IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF NEW YORK

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UNITED STATES OF AMERICA,

v.

Criminal No.
07-CR-202 (FJS)

**INFORMATION**

**JAMES A. HOLLAND,**

Vio: 21 U.S.C. §§ 331(e), 333(a)(1)

Defendant.

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**THE UNITED STATES ATTORNEY CHARGES:**

**Introduction**

A. At all times material to this information:

The FDA Approval Process

1. The United States Food and Drug Administration ("FDA"), an agency of the United States, is responsible for protecting the health and safety of the public by enforcing the Federal Food, Drug, and Cosmetic Act ("FDCA") and its implementing regulations. The FDA's responsibilities under the FDCA include regulating the manufacture, labeling, and distribution of all drugs shipped or received in interstate commerce, including drugs intended solely for investigational use. Under

the FDCA and its implementing regulations, a pharmaceutical manufacturer ("drug sponsor") must apply to the FDA for approval to market new drugs, and was required to demonstrate, often through clinical investigations, the safety and effectiveness of a drug before approval is given. As part of the process of deciding whether a new drug should be approved for marketing, FDA examines the design and conduct of the clinical studies as well as the results.

2. Prior to commencing a clinical study, a sponsor is generally required by FDA regulations to provide the FDA with extensive information regarding the proposed study, including a detailed investigation plan known as the "study protocol." The study protocol contains information about how the clinical study will be conducted, where studies will be done and by whom, how the drug's safety and effectiveness will be evaluated, and what findings would require the study to be changed or halted.

3. Drug sponsors typically hire qualified physicians, known as clinical investigators, to carry out the actual clinical studies of the drug on human subjects, hereinafter referred to as "study subjects." Each physician participating in a drug study as an investigator must sign FDA Form 1572 in which the physician commits to conduct the study in accordance with the study protocol, to personally conduct or supervise the investigation and to comply with FDA regulations.

4. Under Title 21, United States Code, Section 355(i), the FDA is authorized to issue regulations requiring the establishment and maintenance of records relating to the investigational use of new drugs. These regulations impose specific record-keeping requirements upon clinical investigators. When submitted to the FDA as part of a new drug application, these records are part of the basis for the FDA's evaluation of the drug's safety and effectiveness and the agency's determination as to whether the drug can be approved for marketing. Under 21 C.F.R. § 312.62(a), a clinical investigator is required to maintain adequate records of the disposition of investigational

new drugs, including the use by subjects. Under 21 C.F.R. § 312.62(b), a clinical investigator is required to maintain adequate and accurate case histories relating to the clinical use of investigational new drugs, including case report forms and supporting data such as the medical records of individuals administered the investigational drug or employed as a control in the investigation. Under Title 21, United States Code, Section 331(e), it is unlawful for any person to fail to establish or maintain any record required under Title 21, United States Code, Section 355(i), including those records required under 21 C.F.R. 312.62(a) and (b).

5. Although persons enrolled as study subjects are volunteers, a drug sponsor is not necessarily permitted to allow all those willing to volunteer to participate in its clinical studies. Whether an individual may participate depends on whether that individual meets certain criteria, which are set forth in the applicable study protocol and based, in part, on the drug under investigation and how that drug is thought to be useful. The criteria for patient selection are aimed at ensuring that appropriate patients are studied, both so undue risks to patients are avoided and the study results are valid. Study protocols thus provide that only patients who agreed and formally consented by signing an informed consent form and fulfilled all the inclusion/exclusion criteria were eligible for admission to the study, with exceptions to the protocol requiring the agreement of the sponsor. During the course of a drug study, and in accordance with the study protocol, study subjects are administered the study drug or a placebo and visit regularly with the investigator so that the data that are required to be submitted to the FDA can be collected and evaluated.

6. Information about each study subject, including the subject's medical history, laboratory results, and reaction to the drug under study, is provided to the drug sponsor upon completion of a drug study, who in turn may provide the information to the FDA for use in its evaluation of whether the drug should be approved for human use.

7. One procedure commonly used to conduct a clinical study is called a comparative, randomized, open-label, multi-center study (hereinafter referred to as "comparative study"). Generally, in a comparative study, the new drug is given to certain members of the defined test group, while a second drug, designed to treat the same symptoms, is given to other members of the defined test group.

8. A procedure called "randomization" is used, whereby either the new drug or the second drug is randomly assigned to be taken by each study subject. At the end of the study, the raw data is supplied to a statistician, who uses mathematical formulas to determine whether the clinical trial has shown the new drug to be safe and effective when compared with the second drug. The statistician's analysis is then incorporated into a report made to the FDA together with the other data developed during the drug study.

Stratton VA Medical Center

9. The Stratton Veterans Affairs Medical Center, located in Albany, New York, is part of the VA Healthcare Network Upstate New York, within the Veterans Health Administration of the United States Department of Veterans Affairs. The Department of Veterans Affairs (DVA) is a department of the United States (in the executive branch of the government). The Stratton VA Medical Center provides veterans with inpatient and outpatient medical care, including radiation oncology. The Stratton VA Medical Center has been designated as a Comprehensive Cancer Center.

