional as well as for medicinal purposes [Manzi and Pizzoferrato 2000, Appendix 5; Mattila et al. 2001, Appendix 6; and Dikeman et al. 2005, Appendix 2]. Mushroom consumption is considered to be healthy because they are rich in dietary fiber, protein, and minerals but low in calories [Manzi and Pizzoferrato 2000, Appendix 5].

Fruiting bodies of some mushroom are expensive and scarce, so prepared food products are currently being formulated from the mycelia grown in submerged culture [Chang et al. 2001, Appendix 1]. These researchers examined the non-volatile taste components in the mycelia of three medicinal mushrooms, *Agaricus blazei*, *Antrodia camphorata* and *Cordyceps militaris*. They found that all mycelia were high in carbohydrate content, with *A. blazei* carbohydrate composition about 42%. This value was lower than the amount normally found in common mushroom mycelia (53% and 59%).

Manzi and Pizzoferrato [2000, Appendix 5] reported that  $\beta$ -glucan concentration for 8 edible mushrooms ranged from 0.22 to 0.53 g/ 100 g on a dry basis.

75-day Notification Submission for ABPC® (continued)**V. Safety of ABPC®**

The various studies discussed below were sponsored by JAMRI. A final report for each study is provided in Japanese with an English translation provided as well as a summary by a United States board certified toxicologist.

**A. In vitro Studies**

ABPC® was not considered to be mutagenic in the Ames (reverse mutation) assay [Miwa 2004a, Appendix 7]. ABPC® was not considered to be clastogenic in the *In Vitro* Chromosomal Aberration Test on Cultured Chinese Hamster Ovary Cells [Miwa 2004b, Appendix 8].

**B. Acute Animal Study**

ABPC® was considered nontoxic and not lethal at acute oral dosages of 5,000 mg/kg when administered by gavage to rats (CD(SD)IGS) in a single dose oral toxicity test [Koike 2004, Appendix 4].

**C. Subchronic Animal Study**

A 91-day rat feeding study was conducted in accordance with GLPs except that the procedures for analyzing the concentration and the stability may not have followed GLPs. The protocol deviations had no adverse impact on the study.

The study was conducted to determine potential toxicity of ABPC® when administered orally for 91 days to male and female rats (10/sex/group) at dosages of 0, 250, 500 or 1,000 mg/kg. Animals were observed daily before and after dosing. Body weights, and food consumption were measured weekly. Urinalysis, hematology and clinical chemistry parameters were examined at the end of the study. Organ weights and a gross necropsy was performed after the last dose.

None of the animals died. Based a 91 day rat feeding study, ABPC® was not lethal to rats (Crj:CD(SD)IGS) at oral dosages (gavage) of up to 1,000 mg/kg. Test article-related changes included decreased body weights at the lowest dosage, and albumin and A/G ratios at the highest dosage. JAMRI concludes that the NOAEL is 1,000 mg/kg [Koike 2005, Appendix 12].

75-day Notification Submission for ABPC® (continued)**VI. Appendices**

1. Chang, Hui-Ling, et al., "Non-volatile Taste Components of *Agaricus blazei*, *Antrodia camphorata* and *Cordyceps militaris* mycelia" *Food Chemistry* **74**: 203-207 (2001)
2. Dikeman, Cheryl, et al., "Effects of Stage of Maturity and Cooking on the Chemical Composition of Selected Mushroom Varieties," *J. Agric. Food Chem.*, **53**:1130-1138 (2005)
3. Iwade, I., ed., "Kinokorunio Baiyouhou" (The mushrooms and cultivation method) revised fifth edition, Tikyusya, Japan, pp. 342-347 (1985) in Japanese with English translation.
4. Koike, Tsuneo, "Single Dose Oral Toxicity Test of ABPC in Rats," Nihon Bioresearch Inc. Hashima Laboratory, Study Number 402323, July 28, 2004, in Japanese with an English translation of the Final Report and an English Summary.
5. Manzi, Pamela, Pizzoferrato, Laura, "Beta-glucans in edible mushrooms," *Food Chemistry* **68**:315-318 (2000).
6. Mattila, Pirjo, et al., "Contents of Vitamins, Mineral Elements, and Some Phenolic Compounds in Cultivated Mushrooms," *J. Agric. Food Chem.* **49**:2343-2348 (2001).
7. Miwa, Yoshihisa, "Reverse Mutation Test of ABPC on Bacteria (Ames Test)," Nihon Bioresearch Inc. Hashima Laboratory Study Number 900823, June 10, 2004a, in Japanese with English translation of Final Report and an English Summary.
8. Miwa, Yoshihisa, "In Vitro Chromosomal Aberration Test of ABPC on Cultured Chinese Hamster Ovary Cells," Nihon Bioresearch Inc. Hashima Laboratory Study Number 970224, August 5, 2004b in Japanese with English translation of Final Report and an English Summary.
9. Murrill, William A., "New Florida Fungi," *Quart. Jour. Fla. Acad. Sci.*, **8**:175, 193 (1945).
10. Stamets, Paul, ed., *Growing Gourmet and Medicinal Mushrooms*, third edition, Ten Speed Press, Berkeley Toronto, Chapter 21, "Growth Parameters for Gourmet and Medicinal Mushroom Species," pp. 201, 208 - 216, (2000).
11. Wako Pure Chemical Industries, Ltd., Wako Autokit Glucose Enzymatic Method (Mutarotase-GOD), undated (best copy available).

75-day Notification Submission for ABPC® (continued)

VI. Appendices. (continued)

12. Koike, Tsuneo, "The Repetitive Medication Toxicity Examination by the Oral Medication During 91 Days Using the Rat of ABPC," Nihon Bioresearch Inc. Hashima Laboratory Study Number 500324, Final Report through Tables with an English translation of Final Report and an English Summary [Vol. 2 of 3].
13. **Continued:** Appendices of Koike, Tsuneo, "The Repetitive Medication Toxicity Examination by the Oral Medication During 91 Days Using the Rat of ABPC," Nihon Bioresearch Inc. Hashima Laboratory Study Number 500324, and Protocol and Amendments to Protocol, January 25, 2005 in Japanese with an English translation of Protocol [Vol. 3 of 3]

**VII. Authorized Representative**

Mr. Takeru Suyama, Director  
JAPAN APPLIED MICROBIOLOGY RESEARCH INSTITUTE LTD.