DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Reference No. 06-HFD-45-0603

Mr. Terry A. Colip, Chief Financial Officer
Cell Point, L.L.C.
7120 E. Orchard Road, Suite 350
Centennial, Colorado 80111

Dear Mr. Colip:

Between October 18 and November 9, 2004, Ms. Teena Aiken, representing the United States (U.S.) Food and Drug Administration (FDA), conducted an investigation and met with you to review the responsibilities of Cell Point, LLC (Cell Point), as sponsor of two studies conducted at [ ] in which human subjects received investigational drug products. The inspection of Cell Point was prompted by information that the investigational drug product used in the [ ] study was prepared from raw materials that were of human placenta origin and potentially infectious. The purpose of this inspection was to determine whether you were in compliance with the regulations governing the use of investigational drugs and the conduct of clinical trials contained in Title 21 of the Code of Federal Regulations (CFR), Part 312. The inspection included the following two studies:

Protocol [ ] "Biodistribution and Pharmacokinetics of [ ] in Patients with Breast Cancer," of the investigational new drug [ ] and

Protocol [ ] "Comparison of [ ] and [ ] PET Scans for (1) the Evaluation of Patients Suspected of Having Persistent/Recurrent Squamous Cell Carcinoma of the Larynx after Definitive Treatment with Radiation Therapy and (2) the Evaluation of Primary Lung Cancer Patients," of the investigational new drug [ ] conducted under Investigational New Drug Application (IND) [ ]

Ms. Aiken presented and discussed with you the items listed on the Form FDA 483, Inspectional Observations, at the conclusion of the inspection. This inspection is a part of FDA's Bioresearch Monitoring Program, which includes inspections designed to evaluate

the conduct of research and to ensure that the rights, safety, and welfare of the human subjects of those studies have been protected.

From our review of the establishment inspection report, the documents submitted with the report, and Cell Point's February 16, 2005 written response from Mr.[ ] Chief Technology Officer, to FDA, we conclude that Cell Point failed to adhere to the applicable statutory requirements and FDA regulations governing sponsor responsibilities in the conduct of clinical investigations. We wish to emphasize the following:

1. **Cell Point failed to conduct the study under an investigational new drug (IND) application [21 CFR 312.2(a); 21 CFR 312.20].**

   FDA regulations require that a sponsor submit an IND to FDA if the sponsor intends to conduct a clinical investigation with an investigational new drug [21 CFR 312.20(a)] and have an IND in effect before the investigational drug is used in a clinical investigation [21 CFR 312.40(a)(1)]. Our investigation indicates that you initiated and were responsible for the conduct of a clinical investigation intended to evaluate the use of[ ] an investigational new drug, as a diagnostic agent, and that you did not have an IND in effect when the study drug was administered to study subjects.

   Cell Point was the sponsor for a clinical investigation (Protocol[ ]at the [ ]that studied[ ]in ten human subjects to evaluate, among other things, "the use of[ ]for the detection and imaging of treatment-related apoptosis in patients with [primary breast cancer]." In Cell Point's written response of February 16, 2005, Mr. [ ]acknowledged that Cell Point served as sponsor for protocol[ ]and should have had an IND in effect prior to the conduct of the study.

   Mr.[ ]also stated that Cell Point originally believed that the study could be conducted under 21 CFR Part 361 (Prescription Drugs for Human Use Generally Recognized as Safe and Effective and Not Misbranded: Drugs Used in Research) following review and approval by the[ ]Institutional Review Board (IRB) and Radioactive Drug Research Committee (RDRC) and, therefore, did not require an IND. Protocol[ ]fails to meet the criteria for studies to be conducted under 21 CRF part 361. Specifically:

   - Studies intended to evaluate the immediate diagnostic use of a drug are excluded from 21 CFR part 361. Protocol[ ]was intended to evaluate the ability of[ ]to detect treatment-related apoptosis in women being treated for primary breast cancer (an immediate diagnostic purpose within the meaning of 21 CFR 361.1(a)).
   - For studies under 21 CFR part 361, the amount of active ingredient must be known not to cause any clinically detectable pharmacological effect in humans (21 CFR 361.1(b)(2)). There was no documentation to indicate that the proposed dose of[ ](75 micrograms) would not

induce an immunological response in humans.

- For studies under 21 CFR part 361, the dose administered must be based on data from the published literature or other valid human studies (21 CFR 361.1(d)(2)). There is no documentation to indicate that pharmacological dose calculations were made based on data from the published literature or other valid human studies.
- For studies under 21 CFR 361, the radioactive drug used in the research must meet appropriate chemical, pharmaceutical, radiochemical, and radionuclidic standards of identity, strength, quality, and purity as needed for safety and be prepared in sterile and pyrogen-free form [21 CFR 361.1(d)(6)]. You failed to ensure that the[ ]which was derived from human biological material, was appropriately processed or tested to ensure that it was free of transmissible human pathogens and that it was in a sterile and pyrogen-free form.

