DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

By Certified Mail - Return Receipt Requested

Layne O. Gentry, M.D.
St. Luke's Episcopal Hospital
6720 Bertner
M.C. 2-233
Houston, TX 77030

JUN 18 2008

[ ]

Notice of Disqualification of Eligibility to Receive Investigational Drugs

Dear Dr. Gentry and Counsel:

I have reviewed the administrative record of the regulatory proceeding involving Layne O. Gentry, M.D., including the Presiding Officer's Report and the submissions from both the Center for Drug Evaluation and Research (CDER) and Dr. Gentry. Based upon my review, I have concluded that there is no genuine and substantial issue of fact with regard to whether Dr. Gentry repeatedly and deliberately violated 21 CFR Part 312 in connection with three investigational new drug studies of levofloxacin. I am therefore granting CDER's Motion for Summary Decision and, consistent with 21 CFR 312.70(b), I have determined that Dr. Gentry is no longer eligible to receive investigational drugs. Under authority delegated to me by the Commissioner of Food and Drugs, I am issuing this Commissioner's Decision disqualifying Dr. Gentry from eligibility to receive investigational drugs. The reasons for this determination are set forth in the enclosed decision.

Dr. Gentry may seek to have his eligibility to receive investigational drugs reinstated, pursuant to 21 CFR 312.70(f), upon presentation of adequate assurances that the investigator will employ investigational drugs solely in compliance with the provisions of the applicable regulations, i.e., 21 CFR Parts 50, 54, 56, 312.

Sincerely,

John Q. Dyer

John Dyer
Deputy Commissioner for Operations

Enclosure

cc: U.S. Food and Drug Administration
Office of the Chief Counsel (GCF-1)
5600 Fishers Lane
Rockville, MD 20857

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

REGULATORY HEARING ON THE PROPOSAL TO DISQUALIFY

LAYNE O. GENTRY, M.D.

FROM RECEIVING INVESTIGATIONAL NEW DRUGS

COMMISSIONER'S DECISION

The purpose of this proceeding is to determine, pursuant to 21 CFR § 312.70 and 21 CFR part 16, whether Layne O. Gentry, M.D., a clinical investigator, should be disqualified from receiving investigational new drugs. Henry H. Startzman III, M.D., served as the presiding officer (P.O. Dr. Startzman) for this disqualification. P.O. Dr. Startzman issued a summary decision in favor of the Center for Drug Evaluation and Research ("CDER") and recommended that Dr. Gentry be disqualified.

Under authority delegated to me by the Commissioner of Food and Drugs, I am authorized to issue the Commissioner's decision in this matter. Based upon my review of the administrative record in this matter, including P.O. Dr. Startzman's summary decision and the parties' submissions, I conclude that Dr. Gentry repeatedly and deliberately violated the regulations governing clinical investigations. Therefore, I am disqualifying Dr. Gentry from receiving investigational drugs. The reasons for my decision follow.

I. PROCEDURAL BACKGROUND

The charges in this proceeding arise out of three clinical studies of the drug levofloxacin, sponsored by R.W. Johnson Pharmaceutical Research Institute ("the sponsor"). Dr. Gentry was the principal investigator for the three studies, which were conducted at six different clinical sites: one at St. Luke's Episcopal Hospital ("St. Luke's") in Houston, Texas; four in the Costa Rican Social Security Hospital System in San Jose, Costa Rica; and one at Clinica Pavas, also in San Jose, Costa Rica.

Dr. Gentry, who was located at St. Luke's, received authorization under investigational new drug applications ("INDs") #[ ]and #[ ]to begin the three studies in accordance with study protocols[ ][1] [ ]M.D., was the local supervisory subinvestigator for the sites in Costa Rica. The Forms FDA 1572 ("investigator statements") submitted by Dr. Gentry identified St. Luke's Institutional Review Board ("St. Luke's IRB") as the institutional review board ("IRB") for the site at St. Luke's and the[ ]Institutional Review Board[ ]IRB") as the IRB for the sites in Costa Rica.

Between June 20 and 24, 1996, FDA investigators inspected the St. Luke's site to determine whether the clinical studies were in compliance with FDA's regulations for clinical investigations. The FDA investigators issued a Notice of Inspectional Observations ("Form FDA 483") to Dr. Gentry at the close of the inspection. The Form FDA 483 identified two violations. By letter dated July 10, 1996, Dr. Gentry responded to those observations.

---

[1]Study[ ]conducted from August 1992 until March 1993, was designed to evaluate the safety and effectiveness of levofloxacin, as compared to another drug, in the treatment of lower respiratory infections in adults. Study[ ]conducted from August 1992 until July 1994, was designed to evaluate the safety and effectiveness of levofloxacin, as compared to another drug, in the treatment of moderate to severe skin and structure infections in hospitalized adults. Study[ ] conducted from September 1993 until July 1994, was designed to evaluate the safety and effectiveness of levofloxacin, as compared to another drug, in the treatment of mild to moderate skin and skin structure infections in adults. Study[ ]did not include Clinica Pavas as a study site.

From May 19 to 23, 1997, FDA investigators inspected the Costa Rican sites. At the conclusion of the inspection, the investigators issued to Dr. [redacted] a Form FDA 483, which listed numerous violations of FDA's clinical investigator regulations. By letter dated July 8, 1997, Dr. [redacted] responded to the Form FDA 483.

On March 23, 1998, CDER sent Dr. Gentry a Notice of Initiation of Disqualification Proceedings and Opportunity to Explain ("NIDPOE") based on the observations in the Form FDA 483s issued after the inspections in 1996 and 1997. On March 31 and June 17, 1998, Dr. Gentry responded in writing to the NIDPOE. On June 17, 1998, CDER met with Dr. Gentry and his attorneys in an informal conference at which Dr. Gentry had an opportunity to respond to the allegations in the NIDPOE.

In a letter dated April 15, 1999, FDA's Associate Commissioner for Regulatory Affairs informed Dr. Gentry that he would be given an opportunity for a regulatory hearing under 21 CFR part 16 to determine whether he should be disqualified from receiving investigational drugs. The notice of opportunity for a hearing ("NOOH") was issued pursuant to 21 CFR §§ 312.70 and 16.22. The NOOH alleged violations of 21 CFR parts 50, 56, and 312. Dr. Gentry requested a hearing in a letter dated May 14, 1999.

The parties submitted their requests for summary decision on July 7, 2000, and their oppositions on September 8, 2000. CDER subsequently submitted a memorandum of the definitions of "repeated" and "deliberate," and Dr. Gentry subsequently submitted a reply to that memorandum. On January 21, 2001, Dr. Gentry requested that FDA stay the summary decision proceedings until FDA responded to his pending request for records under the Freedom of Information Act ("FOIA"); the request for records under FOIA was denied on February 7, 2001.

Based upon the evidence presented in and attached to CDER's Initial Request for Summary Decision (alternatively "CDER's motion for summary decision"), Dr. Gentry's Request for Summary Decision (alternatively "Dr. Gentry's motion for summary decision"), CDER's opposition to Gentry's motion, Dr. Gentry's opposition to CDER's motion, CDER's Written Response to Request for Clarification, and Dr. Gentry's Reply to CDER's Written Response to Request for Clarification, P.O. Dr. Startzman issued a summary decision on six of the charges in favor of CDER on September 12, 2001. Specifically, in accordance with 21 C.F.R. § 16.26(b), P.O. Dr. Startzman found that there were no genuine and substantial issues of fact with regard to the following six charges:

1. Charge 1(A)(1): Failure to maintain x-ray films for the required period of time, in violation of 21 C.F.R. § 312.62(c);

2. Charge 1(A)(2)(i): Failure to ensure that radiology reports were signed, in violation of 21 C.F.R. § 312.62(b);

3. Charge 1(B): Failure to maintain accurate records, in violation of 21 C.F.R. § 312.62(b);

4. Charge 2: Failure to obtain IRB approval before enrolling certain study subjects, in violation of 21 C.F.R. §§ 50.27, 56.103(a), 312.53(c)(1)(vii), 312.60, and 312.66;

5. Charge 5: Failure to list subinvestigators on Form FDA 1572, in violation of 21 C.F.R. §§ 312.53(c)(1)(viii) and 312.60; and

6. Charge 6(A): Failure to personally conduct or supervise the clinical studies, in violation of 21 C.F.R. §§ 312.53(c)(1)(vi)(c), 312.60, and 312.70.

P.O. Dr. Startzman denied Dr. Gentry's motion for summary decision as to the foregoing charges

and both parties' motions for summary decision with respect to the remaining charges.[2] Based on this decision, P.O. Dr. Startzman recommended that I disqualify Dr. Gentry.

On November 2, 2001, Dr. Gentry submitted a Request for Commissioner's Review. As discussed in Section III.C., *infra*, Dr. Gentry has since submitted additional arguments and documents regarding alleged procedural deficiencies in the proceeding below. To the extent necessary, I address those arguments in Section III.C.

II. SUMMARY DECISION

In this proceeding, CDER charged Dr. Gentry with repeatedly or deliberately failing to comply with 21 C.F.R. Parts 50, 56, and 312. P.O. Dr. Startzman granted summary decision as to six charges and determined that the violations cited in those charges were repeated, deliberate, or both. In reviewing P.O. Dr. Startzman's decision, I will first address the standard for summary decision. Second, I will discuss the appropriate standard for "repeated or deliberate" violations. Third, I will separately address each of the violations on which P.O. Dr. Startzman granted summary decision for CDER.[3] As mentioned above, I will address Dr. Gentry's remaining legal arguments and challenges in Section III, *infra*.

