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GENERAL PROCEDURAL POLICIES

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CVM'S IMPLEMENTATION OF THE AGENCY'S FRAUD, UNTRUE STATEMENTS OF MATERIAL FACTS, BRIBERY AND ILLEGAL GRATUITIES POLICY

During investigations into the illegal conduct of some employees of FDA and generic drug firms, the agency discovered broad patterns of fraud in some abbreviated new drug applications. In response to the findings, the agency adopted a Fraud, Untrue Statements of Material Facts, Bribery, and Illegal Gratuities policy. This policy was issued as Compliance Policy Guide (7150.09) on September 10, 1991 (56 FR 46191). The policy sets forth the agency's general approach to the processing of applications that have been called into question by wrongful acts and applications found to contain unreliable data. The policy provides guidance to agency management to ensure consistent handling of applications from applicants who have compromised an agency review process by engaging in fraud, submission of untrue statements of material facts in applications, bribery and/or the provision of illegal gratuities to agency employees.

1. Purpose:

This guide describes the CVM's internal process for implementing the agency policy on "Fraud, Untrue Statements of Material Facts, Bribery, and Illegal Gratuities" (hereafter referred to as the Application Integrity Policy). It provides guidance when questionable data are suspected or encountered in the review of an application; provides guidance on the withdrawal of approval or refusal to approve applications containing unreliable data or untrue statements of material fact; and provides general guidance on the resumption of the preclearance review of applications submitted by a firm that has satisfactorily implemented a Corrective Action Operating Plan.

2. Terminology:

The following provide working definitions for the purpose of this CVM Policy and Procedures guide.

Applicant--Any person who submits data or other information to FDA to influence or support an agency decision regarding approval to market an FDA-regulated product.

Non-substantive review--Review of submissions that do not require evaluation of data.

Examples would include minor modifications of labeling, protocols that do not rely on data, protocols that rely on validated data, or other Type 1 supplements that do not rely on data.

Application--Any application, petition, amendment, supplement, or other submission made by the applicant. This would include but not be limited to:

Investigational New Animal Drug Applications (INAD)

New Animal Drug Applications (NADA)

Supplements to New Animal Drug Applications Abbreviated New Animal Drug Applications (ANADA)

Medicated Feed Mill Licenses

Food Additive Petitions (FAP)

Drug Experience Reports (DER)

Veterinary Master Files (VMF)

Export Applications.

Fraud-- "Deceit, trickery, sharp practice, or breach of confidence, used to gain some unfair or dishonest advantage"--Webster's Encyclopedic Unabridged Dictionary of the English Language.

Untrue Statements of Material Facts--Omission of information or false information in support of an application regardless of the intent of the applicant (see full explanation 21 CFR 514.15).

Bribery--The act of giving or promising something of value to induce a person to do something illegal or wrong.

Illegal Gratuities--Anything of value given to a person, because of their official position, usually in exchange for illegal acts performed or to be performed.

Validity Assessment--Assessment of reliability of data which has been, or is intended to be, submitted and/or used for agency decision making. Generally, the applicant will undertake an internal review to support the validity assessment process. FDA will perform inspections, data audits, and review the applicant's internal review.

Corrective Action Operating Plan--A written plan and commitment by the applicant based on the internal review, describing what actions the applicant will undertake to correct the residual problems from the wrongful act(s) and to preclude the wrongful act(s) from

recurring.

Questionable Information--Includes but is not limited to information submitted by an applicant which by virtue of detection of protocol deviation, inconsistency or unusual consistency (either internally or historically), omission, or pattern of error or data alteration, method of summary or presentation, ancillary information received from outside sources (tips), information gathered during an FDA inspection, or evaluation by any other method applicable to examination of data IS SUSPECT. The term includes information that is suspected of being materially untrue, fraudulent or submitted by an applicant convicted of bribery or provision of illegal gratuities.

3. Responsibilities:

All employees are responsible for identifying and reporting questionable information found in the review of applications (see section 5 below). Activities related to the Application Integrity Policy will be coordinated by the Office of Surveillance and Compliance. The Director of the Division of Compliance (HFV-230), who is the liaison with the agency wide Application Integrity Policy Implementation Group (AIPIG), a subgroup of the Compliance Policy Council, or designee, will lead a CVM ad hoc team to investigate any report of questionable data. The AIPIG liaison will provide training on Application Integrity Policy responsibilities to new employees. The Director of the Division of Compliance, or designee, will field investigations and maintain a liaison with the Office of Chief Counsel to obtain legal guidance, and will maintain a list-of firms currently affected by the Application Integrity Policy. The list will be disseminated to all Division Directors within the CVM, as well as each Center within the agency. All employees of CVM are responsible for identifying and reporting any suggestion or suspicion of fraud, untrue statements of material facts, bribery, and illegal gratuities. All CVM employees should be cognizant of the many ways fraud may be discovered.