FDA's primary objectives in reviewing an IND are to assure the safety and rights of subjects and to help assure that the quality of the scientific evaluation of drugs is adequate to permit an evaluation of the drug's effectiveness and safety (21 CFR 312.22). Your protocol[ ]failed to consider factors that you would have been required to address in an IND submission (21 CFR 312.23) and your failure to consider these factors may have threatened the rights and safety of your subjects. We note that:

a. Cell Point failed to provide appropriate chemistry, manufacturing, and control information in order to ensure the proper identification, quality, purity, and strength of the investigational new drug, as required by 21 CFR 312.23(a)(7)(i).

The relatively short radioactive half-life of[ ] precluded completion of sterility testing prior to test article administration. For this reason, Cell Point should have ensured that all materials used in producing the investigational new drug were sterile, and that the investigational new drug itself was produced in an aseptic environment. Our investigation determined that sterility testing of the components was not done, and that[ ]was not produced in an aseptic manner.

In addition, our inspection found no evidence that[ ]testing was done prior to[ ]administration. We note that the half-life of[ ]was sufficient to permit[ ]testing (for example, by the[ ]detection method) before the investigational new drug was administered to humans. We acknowledge that batch samples of[ ]were sent to an independent facility for[ ]testing. However, these tests were performed only after the ten study subjects had received the

investigational new drug.

Cell Point's February 16, 2005 response letter to FDA stated that Cell Point had completed the sterility and [ ] tests on each sample before sending them to the clinic for administration to study subjects. However, there was no documentation available on inspection to support Cell Point's claim that the testing was done prior to administration.

b. Cell Point failed to take measures to minimize risks to human subjects as required by 21 CFR 312.23(a)(6)(iii)(*g*).

Our investigation determined that Cell Point failed to ensure that the investigational new drug was free of transmissible human pathogens, and failed to assess the immunological effect of the [ ] Specifically, the [ ] protein used to prepare the [ ] investigational new drug was derived from human placenta and was labeled "not for drug, household or other uses." The Material Safety Datasheet (MSDS) for [ ] stated, "Biohazard... Handle as if capable of transmitting infectious agents." In addition, our investigation found no evidence that the 75-microgram dose of [ ] had been tested to assure that it would not induce an immunological effect.

According to your February 16, 2005, response, "The certificate of analysis of [ ] showed this lot has been tested for [ ] We note that your response also included results dated January 4, 2005, of [ ] assay for the detection of [ ] in [ ] and results dated January 6, 2005, of qualitative real-time [ ] assay for the detection of [ ] However, this limited testing is insufficient to ensure that the product was free of the broad range of transmissible pathogens that may have been present in material derived from human placenta. For example, there was no documentation that the study product was sufficiently tested for other viral contamination, including [ ]

2. Cell Point failed to ensure proper monitoring of the clinical investigation [21 CFR 312.50, 21 CFR 312.56, and 21 CFR 312.53(d)].

During the inspection you failed to provide documentation demonstrating that Cell Point monitored the progress of Protocols [ ] and [ ] as required by 21 CFR 312.50 and 21 CFR 312.56(a). In addition, you failed to provide documentation that Cell Point selected monitors qualified by training and experience to monitor the clinical investigations [21 CFR 312.53(d)].

In Cell Point's written response, Mr.[ ]stated that he, Cell Point's Chief Technology Officer (CTO), monitored activities of both studies very closely. However, Mr.[ ]did not provide supporting documentation for any monitoring activities, such as records of site visits and correspondence with clinical investigators. In addition, Mr.[ ]did not provide documentation that he was qualified by appropriate training and experience to perform such monitoring activities.

This letter is not intended to be an all-inclusive list of deficiencies with your clinical studies of investigational drugs. It is Cell Point's responsibility as the sponsor of the clinical studies to ensure adherence to FDA regulations. Cell Point should address these deficiencies and establish procedures to ensure that any ongoing or future studies will be in compliance with the regulations.

Because of the departures from FDA regulations discussed above, please inform this office, in writing, within 15 working days of your receipt of this letter, of the actions Cell Point has taken or plans to take to prevent similar violations in the future. Failure to adequately and promptly respond may result in further regulatory action.

If you have any questions, please contact Dr. Leslie Ball, at (301) 594-1032, FAX (301) 827-5290. Cell Point's written response and any pertinent documentation should be addressed to:

Leslie K. Ball, M.D.
Branch Chief
Good Clinical Practice Branch II, HFD-47
Division of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research
7520 Standish Place
Rockville, MD 20855

Sincerely yours,

{See appended electronic signature page}

Joseph Salewski
Director (Acting)
Division of Scientific Investigations, HFD-45
Office of Compliance
Center for Drug Evaluation and Research

Linked Applications	Sponsor Name	Drug Name
IND[ ]	CELL	[ ]

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/s/

JOSEPH SALEWSKI
06/15/2006