---

[2]The remaining charges were as follows: failure to date radiology reports (Charge 1(A)(2)(ii)); failure to maintain subject enrollment screening log or source documents (Charge 1(C)); failure to document drug shipments (Charge 3); baseline blood sample violation (Charge 4); submission of false information (Charge 6(B)); reclassification of clinical outcome (Charge 7). P.O. Dr. Startzman also implicitly or explicitly declined summary decision as to certain aspects of the charges on which he granted summary decision. For example, P.O. Dr. Startzman granted summary decision as to Charge 1(A)(1) insofar as CDER relied on 21 C.F.R. § 312.60(c), which requires investigators to retain records for a certain period of time. P.O. Dr. Startzman did not address whether Dr. Gentry violated 21 C.F.R. § 312.60(b) by failing to prepare or maintain these same records, presumably because it was unnecessary to reach that issue once P.O. Dr. Startzman had determined that there was no dispute regarding Dr. Gentry's failure to retain the records.

[3]Because neither party has appealed P.O. Startzman's findings as to the other five charges alleged in the NOOH, I do not have cause to address those findings at this time. In fact, I will not address aspects of charges before me that P.O. Dr. Startzman did not reach or address.

A. The Standard for Summary Decision

I review P.O. Dr. Startzman's grant of summary decision *de novo*. Under 21 C.F.R. § 16.26, summary decision may be granted in favor of a party "if there is no genuine and substantial issue of fact raised by the material submitted." The standard for summary decision in 21 C.F.R. §16.26 is linked inextricably to the standard in federal court for summary judgment. *See John D. Copanos and Sons, Inc.*, 854 F.2d 510, 523 (D.C. Cir. 1988) (comparing the standard for granting summary decision under 21 C.F.R. § 314.200, which contains similar language, to the standard for summary judgment in federal court). Under Rule 56(c) of the Federal Rules of Civil Procedure, summary judgment is proper when there is no genuine issue as to any material fact and the moving party is entitled to judgment as a matter of law. However, "[t]he mere existence of *some* alleged factual dispute between the parties will not defeat an otherwise properly supported motion for summary judgment; the requirement is that there be no *genuine* issue of *material* fact." *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 247-48 (1986) (emphasis in original).

As is the case for summary judgment under Rule 56(e), the key criterion for determining whether summary decision is appropriate under 21 C.F.R. § 16.26 is whether there are disputed facts that might affect the outcome of the proceeding. The opposing party may not rest on mere allegations or denials of the moving party's evidence but must present evidence of its own that establishes a genuine issue of fact. If there are no genuine disputes of fact, summary decision is appropriate.

B. The Standard for Repeatedly or Deliberately

Section 312.70(b) of Title 21 of the Code of Federal Regulations sets forth the standard for disqualification of a clinical investigator as follows:

> After evaluating all available information, including any explanation presented by the investigator, if the Commissioner determines that the investigator has repeatedly or deliberately failed to comply with the requirements of this part, part 50, or part 56 of this chapter, or has deliberately or repeatedly submitted false information to FDA or the sponsor in any required report, the Commissioner will notify the investigator and the sponsor of any investigation in which the investigator has been named as a participant that the investigator is not entitled to receive investigational drugs.

Therefore, a determination that an investigator *either* repeatedly or deliberately failed to comply with the regulations or submitted false information is a sufficient basis for disqualification.

1. The parties' arguments

CDER has consistently maintained throughout this proceeding that, as used in 21 C.F.R. § 312.70(b), "repeatedly" means more than one time and that any two violations of the regulations governing clinical investigations qualify as "repeated," even if committed during the course of a single study. CDER further contends that, as used in the alternative in 21 C.F.R. § 312.70(b), the term "deliberately," while also encompassing intentional conduct, requires only a showing of reckless disregard for the regulations governing clinical investigations. For these standards, CDER relies on what it characterizes as the common or legal understanding of the terms "repeated" and "deliberate" and the holdings of previous presiding officers and commissioners. According to CDER, the evidence is undisputed that Dr. Gentry committed each of the six substantive violations both repeatedly and deliberately under those standards and that, thus, he is subject to disqualification from receiving investigational drugs.

In the proceedings below, Dr. Gentry presented a three-pronged attack on the conclusions reached by CDER regarding the proper standards for "repeatedly" and "deliberately" and the application of those standards to his conduct in this proceeding. First, Dr. Gentry argued at length that CDER's reliance on previous disqualification decisions as binding precedent was inappropriate. He asserted that a number of the opinions cited by CDER to support its interpretation of the "repeatedly or deliberately" standard were unpublished and that CDER's reliance on such opinions, which Dr. Gentry has characterized as "secret law," was impermissible under the Administrative Procedure Act ("APA"), the Freedom of Information Act, and the Due Process Clause of the Fourteenth Amendment. Second, Dr. Gentry argued that the definitions proposed by CDER for "repeatedly" and "deliberately" are broader than the plain meaning of those words. Third, Dr. Gentry argued that the manner in which CDER applied the standards for "repeatedly" and "deliberately" in this proceeding has rendered them a virtual nullity and that, for those terms to have any meaning, the violations underlying a clinical investigator disqualification must reflect "a systematic failure to comply with agency regulations."

In addressing the parties' arguments below, P.O. Dr. Startzman first declined to resolve Dr. Gentry's "secret law" argument, i.e., whether CDER properly relied on prior disqualification decisions in defining "repeated" and "deliberate." P.O. Dr. Startzman also rejected Dr. Gentry's arguments that FDA's public statements regarding the purpose of clinical investigator disqualifications, in preambles and elsewhere, reflect an agency interpretation of 21 C.F.R. § 312.70(b) that would preclude disqualification unless CDER shows that the investigator's violations are widespread or fundamental. He found that "the terms 'repeated' and 'deliberate'

can be defined without reference to the previous clinical investigator decisions," and then he examined "the plain meaning of the words as defined by dictionaries and legal authorities."

Relying on *Webster's Ninth New College Dictionary* (9th ed. 1991), P.O. Dr. Startzman defined "repeatedly" as "again and again" or "more than once." He held that neither the term nor the regulation, 21 C.F.R. § 312.70(b), requires an additional finding that the "repeated" violations occur in more than one study.

In defining the term "deliberate," P.O. Dr. Startzman relied on the meaning several federal courts have given one of its synonyms: "willful." As CDER conceded below, the traditional definition of "deliberate" is "carefully weighed or considered" and "careful or slow in deciding." P.O. Dr. Startzman found that this definition was too restrictive in the context of this case, however. He looked instead to various court definitions of the word "willful," which he found to be synonymous with "deliberate." He found that many courts have interpreted "willful" to mean "demonstrating reckless disregard." See, e.g., McLaughlin v. Richland Shoe Co., 486 U.S. 128, 133 (1988); United States v. Ottley, 509 F.2d 667, 672-73 (2d Cir. 1975); *Black's Law Dictionary* 426, 1270 (6th ed. 1990).

P.O. Dr. Startzman then proceeded to evaluate each of the six substantive charges under the standards he established for "repeatedly or deliberately." He found that the violations for each of the substantive charges on which he granted summary decision were both "repeated" and "deliberate."

In his Request for Commissioner's Review, Dr. Gentry takes issue with both P.O. Dr. Startzman's interpretation of the standards of conduct expressed by the terms "repeatedly" and "deliberately" and the application of the resulting standards to the charges on which P.O. Dr.

Startzman granted summary decision in favor of the Center. According to Dr. Gentry, P.O. Dr. Startzman's "reading of the term 'repeated' is the most extreme interpretation possible." Citing specific examples from P.O. Dr. Startzman's decision, Dr. Gentry maintains that, under the standard for "repeatedly" articulated by P.O. Dr. Startzman, FDA has "the discretion to disqualify an investigator for any *two* mistakes in a study or series of studies, regardless of the materiality of the errors, or the degree of negligence in the mistakes."[4] He contends that such a standard renders "the term 'repeated' a virtual nullity."

Dr. Gentry also relies on public statements by the agency, in preambles and elsewhere, for the proposition that "repeatedly" in the context of investigator disqualifications *must* require a showing of more than the mere existence of two violations. According to Dr. Gentry, those public statements demonstrate that the agency recognizes that clinical studies are susceptible to minor human error and that a clinical investigator should not be disqualified for minor mistakes.

Dr. Gentry also takes issue with P.O. Dr. Startzman's definition for the term "deliberate." He first points out that P.O. Dr. Startzman's interpretation does not square with the dictionary definitions for "deliberate." Relying on *The American Heritage Dictionary of the English Language* (3d ed.1996) and *Webster's New World Dictionary* (2d college ed. 1978), Dr. Gentry argues that the lay definitions for "deliberate" connote a state of mind that is a degree higher than intentional rather than several degrees below. Specifically, Dr. Gentry points out that these dictionaries define "deliberate" to mean "[d]one with or marked by full consciousness of the nature and effects; intentional"; [a]rising from or marked by careful consideration"; and

---

[4]Insofar as Dr. Gentry challenges the application of the standard for "repeatedly or deliberately" to individual charges, I address those challenges below.

"[c]arefully thought out and formed, or done on purpose; premeditated." Noting that P.O. Dr. Startzman nonetheless relies on judicial interpretations of "willful" when that word is used to describe states of mind, Dr. Gentry summarizes P.O. Dr. Startzman's resulting interpretation of "deliberate" as follows:

> [P.O. Dr. Startzman] takes the interpretation of "willful" to such an extreme that an experienced clinical investigator would be said to "deliberately" violate FDA regulations when any subordinate commits a single immaterial regulatory violation, even if the investigator did not intend that violation would occur, did not know about it, and did not have reason to know about it. . . . [This standard] goes well beyond a "reckless disregard" standard to encompass simple negligence. The standard being applied is one in which an "experienced investigator" is held to have deliberately committed any violations by those in his charge, no matter how minor or unintentional.

As he did in objecting to P.O. Dr. Startzman's interpretation of "repeatedly," Dr. Gentry contends that P.O. Dr. Startzman's reading of "deliberate" is inconsistent with FDA's public statements that the agency does not view isolated or inadvertent errors by an investigator to warrant disqualification.