10. The Albany Research Institute, Inc., is a non-profit research and education corporation established to conduct research projects and education activities in connection with the Stratton VA Medical Center.

The Defendant

11. The defendant, **JAMES A. HOLLAND**, was (and is) a licensed physician. Beginning in 1989, the defendant, **JAMES A. HOLLAND**, was employed by the Department of Veterans Affairs. Beginning in August of 1998, the defendant, **JAMES A. HOLLAND**, was employed by the Department of Veterans Affairs at the Stratton VA Medical Center in the oncology program. In June of 2000, **JAMES A. HOLLAND** became the head of the oncology program at the Stratton VA Medical Center. His duties in this position included directing, controlling, managing, and supervising the oncology research program, which included pharmaceutical protocols, adherence to system standards, and compliance with research requirements.

Tax 325 Study

12. Aventis Pharmaceuticals, Inc. ("Aventis")(formerly Rhone-Poulenc Rorer Pharmaceuticals, Inc.) was a pharmaceutical company engaged in developing, testing, and marketing pharmaceutical products, including docetaxel, also known by the brand name of taxotere, developed by Aventis for the treatment of respiratory tract infections.

13. Aventis sponsored an open label, randomized multicentre phase II/III study of docetaxel in combination with cisplatin (CDDP) or docetaxel in combination with 5-flourouracil (5-FU) and CDDP compared to the combination of CDDP and 5-FU in patients with metastatic or locally recurrent gastric cancer previously untreated with chemotherapy for advanced disease. The protocol number for the study was RP 56976-V-325; it sometimes was referred to as Tax 325.

14. The Coalition of National Cancer Cooperative Groups, Inc., conducts clinical research services on behalf of or supported by commercial or government sponsors, and did so for Aventis in connection with Tax 325.

15. The agreement for the Tax 325 Study provided for a grant of $5,000 for each completed, eligible, and evaluated patient/subject, scheduled as follows:

- When patient is randomized $1,666
- After patient has completed half of study $1,667
- After close-out $1,667

16. The Stratton VA Medical Center was a participating site in the Tax 325 study. The defendant, **JAMES A. HOLLAND**, was the principal investigator for the Tax 325 study at the Stratton VA Medical Center and signed an FDA Form 1572 in which he committed to conducting the study in accordance with the study protocol, to personally conduct or supervise the investigation, and to comply with FDA regulations.

17. The study population for Tax 325 was patients with metastatic or locally recurrent gastric cancer previously untreated with chemotherapy for advanced disease. The inclusion criteria for Aventis' Tax 325 study protocol included requirements that each patient had levels of creatinine, total bilirubin, AST (SGOT), and alkaline phosphatase within specified levels, and set a minimum calculated creatinine clearance of 60 ml/mn.

Tax 327 Study

18. Aventis also sponsored a multicenter phase III randomized trial comparing docetaxel administered either weekly or every three weeks in combination with prednisone versus mitoxantrone in combination with prednisone for metastatic hormone refractory prostate cancer. The protocol number for the study was RP56976V-327; it sometimes was referred to as Tax 327.

19. The clinical investigation agreement for the Tax 327 Study, dated February 28, 2000, provided that all work in the study would be performed in accordance with the terms of the protocol,

instructions by the sponsor, good clinical practice, generally accepted professional standards of care, and all applicable laws and regulations. The agreement provided for payment of a maximum of $75,000 on a pro rata basis for 10 patients completing the study, as follows:

- 10% once all required regulatory documents were submitted to the sponsor and approved and the study was initiated;
- 25% once 3 patients were enrolled and completed case report forms for baseline and cycle 1 for these patients were reviewed and forwarded to the sponsor, another 25% once the number reached 6 patients, and another 25% once the number reached 9 patients; and,
- 15% once completed case report forms (through follow-up) for 10 patients were retrieved and forwarded to the sponsor.

An amendment on April 25, 2001 upped the number of patients to 25 and the maximum payment to $192,500.

20. The Stratton VA Medical Center also was a participating site in the Tax 327 study. The defendant, **JAMES A. HOLLAND**, was the principal investigator for the Tax 327 study at the Stratton VA Medical Center and signed an FDA Form 1572 in which he committed to conducting the study in accordance with the study protocol, to personally conduct or supervise the investigation, and to comply with FDA regulations.

DFMO Study

21. ILEX Oncology, Inc., and the National Cancer Institute (NCI), Division of Cancer Prevention (DCP), co-sponsored a phase III, randomized, double-blind study to compare the use of

difluoromethylornithine (DFMO) to the use of a placebo in treating low grade superficial bladder cancer according to the time to the first recurrence of a bladder tumor and toxicities. Patients who met all of the eligibility requirements were randomly assigned a treatment and registered in the study by sending an informed consent document and laboratory normal values to ILEX and faxing a registration form to a foundation which forwarded it by fax to ILEX. Case Report Forms (CRFs) were supplied by ILEX, and were to be filled out completely and returned.

