# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

**21-660**

# ADMINISTRATIVE DOCUMENTS

American BioScience, Inc.

**Patent Certification**

**Paragraph II Certification**

In the opinion and to the best knowledge of American BioScience, Inc., there are no unexpired patents that claim the listed drug [Taxol® (paclitaxel) Injection] referred to in this application or that claim a use of the listed drug.

MG Clark

Mitchall G. Clark
Vice President, Regulatory Affairs

11/6/03

Date

2730 Wilshire Blvd., Suite 110 Santa Monica, California 90403 Tel: (310) 883-1300 Fax: (310) 998-8553

Department of Health and Human Services
Food and Drug Administration

# PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT

***For Each Patent That Claims a Drug Substance (Active Ingredient), Drug Product (Formulation and Composition) and/or Method of Use***

Form Approved: OMB No. 0910-0513
Expiration Date: 07/31/06
*See OMB Statement on Page 3.*

NDA NUMBER
21-660

NAME OF APPLICANT / NDA HOLDER
American BioScience, Inc.

***The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.***

TRADE NAME (OR PROPOSED TRADE NAME)
Abraxane*TM* (*nab* Paclitaxel) for Injectable Suspension

| ACTIVE INGREDIENT(S) | STRENGTH(S) |
|---|---|
| Paclitaxel | 100 mg/vial |

DOSAGE FORM
Sterile powder for injectable suspension

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4).
Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the only information relied upon by FDA for listing a patent in the Orange Book.

**For hand-written or typewriter versions (only) of this report:** If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

***FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.***

***For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.***

## 1. GENERAL

| a. United States Patent Number | b. Issue Date of Patent | c. Expiration Date of Patent |
|---|---|---|
| 6,537,579 | 3/25/2003 | 2/22/2013 |

d Name of Patent Owner
American BioScience, Inc.

Address *(of Patent Owner)*
2730 Wilshire Boulevard, Suite 110

City/State
Santa Monica, CA

| ZIP Code | FAX Number *(if available)* |
|---|---|
| 90403 | 310 998 8553 |
| **Telephone Number** | **E-Mail Address *(if available)*** |
| 310 883 1300 | |

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

N/A

Address *(of agent or representative named in 1.e.)*

City/State

| ZIP Code | FAX Number *(if available)* |
|---|---|
| **Telephone Number** | **E-Mail Address *(if available)*** |

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above? ☐ Yes ☒ No

g If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date? ☐ Yes ☐ No


PSC Media Arts (301) 443-1090 EF

***For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.***

**2. Drug Substance (Active Ingredient)**

| | | |
|---|---|---|
| 2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? | ☐ Yes | ☒ No |
| 2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? | ☐ Yes | ☒ No |
| 2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). | ☐ Yes | ☐ No |
| 2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3. | | |
| 2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) | ☐ Yes | ☒ No |
| 2.6 Does the patent claim only an intermediate? | ☐ Yes | ☒ No |
| 2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) | ☐ Yes | ☐ No |

**3. Drug Product (Composition/Formulation)**

| | | |
|---|---|---|
| 3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? | ☐ Yes | ☒ No |
| 3.2 Does the patent claim only an intermediate? | ☐ Yes | ☒ No |
| 3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) | ☐ Yes | ☐ No |

**4. Method of Use**

***Sponsors must submit the information in section 4 separately for each patent claim claiming a method of using the pending drug product for which approval is being sought. For each method of use claim referenced, provide the following information:***

| | | |
|---|---|---|
| 4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement? | ☒ Yes | ☐ No |
| 4.2 Patent Claim Number *(as listed in the patent)*<br>1-6, 10-15, 22-27, 30-42, 49-51 | Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? ☒ Yes | ☐ No |