2. Dr. Gentry's arguments regarding "secret law."

In its motion for summary decision, CDER originally based its interpretations of "repeated" and "deliberate" on Presiding Officer and Commissioner decisions in previous disqualification matters. Based on those decisions, CDER asserted that "repeated" means "more than one violation in a single study" and that "deliberate" means "intentional," "willful," or "having a reckless disregard for the regulations' requirements."

Some of the decisions cited by CDER had been available at FDA's Division of Dockets Management prior to the initiation of this proceeding. During this proceeding, CDER also provided Dr. Gentry with an index of previous disqualification decisions. In a previous

submission, Dr. Gentry asserted that this index was incomplete in that it omitted at least twenty-one disqualification proceedings that had been resolved through the hearing process. In August 2001, shortly before P.O. Dr. Startzman issued his summary decision, FDA published a Federal Register notice announcing the availability of almost all of the prior decisions.

After reviewing the arguments of both parties, P.O. Dr. Startzman concluded that "Dr. Gentry's 'secret law' argument appear[ed] to have merit," but he found "it unnecessary to resolve the issue." He then proceeded to interpret the terms "repeatedly" and "deliberately" by examining their plain meanings, without reference to previous clinical investigator decisions. I agree with P.O. Dr. Startzman's approach.[5]

3. Public statements by the agency.

Dr. Gentry has consistently maintained throughout this proceeding that public statements by FDA, in preambles to proposed and final rules and elsewhere, make clear that the intended scope of 21 C.F.R. § 312.70(b) is restricted to disqualifying investigators whose violations are widespread, significant, fundamental, material, and/or non-technical. I address some of those specific arguments below, but I provide a general discussion here for the sake of efficiency.

As I make clear in my discussion of the regulatory context for the meaning of "repeatedly" and "deliberately," some reference to the background of the regulations governing clinical investigations is necessary to understand the framework and regulatory purpose of the standards for a disqualification proceeding. For some of his arguments, Dr. Gentry relies on the

[5]Dr. Gentry also notes in his Request for Commissioner's Review that P.O. Dr. Startzman's "adopted . . . interpretations of 'deliberate' and 'repeated' that simply reaffirm" previous decisions by presiding officers and commissioners. Even though P.O. Dr. Startzman's interpretations use reasoning similar to that of previous decisions, neither P.O. Dr. Startzman nor I rely on those previous decisions as precedent. Therefore, Dr. Gentry's arguments regarding reliance on "secret law" are moot.

preamble to a proposed rule from 1978 regarding the disqualification of investigators engaged in studying any FDA-regulated product. 43 Fed. Reg. 35210, 35227 (Aug. 8, 1978). Specifically, he contends that the agency indicated that additional standards for disqualification, such as a showing that the investigator's conduct adversely affected the safety of the patients or the validity of the data, might be advisable to prevent the remedial measure from being abused. *Id.* As Dr. Gentry acknowledges, however, FDA explicitly declined to adopt those additional standards when it finalized 21 C.F.R. § 312.70(b) and opted instead to make clear that the Commissioner could consider such factors in exercising his enforcement discretion not to disqualify an investigator subject to disqualification under the regulation. 52 Fed. Reg. 8798, 8826 (Mar. 19, 1987). I therefore do not find the specific language in this preamble to which Dr. Gentry cites persuasive on the issue of how 21 C.F.R. § 312.70(b) should be interpreted.

Dr. Gentry also relies on two separate rulemakings regarding the disqualification of clinical investigators of unapproved devices to argue that FDA does not intend for the procedure to be used for "technical violations" or for "isolated or inadvertent failures." 41 Fed. Reg. 35282, 35295 (August 20, 1976); 62 Fed. Reg. 120887, 12089 (Mar. 14, 1997). Although I disagree with Dr. Gentry regarding the weight to be given statements made in the preambles associated with other rulemakings, especially given that the quoted statements occurred eleven years before and ten years after the agency finalized 21 U.S.C. § 312.70(b), nothing in my analysis below is inconsistent with those statements.

4. The appropriate standard.

The parties' arguments regarding the appropriate definitions for "repeatedly" and "deliberately," as used in 21 C.F.R. § 312.70(b), present one of the more difficult issues before

me. As discussed below, I am of the opinion that P.O. Dr. Startzman properly granted summary decision in favor of CDER on the six substantive charges now before me. Likewise, the standards for "repeatedly" and "deliberately" adopted by P.O. Dr. Startzman are essentially identical to the standards that I find to be appropriate in the context of a proceeding to disqualify an investigator. However, a closer analysis of the precise regulatory context of those terms and the rationale offered by the agency for the regulatory scheme provide further support for the standards used by P.O. Dr. Startzman.

I agree with both P.O. Dr. Startzman and CDER that the starting point for interpreting language in a regulation should be the plain meaning of the words themselves. An agency's interpretation of a regulation must "conform with the wording and purpose of the regulation." *Public Citizen Inc. v. Mineta*, 343 F.3d 1159, 1166 (9th Cir. 2003). But determining the meaning of regulatory terms should not hinge on the definitions of those words in isolation. *Alaska Trojan Partnership v. Gutierrez*, 425 F.3d 620, 628 (9th Cir. 2005). The context of the regulatory scheme as a whole is also important. *Id.*

One additional step in interpreting the meaning of words in a regulation is to look to the preambles that accompanied the proposed and final rules resulting in the regulations at issue. Courts have recognized that, "while language in the preamble of a regulation is not controlling over the language of the regulation itself, . . . a preamble is evidence of an agency's contemporaneous understanding of its rules." *Wyoming Outdoor Council v. United States Forest Service*, 165 F.3d 43, 53 (D.C. Cir. 1999) (citing *Chemical Mfrs. Ass'n v. DOT*, 105 F.3d 702, 708 (D.C. Cir. 1997); *Booker v. Edwards*, 99 F.3d 1165, 1168 (D.C. Cir. 1996); *Jurgensen v. Fairfax County, Va.*, 745 F.2d 868, 885 (4th Cir. 1984)). With respect to the precise meaning of

"repeatedly or "deliberately," the preambles associated with the original version of the regulation that provided for the disqualification of clinical investigators issued in 1963, and the current regulation, issued in 1987, do not provide much insight. The proposed rule leading to the 1963 regulation did not contain the language "repeatedly" or "deliberately." Under the proposal, the agency would have had the authority to "notify the sponsor that [an] investigator was not entitled to receive investigational-use drugs" if the investigator had "previously failed to comply with the conditions of the [investigational-use] regulations." The final rule added "repeatedly or deliberately" to this language without explanation. Likewise, the preambles associated with promulgation of 21 C.F.R. § 312.70(b) do not touch on the meaning of "repeatedly" or "deliberately."

In the absence of direct guidance from the preambles issued in conjunction with the regulation itself, the only way to determine the meaning of "repeatedly" and "deliberately," as used in 21 C.F.R. § 312.70(b), is to read those terms in context. As courts have long recognized in interpreting statutes, "[t]he plainness or ambiguity of statutory language is determined by reference [not only to] the language itself [but also to] the specific context in which the language is used and the broader context of the statute as a whole." *Robinson v. Shell Oil Co.*, 519 U.S. 337, 340-41 (1997). The same tenets apply to regulatory language. *See Alaska Trojan Partnership*, 425 F.3d at 628. For context to inform the meaning of a word, one should look to the specific use of the word in the regulation in which it is found and the design and purpose of the regulatory scheme of which it is a part.

As recognized by P.O. Dr. Startzman, the purpose of the regulations governing clinical investigations is fairly self-evident: to protect both the safety of the human patients and the

integrity of the data. A review of the background of the regulatory scheme at issue in this proceeding lends credence to that conclusion. As Dr. Gentry points out, FDA began the public process of revising the regulatory conditions applicable to clinical investigations of any product regulated by the agency in 1977. As part of this initiative, FDA issued a proposal regarding the obligations of clinical investigators of regulated articles. In support of this proposal, the agency offered the following justification for imposing such requirements on clinical investigators:

> The results of literally hundreds of clinical investigations are submitted to FDA each year by persons seeking regulatory action by the agency . . . . In evaluating the enormous volume of clinical investigations filed with FDA, many types of scientific and regulatory review must be devoted to these studies apart from determining their ethical and scientific validity, e.g. to interpret the results and to evaluate the status of the affected products in light of the results. Given the limited resources of the agency, the Commissioner believes that FDA must have standards to screen out those clinical investigations that are likely to be unacceptable and thus should not be authorized by FDA or that warrant little further evaluation in support of a product application. The promulgation of [the clinical investigator] regulations provides one process for making this judgment. While compliance with the regulations does not guarantee the ethical or scientific acceptability of, or the validity of data from, a clinical investigation, failure to comply substantially increases the probability that the results will not be useful to FDA. Moreover, as noted elsewhere in this preamble, the regulations reflect principles recognized by the scientific community as essential to sound research involving human and animal subjects.

43 Fed. Reg. at 35221. With respect to the purpose of providing procedures for disqualifying a clinical investigator, the agency made it clear that such procedures are essential to protecting human subjects in future studies and ensuring the integrity of the data:

> Disqualification is principally a remedial action to prevent future violations and to assure that the rights and safety of the subjects are appropriately protected and that data in support of the applications are produced under circumstances that increase the likelihood of their scientific validity.

Id. The agency later rejected some of the requirements proposed in 1978 in finalizing the

obligations on clinical investigators in part 312. But the policy justifications advanced by the agency in that related rulemaking, even if it did not advance past the proposal phase, clearly provide support for the common-sense conclusion that the purpose of a regulatory scheme that governs the conduct of clinical studies is to protect the safety of human subjects and the integrity of the clinical data.