22. The clinical investigation agreement for the DFMO Study, dated March 10, 2000, provided that the study would be performed in accordance with the protocol, instructions by the sponsor, good clinical practice, generally accepted professional standards of care, and all applicable laws and regulations. The agreement provided for payment of $2,500 per qualified, evaluable patient, with $625 paid upon receipt of registration documents, $1,250 paid when each qualified, evaluable patient completed or discontinued early from the one-year treatment period of the study and the required study documents (CRFs) were received and reviewed by the sponsor, and the remaining $625 paid when each qualified, evaluable patient completed or discontinued early from the first year of follow-up and the required study documents (CRFs) were received and reviewed by the sponsor. The requirements for payment included that procedures were performed in full compliance with the protocol, the data submitted be complete and accurate, and the patient have met the inclusion and exclusion criteria.

23. The Stratton VA Medical Center also was a participating site in the DFMO study. The defendant, **JAMES A. HOLLAND**, was the principal investigator for the DFMO study at the Stratton VA Medical Center and signed an FDA Form 1572 in which he committed to conducting

the study in accordance with the study protocol, to personally conduct or supervise the investigation, and to comply with FDA regulations.

24. From about 1999, Paul H. Kornak was employed at the Stratton Veterans Affairs Medical Center, Albany, New York, first by Albany Research Institute, Inc., initially as a Research Assistant and then as Study Director of VA Cooperative Studies, and then by the Department of Veterans Affairs (at the Stratton Veterans Affairs Medical Center) as a Program Specialist, with duties which included coordination of research protocols. Under the supervision of the defendant, **JAMES A. HOLLAND**, Kornak was responsible for liaison planning, organizing, coordinating, implementing, directing, integrating, controlling, and evaluating research elements in the oncology research program, which included VA Cooperative Studies and pharmaceutical protocols, as well as data management, adherence to system standards, and compliance with research requirements. Under the supervision of the defendant, **JAMES A. HOLLAND**, Kornak was the site coordinator at the Stratton VA Medical Center for the Tax 325, Tax 327, and DFMO studies.

## COUNT 1

B. The Introduction is incorporated by this reference.

C. From on or about May 14, 1999, up to and including on or about July 10, 2002, in the Northern District of New York, the defendant, **JAMES A. HOLLAND**, did, in connection with leading, supervising, managing, conducting, and coordinating clinical trials and studies at the Stratton VA Medical Center, including the Tax 327, Tax 325, and the DFMO studies, wrongfully and unlawfully fail to establish and maintain adequate and accurate case histories of some

individuals administered investigational drugs and employed as controls in the studies, in that the case histories included materially false documentation and/or information provided by a subordinate, Paul H. Kornak, that enabled persons to be enrolled as study subjects who did not qualify under the study protocol. Case histories for such patients contained false and misleading documents, including some which falsely reflected:

- That patients had blood drawn on certain dates;
- Laboratory analysis of samples from study subjects;
- That study subjects had electrocardiograms done on certain dates;
- The results of electrocardiograms of study subjects;
- The results of ejection fraction testing; and,
- A false radiology display report; and,
- Dates on a final surgical pathology report, a letter, an operative note, urethrocystogram retrograde supervision and interpretation report, and a urology clinic progress note.

The above described false and misleading documents were created and submitted by a direct subordinate of the defendant, **JAMES A. HOLLAND**. The defendant, **JAMES A. HOLLAND**, had the responsibility, authority, and duty to ensure that adequate and accurate case histories were maintained and promptly detect and correct inadequate and inaccurate cases histories, but wrongfully and unlawfully failed to do so, including by failing to review or check the accuracy of the above described case histories and reports of laboratory analysis, electrocardiograms, ejections fraction testing, radiology reports, surgical reports, and operative and progress notes. One example was the

defendant, **JAMES A. HOLLAND**, causing to be administered to James J. DiGeorgio the chemotherapeutic drugs docetaxel, cisplatin, and 5-FU in connection with Tax 325 on or about May 31, 2001, based upon documents and records made by Kornak which falsely stated and represented the results of blood chemistry analysis of a sample provided by James J. DiGeorgio on May 25, 2001. The false documents purported that James J. DiGeorgio met the inclusion and exclusion criteria for participation in Tax 325 when the actual results did not meet the inclusion and exclusion criteria and showed impaired kidney and liver function. The defendant, **JAMES A. HOLLAND**, did not review the actual report of laboratory analysis or check the accuracy of the documents and records made by Kornak, and James J. DiGeorgio thus was administered the chemotherapeutic drugs. James J. DiGeorgio died on or about June 11, 2001.

E. All in violation of Title 21, United States Code, Sections 331(e) and 333(a)(1).

Dated: April 24, 2007

GLENN T. SUDDABY
United States Attorney

By: 
Grant C. Jaquith
Assistant U.S. Attorney
Chief, Criminal Division
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