| | |
|---|---|
| **4.2a** If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product. | Use: *(Submit indication or method of use information as identified specifically in the approved labeling.)*<br>Claims 10-15 - Abraxane (*nab* paclitaxel) for injectable suspension is a nanoparticle albumin-bound (*nab*) form of paclitaxel. *See Description.* Each single-use vial contains 100 mg of paclitaxel and approximately 900 mg of human albumin. *See Description.* This formulation is free from solvents. *See Description.* Abraxane (*nab* paclitaxel) for injectable suspension is indicated for the treatment of [redacted] breast cancer. *See Indication.* Abraxane does not contain Cremophor-EL, therefore hypersensitivity reactions to Abraxane are rare. *See Adverse Reactions: Hypersensitivity Reactions (HSRs).* For metastatic breast cancer, Abraxane (*nab* paclitaxel for injectable suspension) at a dose of 260 mg/m$^2$ administered intravenously over 30 minutes every 3 weeks has been shown to be effective. *See Dosage and Administration.*<br><br>Claims 22-27, 32-34, 39-42, and 49-51 - Abraxane (*nab* paclitaxel) for injectable suspension is a nanoparticle albumin-bound (*nab*) form of paclitaxel. *See Description.* Abraxane is supplied as a white to yellow, sterile, lyophilized powder intended for reconstitution with 0.9% Sodium Chloride Injection, USP prior to intravenous infusion. *See Description.* Each single-use vial contains 100 mg of paclitaxel and approximately 900 mg of human albumin. *See Description.* Abraxane (*nab* paclitaxel) for injectable suspension is indicated for the treatment of [redacted] breast cancer. *See Indication.* For metastatic breast cancer, Abraxane (*nab* paclitaxel for injectable suspension) at a dose of 260 mg/m$^2$ administered intravenously over 30 minutes every 3 weeks has been shown to be effective. *See Dosage and Administration.* Abraxane is supplied as a sterile lyophilized powder for reconstitution before use. *See Dosage and Administration: Preparation for Intravenous Administration.* Reconstitute each vial by injecting 20 mL of 0.9% Sodium Chloride Injection, USP. *See Dosage and Administration: Preparation for Intravenous Administration.* Each mL of the reconstituted nanoparticle formulation will contain 5 mg/mL paclitaxel. *See Dosage and Administration: Preparation for Intravenous Administration.*<br><br>Claim 30 - Abraxane (*nab* paclitaxel) for injectable suspension is a nanoparticle albumin-bound (*nab*) form of paclitaxel. *See Description.* Each single-use vial contains 100 mg of paclitaxel and approximately 900 mg of human albumin. *See Description.* This formulation is free from solvents. *See Description.* Abraxane (*nab* paclitaxel) for injectable suspension is indicated for the treatment of [redacted] breast cancer. *See Indication.* Neutropenia, the most important hematologic toxicity, was dose dependent and was generally rapidly reversible. *See Adverse Reactions: Hematologic.* Grade 4 (<500 cells/mm$^3$) neutropenia occurred in 12% of patients treated with Abraxane. *See Adverse Reactions: Hematologic.* Among patients treated in the Phase 3 metastatic breast cancer study, neutrophil counts declined below 500 cells/mm$^3$ (Grade 4) in 9% of the patients treated with a dose of 260 mg/m$^2$ compared to 22% in patients receiving Cremophor-based paclitaxel injection at a dose of 175 mg/m$^2$. *See Adverse Reactions: Hematologic.* Among patients Abraxane does not contain Cremophor-EL, therefore hypersensitivity reactions to Abraxane are rare. *See Adverse Reactions: Hypersensitivity Reactions (HSRs).* For metastatic breast cancer, Abraxane (*nab* paclitaxel for injectable suspension) at a dose of 260 mg/m$^2$ administered intravenously over 30 minutes every 3 weeks has been shown to be effective. *See Dosage and Administration.* Abraxane is supplied as a sterile lyophilized powder for reconstitution before use. *See Dosage and Administration: Preparation for Intravenous Administration.* Reconstitute each vial by injecting 20 mL of 0.9% Sodium Chloride Injection, USP. *See Dosage and Administration: Preparation for Intravenous Administration.*<br><br>Claim 31 - Abraxane (*nab* paclitaxel) for injectable suspension)is a nanoparticle albumin-bound (*nab*) form of paclitaxel. *See Description.* Each single-use vial contains 100 mg of paclitaxel and approximately 900 mg of human albumin. *See Description.* Abraxane (*nab* paclitaxel) for injectable suspension is indicated for the treatment of [redacted] breast cancer. *See Indication.* In general, the frequency and severity of neurologic manifestations were dose-dependent in patients receiving single-agent Abraxane. *See Adverse Reactions: Neurologic.* Peripheral neuropathy was observed in 64% of all patients (10% severe). *See Adverse Reactions: Neurologic.* Peripheral neuropathy was the cause of Abraxane discontinuation in 13/366 (4%) of all patients. *See Adverse Reactions: Neurologic.* Sensory symptoms have usually improved or resolved within 22 days of interrupting Abraxane therapy. *See Adverse Reactions: Neurologic.* Pre-existing neuropathies resulting from prior therapies are not a contraindication for Abraxane therapy. *See Adverse Reactions: Neurologic.* No incidences of grade 4 peripheral neuropathies were reported in the clinical trial. *See Adverse Reactions: Neurologic.* Other than peripheral neuropathy, serious neurologic events following Abraxane administration have been rare (<1%) and have included ischemic stroke, metabolic encephalopathy, confusion, dizziness/lightheadedness, and mood alteration/depression. *See Adverse Reactions: Neurologic.* For metastatic breast cancer, Abraxane (*nab* paclitaxel for injectable suspension) at a dose of 260 mg/m$^2$ administered intravenously over 30 minutes every 3 weeks has been shown to be effective. *See Dosage and Administration.* Abraxane is supplied as a sterile lyophilized powder for reconstitution before use. *See Dosage and Administration: Preparation for Intravenous Administration.* Reconstitute each vial by injecting 20 mL of 0.9% Sodium Chloride Injection, USP. *See Dosage and Administration: Preparation for Intravenous Administration.* |

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