In addition to the general purpose of the regulations at stake in this proceeding, the structure and design of the regulations surrounding 21 C.F.R. § 312.70(b) are also instructive in determining the meaning of "repeatedly" and "deliberately." The regulations governing the responsibilities of clinical investigators, along with those governing sponsors of clinical trials, are found in subpart D of 21 C.F.R. part 312. Under those regulations, investigators are held to a high standard. The first of the regulations addressing the duties of investigators in subpart D sets out those responsibilities in clear terms. Under 21 C.F.R. § 312.60, an investigator has an affirmative duty to ensure that the study is conducted in accordance with, *inter alia*, all applicable regulations: "An investigator is responsible for ensuring that an investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations." Each of the regulations that follow, 21 C.F.R. §§ 312.61 to 312.69, imposes additional obligations on an investigator. But, given its scope, 21 C.F.R. § 312.60 makes clear that the investigator's duties go well beyond those enumerated responsibilities, and include supervision of the investigation in a manner that prevents violations of any governing regulations. In other words, it serves as a framework for all of the regulations governing the responsibilities of investigators. Indeed, a violation of any of the other regulations, including 21 C.F.R. §§ 312.61 to 312.69, would also be a violation of 21 C.F.R. § 312.60.

As noted above, under 21 C.F.R. § 312.70(b), investigators are subject to disqualification if they have "repeatedly or deliberately failed to comply with the requirements of [part 312], part 50 or part 56." By virtue of the literal terms of 21 C.F.R. § 312.60, an investigator's *failure to ensure* that the clinical investigation is conducted according to applicable regulations may subject an investigator to disqualification. Dr. Gentry argues there is a distinction to be made between direct violations of the regulations governing clinical investigations, whether they occur through commission or omission, and supervision that fails to prevent such violations. Given the interplay between 21 C.F.R. §§ 312.60 and 312.70(b), however, any such distinction becomes meaningless with respect to the underlying conduct that subjects an investigator to disqualification.

Under 21 C.F.R. § 312.60, an investigator must ensure that the investigation is conducted in accordance with both the applicable regulations and the investigator statement, which requires the investigator to agree to personally conduct or supervise the investigation. Therefore, an investigator's failure to supervise an investigation can result in disqualification as readily as his own direct violation of the regulations if such failure is repeated or deliberate. As a consequence, any interpretation or application of "repeatedly" or "deliberately" must account for not only direct violations of the regulations but also circumstances in which there has been an abrogation of supervisory responsibilities.

a. deliberately

When viewed in that light, the meaning of the term "deliberately," in particular, comes into focus. As argued at length by Dr. Gentry in the proceedings below, the lay definition of "deliberate" may connote a *mens rea* on par with "intentional." When the issue is whether an

investigator has "deliberately" shirked the duties imposed on him by 21 C.F.R. § 312.60, however, the standard takes on new dimensions. One can deliberately fail to take steps to ensure compliance with the regulations without any knowledge of the specific violations that are occurring as a result of such failure. While it is true, as Dr. Gentry argues, that mere negligence with respect to the conduct of an investigation could clearly not satisfy any *mens rea* standard described as "deliberate" or "intentional," a demonstrated indifference to the regulatory requirements for investigations could clearly serve as the basis for disqualification if it could be characterized as "deliberate."

The Supreme Court has had occasion--in a different context--to explore the meaning of "deliberate" when used in connection with a failure to act. In *Estelle v. Gamble*, 429 U.S. 97 (1976), the Supreme Court formulated a standard for evaluating whether prison officials have subjected an inmate to cruel and unusual punishment by denying him or her medical care. The Court concluded that "deliberate indifference to serious medical needs of prisoners constitutes" a violation of the Eighth Amendment proscription against cruel and unusual punishment. *Id.* at 104. In the years that followed, federal courts interpreted the term "deliberate indifference" to mean a standard of care "lying somewhere between the poles of negligence at one end and purpose or knowledge at the other," and the term came to be equated with "recklessness." *Farmer v. Brennan*, 511 U.S. 825, 836 (1994).

In 1994, however, the Court found that formulation of the standard for deliberate indifference to be inadequate:

> [T]he term recklessness is not self-defining. The civil law generally calls a person reckless who acts or (if the person has a duty to act) fails to act in the face of an unjustifiably high risk of harm that is either known or so obvious that it should be

> known. The criminal law, however, generally permits a finding of recklessness when a person disregards a risk of harm of which he is aware.

Id. at 836-37 (internal citations omitted). After acknowledging that there is a clear place in society for an objective standard for both "recklessness" and "deliberate indifference," the Court opted for the subjective standard associated with criminal law. In doing so, however, the Court made clear that its conclusion in that regard stemmed from its view that the Eighth Amendment only proscribes the infliction of *punishment*, which connotes some form of subjective intent, *id.* at 838-39, and not from "a parsing of the phrase 'deliberate indifference'":

> Use of "deliberate," for example, arguably requires nothing more than an act (or omission) of indifference to a serious risk that is voluntary, not accidental. And even if "deliberate" is better read as implying knowledge of a risk, constructive knowledge is familiar enough that the term "deliberate indifference" would not, of its own force, preclude a scheme that conclusively presumed awareness from a risk's obviousness.

Id. at 840.

I agree with the Supreme Court that the term "deliberate," when used to describe a category of violations that might lead to legal consequences, does not necessarily require a showing of subjective intent on the part of the person in question. As discussed *supra*, the purpose of the scheme here is to protect the safety of patients and to preserve the integrity of the data needed to assess the safety and effectiveness of drugs before being sold to the general public through disqualifying investigators who do not fulfill the responsibilities imposed on them.

In the context of such a remedial, as opposed to punitive, scheme, an objective standard for "deliberate" or "deliberately" is a better fit because the inquiry should focus on preventing risk rather than imposing punishment for culpable conduct. Even if the investigator did not intend for the violations to occur, conduct demonstrating a reckless disregard for the regulatory

requirements calls into question the investigator's fitness for conducting clinical trials. Although intentional violations of the regulations would further call the investigator's fitness into question, reckless conduct also has a detrimental effect on the safety of the patients and the integrity of the data. Given that the aim of the regulations governing clinical investigations, including 21 C.F.R. § 312.70(b), is to protect those very aspects of a clinical investigation, interpreting "deliberately" to mean "intentional" for the remedial measure of disqualification would thus be inconsistent with the regulatory scheme.

Inasmuch as the Supreme Court has acknowledged that inferring an objective standard from "deliberate" is permissible when the regulatory scheme warrants such an inference, there is thus no doubt that the standard for "deliberately" should be an objective one here. The question is how to frame that objective standard. In my view, federal courts struck the proper balance in their original formulation of the "deliberate indifference" standard for certain constitutional violations. "Deliberately," when used as an objective standard, should be a standard of care "lying somewhere between the poles of negligence at one end and purpose or knowledge at the other" and is best equated with "recklessness." *Farmer*, 511 U.S. at 836. Ignoring an obvious risk that a violation would occur or remaining willfully blind to risks of which the investigator *should have* known had he or she been fulfilling his or her regulatory obligations would both qualify as "deliberately" under this standard, as would intentional violations of the regulations.

As P.O. Dr. Startzman recognized, such a construction of "deliberately" in the context of the clinical investigation regulations necessarily touches upon the supervisory responsibilities of the investigator. When a clinical investigator is vested with the responsibility *to ensure* that violations do not occur, *see* 21 C.F.R. § 312.60, *recklessly disregarding* whether such violations

are likely to occur satisfies the standard of "deliberately" as readily as undertaking conduct that directly violates those regulations. In other words, investigators may be disqualified on the basis of nonfeasance, i.e., a failure to prevent a regulatory violation, just as they may be disqualified for misfeasance, i.e., direct regulatory violations. For the nonfeasance version of "recklessness," the range of evidence that might satisfy the standard overlaps extensively with the standard discussed below for "repeatedly." Evidence as to "repeated" violations of the regulations could also serve to show that the investigator recklessly disregarded the regulatory requirements. Certainly, such evidence would go a long way toward demonstrating that the investigator deliberately violated 21 C.F.R. § 312.60 by failing to supervise the clinical investigation properly.

In short, after extensive evaluation of the plain meaning of "deliberately" in the context of the design and purpose of the regulatory scheme of which it is a part, I agree with P.O. Dr. Startzman's ultimate conclusion that the term equates with "recklessness" in regard to the regulatory requirements applying to clinical investigations.

b. repeatedly

In the proceeding below, P.O. Dr. Startzman looked to the dictionary definition of "repeatedly" and concluded that the term means "again and again" or "more than once" whether in single study or across multiple studies. *See Webster's Ninth New College Dictionary* (1991). There is ample support for this interpretation. In fact, even Dr. Gentry agreed with that interpretation in his motion for summary decision when he acknowledged that the dictionary definition of "repeated" includes "said, done, or occurring again and again."

Insofar as Dr. Gentry takes issue with the P.O. Dr. Startzman's interpretation of

"repeatedly," his issue appears to be with the application of the standard to the undisputed evidence before him. Specifically, he argues that P.O. Dr. Startzman's application of the "repeatedly" standard renders his reading "the most extreme interpretation possible." According to Dr. Gentry, such an application of the standard "would give FDA discretion to disqualify an investigator for any *two* mistakes in a study or series of studies, regardless of the materiality of the errors, or the degree of negligence involved in the mistakes." As a specific example, he cites to P.O. Dr. Startzman's apparent conclusion that missing signatures on two radiology reports in a single patient's file could lead to disqualification.

In my view, for a violation to be "repeated," the underlying conduct must be undertaken on multiple occasions, whether within a single study or across several studies. As discussed in more detail below in the discussion of specific charges, however, there is no need in this proceeding to resolve the limits of how the term "repeatedly" should be applied. Whenever the limits of the standard for "repeatedly" are arguably at play in upholding P.O. Dr. Startzman's grant of summary decision, I am of the opinion that the uncontroverted evidence shows that the violation or violations at issue were deliberate under the standard articulated above. Furthermore, in many instances, the violations occurred across multiple studies. As a result, any further discussion of "repeatedly" is rendered moot.

In conclusion, I agree with P.O. Dr. Startzman that "repeatedly" means "again and again" or "more than once." As applied, the standard encompasses multiple violations of the regulations, whether in a single study or multiple studies.