4. Means of Discovery of Invalid Submission:

Vehicles through which fraud, untrue statements of material fact, bribery and illegal gratuities may be uncovered include:

- Information from informants using any possible means of communication
- Reviews of applications submitted to CVM
- Reviews of establishment inspection reports
- Reviews of reports of investigations conducted by other FDA Centers, FDA

Field Offices or other Federal Agencies.

Reviewers must carefully and completely evaluate unusual events or occurrences found in applications, routinely evaluate raw/source-data records, and critically examine altered data, unexpected changes in protocol, and unexplained changes such as increases or decreases within and among experimental units.

5. CVM Employee Responsibility on Discovery of Wrongful Acts:

a. **Reviewer**

If, by whatever means, an application reviewer detects what he or she believes to be questionable information, the reviewer must expeditiously inform his or her Team Leader.

b. **Team Leader**

The reviewer and Team Leader need to determine whether the questionable information may jeopardize the application's integrity or whether the issue may be resolved by issuing an incomplete letter for the application and requesting submission of additional information. If the Team Leader and the reviewer agree that the information in question may jeopardize the application's integrity or the reviewer and the Team Leader fail to reach consensus on the issue of application integrity, both should expeditiously meet with the reviewer's Division Director.

c. **Division Director**

If, after thorough discussion with the reviewer and Team Leader, the Division Director believes that the identified information is questionable and may jeopardize the integrity of the application, a memo must be prepared for the Division Director's signature to the Director, Division of Compliance. This memo should set out the issue of concern. Copies of this memorandum should be sent to the reviewer's Office Director and, if not a S&C reviewer, the Director of the Office of Surveillance and Compliance for their information.

However, if the discussion does not convince the Division Director that the information is questionable and may jeopardize the integrity of the application, either the Team Leader or the reviewer has the option to prepare a memorandum

to the Division Director documenting the basis for his or her concern. Copies of the memorandum should be sent to the Office Directors of the Office of New Animal Drug Evaluation and the Office of Surveillance and Compliance. Upon receipt of this memo, the informed Office directors will convene an ad hoc team to investigate the concern and resolve the difference of opinion existing within the Division. This team may, for example, be comprised of independent reviewers who have expertise in the area of concern, a Division of Compliance CSO, and the Director of the Division of Compliance.

d. **Director, Division of Compliance (AIPIG liaison)**

Upon receipt of the memorandum setting out the issue of concern from the responsible Division Director, the Director of the Division of Compliance will form an ad hoc team including a representative of the division which discovered the questionable information, the primary reviewer, and any other useful employee such as a CSO (as the project continues additional persons may be added to the committee including a representative of OCC). The first meeting will be to determine the need for further investigation. The Director of the Division of Compliance, or designee, is the leader of the ad hoc team. Often the initial finding will require field investigations to verify and obtain information on the pattern of the findings.

e. **All Employees**

In the specific case of an employee who is offered a bribe or suspects bribery of an agency employee or gains knowledge of illegal gratuities the employee is to immediately report this information directly to the HHS Inspector General (202-619-1900), the FDA Division of Ethics and Program Integrity (301-827-5511), or to the direct supervisor. The information should not be reported to the direct supervisor if there is suspicion of managerial involvement.

6. Examples of Recommendations of the AD HOC Team Review:

The Ad Hoc Review Team may reach one or more of the following recommendations (this list is not exhaustive).

Once the Ad Hoc team reaches consensus on a recommendation, a should issue from the

Director, Division of Compliance to Director with concurrence from the Office Directors of New Animal Drug Evaluation and Surveillance and Compliance which provides information and the proposed recommendations.

- a. The identified issue brought before the ad hoc team is determined not to be suspect.
- b. For a pending application, the information identified is unacceptable and cannot be used for decision-making purposes (resulting in the rejection of a study or studies), but further administrative action by FDA is not warranted.
- c. Available information demonstrates unacceptable practice(s) on the part of the clinical investigator, but not the applicant. Action should be taken against the investigator (such as making the individual ineligible to receive investigational drug products) and the study rejected (see a full explanation in 21 CFR 511.1 (c)).
- d. Further investigation is warranted before reaching a conclusion, in which case the ad hoc team will recommend the direction of the investigation. The investigation may entail, but not be limited to:
  - (1) Field investigation (usually with CVM involvement) of suspected data collection practices, applicant evaluation and submission processes, and the extent of process failure which caused submission of the questionable information.
  - (2) Review or re-review of additional information submitted in the suspect application or in other applications in an effort to determine if the suspect information may represent a previously undetected pattern or practice.