C. The Violations

I now turn to applying the "repeatedly or deliberately" standard discussed above to the

individual violations and the record as a whole. Dr. Gentry contends that there remain genuine and substantial issues of fact with respect to whether Dr. Gentry repeatedly or deliberately violated the regulations governing clinical investigations. I begin by addressing Dr. Gentry's arguments in the context of each of the first five charges on which P.O. Dr. Startzman granted summary decision. I conclude by addressing the sixth charge, which relates to his failure to personally conduct or supervise the three clinical studies at issue in this case, and P.O. Dr. Startzman's conclusion that the undisputed evidence demonstrates that Dr. Gentry is subject to disqualification under 21 C.F.R. § 312.70(b).

1. Failure to Retain X-Ray Films

In granting CDER summary decision on this charge, P.O. Dr. Startzman found that there was no genuine issue of material fact with respect to CDER's allegations that Dr. Gentry repeatedly and deliberately violated 21 C.F.R. § 312.62(c) because he failed to retain the x-ray films for any of the sixty subjects in Study[ ]for the required period of two years. Dr. Gentry has admitted throughout this proceeding that the hospital where the study was being conducted destroyed the x-ray films after[ ]months. His sole argument in response to this charge is that the violation of 21 C.F.R. § 312.62(c) was neither repeated nor deliberate.

Under 21 C.F.R. § 312.62(b), an investigator must "prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation." Under 21 C.F.R. § 312.62(c), "an investigator shall retain records required to be maintained under this part for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated." Under 21 C.F.R.

§ 312.62(c), Dr. Gentry was required to retain the x-ray films for all sixty patients enrolled in Study[ ] When FDA investigators inspected the records for Study[ ] the x-ray films for the sixty patients enrolled in the study were not available for inspection. Dr. Gentry admits that he did not retain the x-ray films, in violation of 21 C.F.R. § 312.62(c).

Although Dr. Gentry admits that he did not retain the x-ray films, in violation of 21 C.F.R. § 312.62(c), he contends that the violation was not repeated because the loss of the x-rays was a result of a single failure to verify the record-retention policies for the hospital. Dr. Gentry further argues that the undisputed record does not establish that he violated 21 C.F.R. §312.62(c) deliberately and that, in fact, the record establishes no more than mere negligence. He asserts that he had a good faith belief that the hospital would retain the x-ray films based on his prior dealings with the hospital system at issue and that he should have been given an opportunity to demonstrate that good faith belief at an evidentiary hearing.

Having reviewed the record and P.O. Dr. Startzman's written decision, I conclude that there is no genuine and substantial issue of fact with respect to the charge that Dr. Gentry deliberately violated 21 C.F.R. § 312.62(c). As discussed above, a regulatory violation need not be intentional for it to be deliberate as that term is used in 21 C.F.R. § 312.70(b). The conduct underlying the violation must merely evince a reckless disregard for the duties and obligations imposed on investigators by FDA's regulations. The undisputed record before me establishes that not only did Dr. Gentry fail to ensure the retention of the patients' x-ray films in violation of 21 C.F.R. § 312.62(c), he never verified that there was a system in place for retaining those x-ray films.

Dr. Gentry maintains that he had a good faith belief that the hospital would retain the x-

ray films, but he admits that the belief was premised solely on his prior dealings with the hospital. The record shows that Dr. Gentry's belief was unfounded and inconsistent with the hospital's practices at the time Study[ ]began. At best, Dr. Gentry's belief was an assumption that had no basis in fact.

Under 21 C.F.R. § 312.62(c), Dr. Gentry had a duty to retain x-ray films as part of the records for Study[ ] The obligation did not require him to keep the records in his own physical possession. But whatever steps he took to ensure that the records of the study would be retained--and the record does not reveal what those steps were--they were inadequate to uncover that the hospital's practices called for the destruction of certain records[ ]months after they were created. Given the affirmative duty imposed on Dr. Gentry under 21 C.F.R. § 312.62(c), his failure to uncover this aspect of the hospital's record-retention policy speaks for itself. Such failure indicates that he did not make even the most basic inquiries into the hospital's record-retention policies before initiating Study[ ]Dr. Gentry may not have destroyed the x-ray films himself, but the record does not disclose any effort on his part to ensure that all of the records for the study would be retained. Nor does Dr. Gentry offer any explanation for why the hospital's practice regarding the destruction of x-ray films slipped past him, other than his assumption that the hospital's policies had not changed since the last clinical study he conducted there.

Under the foregoing circumstances, Dr. Gentry's assertion that he had a good faith belief that the records would be retained does not create a genuine and substantial issue of fact. His own admitted reliance on an unfounded assumption regarding the hospital's record-retention policies establishes that Dr. Gentry acted with reckless disregard for the requirements of 21

C.F.R. § 312.62(c). Accordingly, I agree with P.O. Dr. Startzman that summary decision on this charge is appropriate.

Having reviewed the record and P.O. Dr. Startzman's written decision, I conclude that there is no genuine and substantial issue of fact with respect to the charge that Dr. Gentry deliberately failed to comply with 21 C.F.R. § 312.62(c) by failing to retain x-ray films for the required two years in Study[ ].

2. Failure to Maintain Signed Radiology Reports

P.O. Dr. Startzman determined that Dr. Gentry repeatedly and deliberately violated 21 C.F.R. § 312.62(b) by failing to ensure that two radiology reports for Study[ ]were signed. Under 21 C.F.R. § 312.62(b), investigators must maintain case histories containing "case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes." Dr. Gentry does not deny that two of the radiology reports maintained for Study[ ]bore the typed name of the radiologist who evaluated the x-ray films but not the radiologist's handwritten signature.[6] The undisputed record before me also establishes that the hospital's routine practice did not provide for handwritten signatures. In concluding that the radiology reports required handwritten signatures under 21 C.F.R. § 312.62(b), P.O. Dr. Startzman determined that the modifier "signed" requires a handwritten signature.

[6]As noted above, P.O. Dr. Startzman found that summary decision was inappropriate on the issue of whether 21 C.F.R. § 312.62(b) required that the radiology reports be dated. Because I am addressing only those charges for which summary decision was granted, I have no cause to address P.O. Dr. Startzman's resolution of that issue.

Dr. Gentry does not dispute P.O. Dr. Startzman's determination that the two radiology reports do not bear handwritten signatures. Dr. Gentry initially objected to CDER's definition of "signed." He argued before P.O. Dr. Startzman that the modifier "signed" did not exclude typewritten names and that, thus, a radiologist's typed name on a radiology report satisfied the requirement under 21 C.F.R. § 312.62(b) that such reports be signed. Dr. Gentry now takes issue with CDER's position--and P.O. Dr. Startzman's--that the word "signed" modifies medical records. Dr. Gentry claims, for what appears to be the first time, that "signed" modifies only "consent forms" and does not modify "medical records." He argues that, as a result, 21 C.F.R. § 312.62(b) does not require medical records to be signed.

As a preliminary matter, Dr. Gentry's arguments that 21 C.F.R. § 312.62(b) does not require medical records to bear handwritten signatures is inconsistent with his concessions in his responses to the NIDPOE, both in writing and at the informal conference, that the unsigned radiology reports constituted a violation of 21 C.F.R. § 312.62(b). The explanation he provided for the violation in the NIDPOE was that he was unaware that the hospitals' radiologists did not sign the radiology reports. In fact, he represented that, when he learned of the hospitals' policies, he took immediate corrective action by hiring an independent radiologist who agreed to authenticate radiology reports with his own handwritten signature. Therefore, insofar as Dr. Gentry intends to suggest that the legal arguments on which he has relied in this proceeding are consistent with his understanding of the regulation when he conducted Study[ ]the record before me prevents any such suggestion from rising to the level of a disputed fact with respect to the charge of deliberateness. As a result, Dr. Gentry's arguments regarding the scope of 21 C.F.R. § 312.62(b) raise questions of regulatory interpretation, not fact.

As determined by P.O. Dr. Startzman, the word "signed" requires a handwritten signature. I agree with his interpretation. The word "signed" is a verbal adjective derived from the verb "sign." *See Merriam-Webster's Collegiate Dictionary* (10th ed. 2002). "Sign" means "to affix a signature to." *Id.* The primary lay definition of "signature" is "a person's name, or a mark representing it, as signed or written by himself or by deputy, as in subscribing a letter or other document." *Id. Black's Law Dictionary* (6th ed. 1990) defines "signature" as, *inter alia*, the "name or mark of a person, written by that person or at his or her direction." Although *Black's Law Dictionary* includes among its definitions of "signature" typewritten names at the end of an instrument, a critical element of this type of "signature" is that it be designed "to attest to the validity" of the instrument to which it is attached. *Id.*

In light of the foregoing definitions, P.O. Dr. Startzman's conclusion that the adjective "signed," as used in 21 C.F.R. § 312.62(b), requires something more than a typewritten name on the instruments it modifies was reasonable. Moreover, I am of the opinion that P.O. Dr. Startzman's interpretation of "signed" is the correct one because any ambiguity in the meaning of the word "signed" should be resolved in a manner consistent with the purpose of the regulation. The regulations governing clinical investigations of unapproved drugs, or unapproved indications, are designed to protect not only the safety and health of the patients enrolled in the study but also the integrity of the data submitted for approval. The typewritten name of the radiologist, without more indicia of reliability, is inadequate to protect the integrity of the data.

Given the importance of signatures in protecting the integrity of data, it cannot be gainsaid how important the signatures of medical practitioners are in the context of a clinical trial. Medical reports have little value if they are not authenticated by an attending practitioner

whose identity can be verified by reference to a handwritten signature or an electronic signature under 21 CFR part 11. Without the reliability conferred by signatures, medical reports could be fabricated and manipulated in ways that they cannot when signed by the appropriate medical practitioner. The signature is the imprimatur of the person who generated the document or caused the document to be generated. A typewritten name on a paper document lends the report no such indicia of reliability. Because it is undisputed that the radiologist in this case simply dictated the two radiology reports at issue and an assistant typed the radiologist's name at the bottom, I find that the radiology report was not "signed" as that term is used in 21 C.F.R. § 312.62(b).

Dr. Gentry also argues that the adjective "signed" in 21 C.F.R. § 312.62(b) describes only "consent forms" and does not describe "medical records." As noted above, he does not contend that he understood the regulation to require something less than a handwritten signature on medical records when he conducted Study[ ]Indeed, there is no punctuation or phrasing in the regulation to indicate that "signed" is intended to modify only "consent forms" and not "medical records."

Insofar as there is any ambiguity in the regulation, I must resolve it in favor of the purpose for which the regulation was intended. As discussed above, one of the overarching purposes of the regulations governing clinical investigations--and this regulation in particular--is to ensure that medical records are prepared and maintained in a manner that promotes an accurate and comprehensive reflection of the data compiled. Requiring the medical practitioner's signature on his or her reports serves that purpose by protecting the integrity of the data. In short, whatever ambiguity there is with respect to the words modified by "signed," the context of

the language and the overriding purpose of 21 C.F.R. § 312.62(b) and the regulations governing clinical investigations as a whole, convince me that the word "signed" should be read to modify "medical records."

Because I cannot square Dr. Gentry's interpretation of 21 C.F.R. § 312.62(b) with its clear regulatory purpose or the intent evidenced by its language, I find that the regulation required that the radiology reports bear a handwritten signature or suitable substitute authorized by regulations. It is undisputed in this case that two records did not bear the required signature. Therefore, I find that P.O. Dr. Startzman properly granted summary decision on this charge because Dr. Gentry's failure to comply with 21 C.F.R. § 312.62(b) was deliberate. In a vein similar to the charge regarding Dr. Gentry's failure to retain x-ray films for all patients, the violation was deliberate because he recklessly disregarded the regulatory requirement by failing to make even the most basic inquiries as to the hospital's policies regarding the manner in which radiology reports would be finalized by radiologists at the hospital.

Having reviewed the record and P.O. Dr. Startzman's written decision, I conclude that there is no genuine and substantial issue of fact with respect to the charge that Dr. Gentry deliberately failed to comply with 21 C.F.R. § 312.62(b) by failing to ensure that the radiology reports were signed in Study[ ].

3. Failure to Maintain Adequate and Accurate Case Histories

P.O. Dr. Startzman concluded that Dr. Gentry also repeatedly and deliberately violated 21 C.F.R. § 312.62(b), which required that he maintain adequate and accurate case histories, in that there were seven record discrepancies, involving five subjects in Study[ ]Dr. Gentry

does not dispute that the discrepancies exist.[7] Instead, he argues that the discrepancies were not material to FDA's drug approval process.

At the outset, I note that Dr. Gentry's argument does not raise any issue of fact. Rather, Dr. Gentry's argument, that the inaccuracies in the case histories must be material to FDA's drug approval process for those inaccuracies to be violations of 21 C.F.R. § 312.62(b), raises an issue of regulatory interpretation. It is true that numerous federal statutes explicitly or implicitly require a showing of materiality as a condition of civil or criminal liability and that certain provisions of the FDCA involve a materiality requirement. But 21 C.F.R. § 312.62(b) imposes no such requirement. By its own terms, the regulation requires that the investigator "prepare and maintain adequate and *accurate* case histories that record *all* observations and other data *pertinent* to the investigation (emphasis added)." Insofar as the regulation's requirement regarding accuracy is at all limited, the limitation is pertinence to the study, not materiality to FDA's drug approval process. The record discrepancies undergirding P.O. Dr. Startzman's summary decision on this charge are indisputably pertinent to the study. As a result, the uncontroverted evidence establishes that Dr. Gentry violated 21 C.F.R. § 312.62(b) by failing to prepare and maintain accurate records for Study[ ]

I also find that P.O. Dr. Startzman's grant of summary decision on this charge was appropriate because the discrepancies at issue occurred across five patients' files and thus

---

[7] Specifically, the seven record discrepancies involved the following: duplicative medication dosing records, which showed different drug administration patterns, for two subjects (1403 and 1903); incorrect subject numbers on medication labels on Case Report Forms ("CRFs") for two subjects (1403 and 1916); administration of study medications past the post-therapy date – i.e., the date a subject completes the prescribed course of therapy – for two subjects (1403 and 2117); and a discrepancy between the hospital medication chart and the CRF about whether one subject (1920) received concomitant therapy – i.e., therapy with drugs in addition to the test drug.

constituted a "repeated" failure to comply with the regulations. By its own terms, 21 C.F.R. § 312.62(b) requires that the investigator maintain "adequate and accurate case histories"--plural. This is not a case in which there are discrepancies in a single patient's case history so I need not address Dr. Gentry's argument regarding whether multiple discrepancies in a single patient's case history would satisfy the "repeatedly" standard. In this case, there is documentation of discrepancies across multiple patients' files which clearly meets the "repeatedly" standard in my view. Each inaccurate case history therefore represents a failure on the part of Dr. Gentry to comply with the 21 C.F.R. § 312.62(b) by maintaining an accurate case history. Furthermore, I agree with P.O. Dr. Startzman that the uncontested record discrepancies here reflect a reckless disregard for that regulation's requirements. The internal inconsistencies within the patient's files indicate that there was little, if any, review of the records by Dr. Gentry to ensure that they were adequate and accurate. Although Dr. Gentry takes issue with P.O. Dr. Startzman's conclusion regarding the lack of review by Dr. Gentry himself, he provides no evidence that he actually reviewed the records for accuracy and internal consistency or even directed someone else to do so.

Having reviewed the record and P.O. Dr. Startzman's written decision, I conclude that there is no genuine and substantial issue of fact with respect to the charge that Dr. Gentry repeatedly and deliberately failed to comply with 21 C.F.R. § 312.62(b) by failing to prepare and maintain adequate accurate case histories for Study[ ]

4. Failure to Obtain IRB Approval

In addition, P.O. Dr. Startzman concluded that Dr. Gentry violated 21 C.F.R. §§ 50.27, 56.103, 312.53(c)(1)(vii), 312.60, and 312.66 by failing to obtain required IRB approval for the

enrollment of new patients at Hospital Calderon Guardia. This finding was based upon the fact that Dr. Gentry enrolled twenty-five subjects across two studies, Studies[ ]and[ ] at Hospital Calderon Guardia in Costa Rica before obtaining approval from the Institutional Review Board ("IRB") of record ("the[ ]IRB") for those studies. Dr. Gentry concedes both that the[ ]IRB was the IRB listed on the investigator statements for the Costa Rican sites in Studies[ ]and[ ]and that he failed to obtain approval from the[ ]IRB before enrolling subjects. However, he contends that the regulations did not require him to obtain approval from a particular IRB for these studies and that he obtained approval from "local IRBs" for the studies before enrolling the patients.[8]

In addressing this charge, P.O. Dr. Startzman devoted much of his discussion to whether Dr. Gentry had created a material factual dispute with respect to whether the "local IRBs" satisfied the requirements for IRBs under the regulations and whether they could and did perform all of the functions required of IRBs. I find it unnecessary to address these issues because Dr. Gentry did not list any of the "local IRBs" on the investigator statement submitted to FDA. The investigator statement listed only St. Luke's Episcopal Hospital IRB ("the St. Luke's IRB") and the[ ]IRB as the IRBs responsible for review and approval of the studies. Dr. Gentry's failure to obtain approval from one of these IRBs constituted a violation of 21 C.F.R. §§ 312.60 and 312.66 for each study.

Under 21 C.F.R. § 312.53(c)(1), the sponsor must obtain a signed statement from the investigator prior to the start of the investigation. That statement must include "the name and

[8]The parties appear to agree that the regulations did require IRB approval for enrollment of the twenty-five patients at Hospitals Calderon Guardia.

address of the IRB that is responsible for review and approval of the study(ies)." Dr. Gentry also committed to seeking approval of "*the* IRB" before making changes to the research in Studies [ ]and[ ]when he signed and submitted the investigator statements for those studies. *See* 21 C.F.R. § 312.53(c)(1)(vii) (emphasis added). Under 21 C.F.R. § 312.60, "[a]n investigator is responsible for ensuring that an investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations." Under 21 C.F.R. § 312.66, an investigator must report all changes in clinical studies to "*the* IRB" and may "not make any changes to the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects" (emphasis added).

Before the presiding officer, Dr. Gentry argued nonetheless that he was not required to seek approval from the[ ]IRB, as contended by CDER, because none of the regulations cited by CDER expressly requires that the IRB approval be from an IRB listed in the investigator statement. In the NOOH and throughout this proceeding, CDER has cited 21 C.F.R. §§ 50.27, 56.103, 312.53(c)(1)(vii), 312.60, and 312.66 in support of this charge.[9]

While I agree with CDER and P.O. Dr. Startzman that 21 C.F.R. § 312.60, and 312.66 support this charge, I disagree that 21 C.F.R. § 312.53(c)(1)(vii) supports a charge against a clinical investigator. A close examination of the terms of 21 C.F.R. § 312.53(c) makes it clear that it imposes an obligation on the sponsor of the study, not the clinical investigator of the

[9]Although P.O. Dr. Startzman found that Dr. Gentry violated all the regulations as charged by CDER, his opinion does not appear to include a discussion of his findings as to the violations of 21 C.F.R. §§ 50.27 and 56.103. 21 C.F.R. § 50.27 sets out requirements regarding informed consent and provides for use of a written informed consent form approved by the IRB. 21 C.F.R. § 56.103 provides that a clinical investigation shall not begin unless it has been "reviewed and approved by .... . . an IRB." Nor does Dr. Gentry address these provisions. Therefore, my opinion will discuss only 21 C.F.R. § 312.60 and 312.66.

study. The title of section 312.53(c) is "*Obtaining information from the investigator.*" The lead-in to the section reads "Before permitting an investigator to begin participation in an investigation, the sponsor shall obtain the following: (1) A signed investigator statement (Form FDA 1572) containing [various listed elements including a commitment by the investigator with regard to IRB review.]" It is clear that the regulations at 21 C.F.R. § 312.60 impose the requirement on the investigator to conduct the investigation in accordance with the signed investigator statement that the sponsor is required to obtain under 21 C.F.R. § 312.53(c).

Returning to the other regulations cited by CDER for this charge, those regulations clearly require approval by such a listed IRB when read in context and in conjunction with other regulations. Under 21 C.F.R. § 312.60, the investigator must conduct the studies in accordance with not only the regulations but also the investigator statement. The investigator's statement includes the name and address of the IRB that is responsible for reviewing and approving the study. 21 C.F.R. § 312.66 refers to the "IRB approval." The only reasonable interpretation of "IRB approval," as used in 21 C.F.R. § 312.66, is approval by an IRB listed in the investigator statement.

In short, the regulations cited by CDER, except for 21 C.F.R. § 312.53(c)(1)(vii), clearly required that Dr. Gentry obtain approval by either the St. Luke's IRB or the[ ]IRB, i.e., the IRBs listed in the investigator statements, before changes to Studies[ ]and[ ]could be made. As apparently conceded by Dr. Gentry, enrolling twenty-five new study subjects, ten in one study and fifteen in the other, constitutes changes to the underlying studies requiring IRB approval. Because he did not obtain approval from either of the IRBs listed in the investigator statements, Dr. Gentry violated 21 C.F.R. § 312.60 by failing to conduct the studies according to

the investigator statement and violated 21 C.F.R. § 312.66 by failing to obtain IRB approval before making such changes. Furthermore, I agree with P.O. Dr. Startzman that the undisputed evidence shows that Dr. Gentry both repeatedly and deliberately failed to comply with these regulations: (1) because he did not obtain the proper IRB approval for two separate studies and (2) because he acted with reckless disregard for the regulatory requirement.

Having reviewed the record and P.O. Dr. Startzman's written decision, I conclude that there is no genuine and substantial issue of fact with respect to the charge that Dr. Gentry repeatedly and deliberately failed to comply with 21 C.F.R. §§ 50.27, 56.103, 312.60, and 312.66 by failing to obtain proper IRB approval for enrollment of twenty-five patients across two different studies: Studies[ ] and[ ]

5. Failure to List Three Subinvestigators on FDA Form 1572

P.O. Dr. Startzman determined that Dr. Gentry violated 21 C.F.R. §§ 312.53(c)(1)(viii) and 312.60 because he failed to include the names of three subinvestigators on the investigator statements for Studies[ ] Dr. Gentry does not dispute that he failed to list the physicians that CDER asserts were subinvestigators for those studies, i.e., Drs. [ ] in the investigator statements. Rather, Dr. Gentry argues that, insofar as those three physicians qualified as "subinvestigator[s]" under 21 C.F.R. § 312.3(b), he lacked sufficient notice as to whom FDA would consider to be a "subinvestigator." He contends that he should thus not be disqualified for his failure to list the three physicians in the investigator statements. In support of this position, Dr. Gentry relies, *inter alia*, on statements attributed to Dr. Robert Temple, the Associate Director for Medical Policy at CDER, that the definition of subinvestigator is "variable and imprecise."

As discussed above, I disagree with the finding by P.O. Dr. Startzman that Dr. Gentry violated 21 C.F.R. § 312.53(c) because that section imposes requirements on the sponsor, not on the clinical investigator. Therefore, I will only consider whether summary decision was appropriate on CDER's charge that Dr. Gentry violated 21 C.F.R. § 312.60 by failing to list the three subinvestigators' names on the Form FDA 1572.

I disagree with Dr. Gentry that the definition of subinvestigator in FDA's regulations is unclear. Under 21 C.F.R. § 312.3(b), the definitions for both "investigator" and "subinvestigator" are interrelated. "Investigator" means "an individual who actually conducts a clinical investigation (i.e., under whose immediate direction the drug is administered or dispensed to a subject). In the event an investigation is conducted by a team of individuals, the investigator is the responsible leader of that team." 21 C.F.R. § 312.3(b). "Subinvestigator" means "*any* other individual member of that team." *Id.* (emphasis added). In addition, the preamble to the final rule states that "subinvestigator" includes "*all* other professionals who assist the principal in the design and conduct of the investigation." 52 Fed. Reg. 8798, 8809-10 (March 19, 1987) (emphasis added). Furthermore, the investigator statements themselves provided notice to Dr. Gentry that the term subinvestigator encompassed all professionals--physicians, in particular--that assisted in the conduct of the studies. The form provides for him to list the "[N]AMES OF THE SUBINVESTIGATORS (e.g., research fellows, residents, associates) WHO WILL BE ASSISTING THE INVESTIGATOR IN THE CONDUCT OF THE INVESTIGATION." Finally, 21 C.F.R. § 312.61 permits the administration of study medication to subjects only "under the investigator's personal supervision or the supervision of a subinvestigator responsible to the investigator."

The undisputed evidence in this proceeding shows that Dr.[ ] the supervisory subinvestigator in Costa Rica, delegated responsibility for conducting many of the critical functions for conducting a clinical trial to Drs.[ ]. Those three physicians recruited and screened candidates for enrollment in the study, explained the consent forms to study subjects, conducted physical examinations, and provided follow-up on the subjects' clinical responses. Perhaps most importantly, Drs.[ ] administered study medications to subjects, apparently without supervision by Dr. Gentry or Dr. [ ] but could only do so under FDA's regulations if they were subinvestigators. *See* 21 C.F.R. § 312.61. In any event, as physicians assisting in the conduct of the clinical trial by performing critical functions, Drs.[ ] were subinvestigators, as that term is defined in 21 C.F.R. § 312.3(b) and the Form FDA 1572, whose names should have been listed on the investigator statements. Accordingly, by failing to list those three physicians on the investigator statements--or amend the investigator statements when those physicians began performing the functions of subinvestigators--Dr. Gentry conducted an investigation that was not according to the signed investigator's statement. This was a violation of 21 C.F.R. § 312.60.

Dr. Gentry's attempts to muddy the definition of subinvestigator without specific reference to the roles performed by Drs.[ ] are unconvincing. As P.O. Dr. Startzman found, the regulations and Federal Register documents cited by Dr. Gentry in support of his arguments actually serve to undercut his position inasmuch as they contain definitions of subinvestigator or explanatory language that is consistent with the definition in 21 C.F.R. § 312.3(b). Furthermore, even if Dr. Gentry is correct that the precise parameters of the definition of "subinvestigator" are unclear, the three physicians here fall squarely within that

definition. Further, Dr. Gentry has never explained why he believes the definition of subinvestigator to be vague in terms of whether those three physicians were subinvestigators. A fair interpretation of the remarks attributed to Dr. Temple is that he views the current definition of "subinvestigator" to be too broad.[10] Dr. Gentry clearly agrees. But for the putative over-breadth of the definition to be meaningful in this proceeding, Dr. Gentry would have to show, at the very least, that FDA has interpreted the definition in a manner that excludes Drs. [ ] from the definition. He has made no such showing. Indeed, based on the undisputed evidence, I find that those physicians would meet the definition of subinvestigator under any reasonable interpretation of 21 C.F.R. § 312.3(b). Therefore, as noted above, Dr. Gentry violated 21 C.F.R. § 312.60 when he failed to list them as subinvestigators on the investigator statement and, as a result, he did not conduct the study in accordance with the signed investigator's statement. Furthermore, I agree with P.O. Dr. Startzman that the undisputed evidence shows that Dr. Gentry both repeatedly and deliberately failed to comply with the regulation: (1) because he conducted three studies that were not in accordance with the signed investigator statements when he did not list subinvestigators on the investigator statements for three separate studies and (2) because he acted with reckless disregard for the regulatory requirement that he conduct all studies in accordance with the signed investigator statement

---

[10]As reported in FDA Webview, Dr. Temple's comments were as follows:

> Temple said part of the problem [identified in an Inspector General report criticizing aspects of the IND process] lies in FDA's "variable and imprecise" definitions of investigator, sub-investigator and others who must sign the Form FDA-1572. "The people who get listed are fairly broadly defined, essentially by their major roles, and we all believe that needs further definition. . . . This is a work in progress. We're not happy with the current definitions. "

because those signed statements did not include the names of the three subinvestigators.

Having reviewed the record and P.O. Dr. Startzman's written decision, I conclude that there is no genuine and substantial issue of fact with respect to the charge that Dr. Gentry repeatedly and deliberately violated 21 C.F.R. § 312.60 because he failed to include the names of three subinvestigators on the investigator statements for Studies[ ] and, therefore, he conducted studies that were not according to the signed investigator statements for those studies.

6. Failure to Personally Conduct or Supervise Studies

The final charge on which P.O. Dr. Startzman granted summary decision in favor of CDER is a repeated and deliberate violation of 21 C.F.R. §§ 312.53(c)(1)(vi)(c) and 312.60 in that Dr. Gentry failed to personally conduct or supervise Studies[ ] as required by FDA regulations and in accordance with the obligations to which he committed when he signed the investigator statements.

Dr. Gentry challenges this finding on the grounds that CDER failed to allege any specific facts to support this charge and that the P.O. Dr. Startzman erred in finding this violation based solely on the existence of the other violations discussed above. Dr. Gentry argues that evidence that some violations occurred is not sufficient to support a charge of failure to supervise. According to Dr. Gentry, CDER should have been required to present evidence relating to his failure to perform supervisory duties. He further claims that using a group of violations to establish a separate violation is "double counting."

Contrary to Dr. Gentry's position, except with regard to 21 C.F.R. § 312.53(c)(1)(vi)(c),[11] the uncontroverted evidence supports P.O. Dr. Startzman's finding on this charge. The Presiding Officer considered the undisputed facts that Dr. Gentry failed to ensure that x-rays were retained, that radiology reports were signed, that case histories were accurate, that proper IRB approval was obtained, and that all subinvestigators were listed on the investigator statements. By signing the investigator statements, Dr. Gentry agreed that he would ensure that those tasks were performed and that he would "personally conduct or supervise" the investigations. If he was not directly performing those duties himself, therefore, he was obligated to supervise the performance of those duties by others. "Supervision" means a "critical watching and directing (as of activities or a course of action)." *See Merriam-Webster's Collegiate Dictionary* (10th ed. 2002). The violations described in connection with the five other substantive charges demonstrate that he repeatedly and deliberately did not perform the personal supervision to which he committed--"repeatedly" because he failed to ensure that violations did not occur in three separate studies and "deliberately" because the violations reflect a reckless disregard for the regulations governing clinical investigations. For example, evidence that the case histories contained errors establishes that Dr. Gentry repeatedly and deliberately failed to review such records to the extent necessary to ensure that they were accurate. The regulations do not prohibit this finding by P.O. Dr. Startzman simply because it is based on the same evidence as other

[11]As discussed with regard to other charges, 21 C.F.R. § 312.53(c)(1) imposes requirements on sponsors, not clinical investigators. The connection between 21 C.F.R. § 312.53(c)(1) and the clinical investigator is made through 21 C.F.R. § 312.60 which imposes a requirement on the clinical investigator to conduct the study in accordance with the signed investigator's statement that the sponsor is required to obtain under 21 C.F.R. § 312.53(c)(1).

violations.

Whether one frames P.O. Dr. Startzman's findings on the other five substantive charges as individual grounds for disqualifying Dr. Gentry or considers them collectively, however, the uncontroverted evidence subjects Dr. Gentry to disqualification under 21 C.F.R. § 312.70(b). The five other substantive charges represent multiple violations of the regulations, spanning three separate studies. Furthermore, as noted above, the number and type of violations presented reflect Dr. Gentry's reckless disregard for the regulatory requirements applicable to him. Consequently, I conclude both (1) that P.O. Dr. Startzman correctly granted summary decision as to the charge that Dr. Gentry repeatedly and deliberately failed to comply with 21 C.F.R. § 312.60 by failing to conduct the studies in accordance with the signed investigator statements, which included a commitment to personally conduct or supervise the investigations and (2) that the resulting repeated and deliberate violations, taken together or apart, subject Dr. Gentry to disqualification under 21 C.F.R. § 312.70(b).

Having reviewed the record and P.O. Dr. Startzman's written decision, I conclude that there is no genuine and substantial issue of fact with respect to the charge that Dr. Gentry repeatedly and deliberately violated 21 C.F.R. § 312.60 by failing to personally conduct or supervise Studies[ ]

III. PROCEDURAL CHALLENGES

Finally, Dr. Gentry argues that there were procedural deficiencies in the proceeding below that rendered the granting of summary decision and any disqualification on that basis fundamentally unfair and thus a violation of due process. He also contends that disqualifying

him on the basis of the proceeding below would be arbitrary and capricious. I address each of these arguments in turn.

A. Lack of Fair and Impartial Proceeding

Dr. Gentry argues that he was not provided the fair and impartial hearing to which he was entitled under 21 C.F.R. § 16.42(b) and the Due Process Clause of the Fifth Amendment. In support of his argument, Dr. Gentry lists several procedures that he claims were "unfair and biased."

1. The "NIDPOE" process.

Dr. Gentry argues that initiating this proceeding via a Notice of Initiation of Disqualification Proceedings and Opportunity to Explain ("NIDPOE") was a violation of the APA and his constitutional right to due process in that the NIDPOE procedure is not outlined in any public document and was never published by FDA for public review and comment. However, 21 C.F.R. § 312.70, which governs the disqualification process and which *was* promulgated using the notice-and-comment rulemaking, clearly states that CDER will initiate the disqualification process by issuing to the investigator "written notice of the matter complained of and offer the investigator an opportunity to explain the matter in writing, or, at the option of the investigator, at an informal conference." The NIDPOE issued in this matter provided Dr. Gentry with the written notice to which he was entitled, and he received both an opportunity to respond in writing and an informal conference. CDER's practice of calling the written notice a "NIDPOE" does not render the notice or the process accompanying such notice a violation of the Constitution or the APA.

2. CDER's failure to allege specific facts to which Dr. Gentry could respond.

Dr. Gentry argues that the allegations in the NIDPOE were insufficiently particularized to provide him with a reasonable opportunity to respond to the charges against him. He makes a similar argument with respect to the NOOH and complains that the Hearing Coordinator denied his request for a more particularized NOOH. However a review of the record before me discloses that the summary decision process provided Dr. Gentry with an opportunity to address not only every allegation on which CDER was basing its charges but also the evidence on which it was relying to support those allegations.

3. Constantly changing allegations.

Dr. Gentry objects to CDER's addition of (1) the failure to supervise charge, which was not raised in previous 483's, at the NIDPOE stage and (2) a charge concerning the submission of false information at the Notice of Opportunity for a Hearing ("NOOH") stage. He claims that CDER's altering those charges prevented him from effectively defending himself. However, Dr. Gentry was able to, and in fact did, address in detail the failure to supervise charge both in writing and at the informal conference. The submission of false information charge is irrelevant on review because the P.O. Dr. Startzman did not grant summary decision to CDER as to that charge.

4. Lack of discovery or an effective FOIA process.

Dr. Gentry argues that the proceeding below was unfair because it provided him with "no right of discovery, whether in the form of document requests, interrogatories, or depositions of the FDA investigators whose allegations [were at issue]." He argues that access to information

through the Freedom of Information Act was inadequate to provide him with the evidence necessary to defend himself and adequately challenge CDER's motion for summary decision.

Dr. Gentry had access to all the documents upon which CDER relied for summary decision. Insofar as Dr. Gentry was aware of facts pertaining to his own conduct that showed he did not "repeatedly or deliberately fail to comply" with the regulations--and he was uniquely positioned to be aware of such facts--he was free to enter evidence regarding his own recollections in response to CDER's motion for summary decision. Instead, many of his FOIA requests, as demonstrated by his submissions to the record since entry of P.O. Dr. Startzman's decision, have focused on supporting his legal arguments regarding alleged procedural deficiencies and the supposed arbitrariness and capriciousness of any final decision to disqualify him. In fact, he has not pointed to one document he requested through the FOIA process that was not provided to him and was--even theoretically--related to CDER's *evidence* regarding the factual bases for his disqualification. Even criminal defendants, whose liberty is at stake, have no constitutional due process right to engage in full-scale discovery. *Spicer v. Roxbury Correctional Institute*, 194 F.3d 547, 555 (4th Cir. 1999). I therefore find that the failure to provide Dr. Gentry with an opportunity to engage in discovery did not prejudice his ability to respond to CDER's Motion for Summary Decision.

5. Reliance on secret law.

As discussed above, there is no need for me to address this issue. As the P.O. Dr. Startzman did, I can interpret the meaning of the "repeated or deliberate" standard without looking to previous disqualification decisions.

6. "Biased" summary decision.

Dr. Gentry argues that the Presiding Officer's summary decision was "biased" in that Presiding Officer: (1) failed to resolve doubts in Dr. Gentry's favor; (2) impermissibly shifted the burden of proof to Dr. Gentry; (3) assumed facts not in evidence; and (4) failed to decide any issue in favor of Dr. Gentry. As discussed at length above, I find that P.O. Dr. Startzman's ultimate resolution of each of the charges on which he granted summary decision was appropriate. Therefore, I find that Dr. Gentry's arguments to the contrary are meritless.

B. Arbitrary and Capricious Disqualification

Dr. Gentry further argues that disqualifying him would be arbitrary and capricious because FDA lacks consistent standards for disqualification, resulting in the inconsistent treatment of similarly situated persons. As discussed at length above, FDA's standards for disqualification are consistent. The regulations make it clear that disqualification for violations of the clinical investigator regulations is the rule and not the exception. Section 312.70 provides that:

> [I]f the Commissioner determines that the investigator has repeatedly or deliberately failed to comply with the requirements of [part 312], part 50, or part 56 . . . the Commissioner *will* notify the investigator . . . that [he] is not entitled to receive investigational drugs.

21 C.F.R. § 312.70 (emphasis added). Although the preamble to the final rule explains that the Commissioner has discretion not to disqualify an investigator if he or she believes the violations are insignificant or lesser sanctions would be adequate, the preamble makes clear that this discretion should be exercised only in extraordinary circumstances. *See* 52 Fed. Reg. 8798, 8826

(1987). The existence of such enforcement discretion does not detract from the clear and consistent standards set forth in the regulations. Nor does it make a Commissioner's decision to follow those standards arbitrary and capricious. In this case, the standard for disqualification was clear and contained the relevant standard, i.e., repeated or deliberate violation of the clinical investigator regulations. Moreover, Dr. Gentry failed to create issues of material fact with respect to whether he was subject to disqualification under those standards.

The preamble to the final rule does provide that the Commissioner retains the discretion to decline disqualifying a clinical investigator under extraordinary circumstances if the violations at issue were insignificant or lesser sanctions would suffice to accomplish the remedial purpose. Given the record before me, however, I find that such extraordinary circumstances do not exist. Dr. Gentry's arguments regarding the conduct of other clinical investigators and the significance of his own violations do not convince me otherwise. The uncontroverted evidence before me shows that Dr. Gentry recklessly disregarded the regulatory requirements governing clinical investigations on numerous occasions across three separate investigations. I find that his violations are sufficiently serious and numerous to warrant disqualification.

IV. CONCLUSION

On the basis of the record before me, I conclude that Dr. Gentry is no longer entitled to receive investigational drugs. Dr. Gentry may seek to have his eligibility to receive investigational drugs reinstated pursuant to 21 C.F.R. § 312.70(f).

John R. Dyer
Deputy Commissioner for Operations

6/18/02
Date