DEPARTMENT OF HEALTH AND HUMAN SERVICES

U.S. FOOD AND DRUG ADMINISTRATION

REGULATORY HEARING ON THE PROPOSAL TO DISQUALIFY

CAREY L. QUARLES, Ph.D.

FROM RECEIVING INVESTIGATIONAL NEW ANIMAL DRUGS

DECISION ON PARTIES' MOTIONS FOR SUMMARY DECISION

I. Introduction

In this disqualification proceeding, the Center for Veterinary Medicine [CVM] asserts that Carey L. Quarles, Ph.D., repeatedly or deliberately submitted false information to the study sponsor, American Cyanamid Company, in violation of 21 C.F.R. § 511 CVM alleges that Dr. Quarles submitted false information in four studies: A-88-29, A-88-37, A-88-41, and A-89-8. On this basis, CVM requests that Dr. Quarles be disqualified from receiving investigational new animal drug products. Dr. Quarles responds by denying that he repeatedly or deliberately submitted false information to the study sponsor. Both CVM and Dr. Quarles request summary decision in their favor.

As provided in Title 21 of the Code of Federal Regulations [C.F.R.] Part 16 and § 511.1, I have reviewed:

- the Motion for Summary Decision and the supporting exhibits submitted by the Center for Veterinary Medicine,
- the Motion for Summary Decision and the supporting exhibits submitted by Dr. Carey L. Quarles,
- CVM's Opposition to Dr. Quarles' Initial Request for Summary Decision, and
- Dr. Quarles' Response to CVM's Request for Summary Decision.

I have concluded that Dr. Quarles submitted false information to the study sponsor three times. CVM's allegations in these three instances are supported by uncontroverted evidence sufficient to warrant granting CVM's motion for summary decision. In other words, Dr. Quarles has failed to overcome CVM's evidence that he repeatedly and deliberately violated 21 C.F.R. § 511.1. These three instances of falsification are sufficient to support a recommendation that Dr. Quarles be disqualified.

As for CVM's other allegations of Dr. Quarles' submission of false information to the sponsor, I find that there remain genuine and substantial issues of fact and that resolution of these issues would require a hearing. However, because the three aforementioned instances of falsification are sufficient to support a recommendation of disqualification, I find that a hearing is not necessary on these other allegations.

As provided in 21 C.F.R. § 16.26(b), this summary decision constitutes ~~my~~ ~~ruling~~ on the parties' motions. As described in detail below, I find that Dr. Quarles repeatedly and deliberately submitted false information in violation of 21 C.F.R. § 511.1. I recommend to the Commissioner that Dr. Quarles be disqualified from being eligible to

receive investigational new animal drugs. In accordance with 21 C.F.R. §§ 16.95 and 51 , this decision will be referred to the Commissioner of Food and Drugs, who will make a final decision.

II. Regulatory Basis for Disqualification

CVM charges Dr. Quarles with falsification under 21 C.F.R. § 51 1(c)(2), which provides:

> If, after evaluating all available information, including any explanation presented by the investigator, the Commissioner determines that the investigator . . . has repeatedly or deliberately submitted false information to the sponsor of an investigation, the Commissioner will notify the investigator and the sponsor of any investigation in which he has been named as a participant that the investigator is not entitled to receive investigational use new animal drugs with a statement of the basis for this determination.

The word "repeatedly" means more than once, or "again and again."[1] The term "deliberately" includes conduct that is "willful."[2] Willful conduct includes conduct demonstrating reckless disregard. When a clinical investigator engages in conduct that the investigator either knew, or showed reckless disregard for the possibility, that the information submitted by the investigator was false, the clinical investigator is liable to being found to have "deliberately" violated the regulations. Similarly, an investigator whose conduct shows a reckless disregard for whether the false information is submitted in a report to a sponsor is liable to being found to have "deliberately" violated the regulations.

Pursuant to 21 C.F.R. § 16.26, the Presiding Officer of a Part 16 hearing is authorized to issue a summary decision on any issue in the hearing if the Presiding

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[1] Webster's Ninth New College Dictionary (Merriam-Webster, Inc. 1991).

Officer determines from material submitted in connection with the hearing, or from matters officially noticed, that there is no genuine and substantial issue of fact regarding that issue.[3] Under § 16.26(b), a hearing commences upon receipt by FDA of a request for a hearing submitted under 21 C.F.R. § 16.22(b). A summary decision may be issued any time after the clinical investigator submits a request for a hearing in response to a Notice of Opportunity for Hearing [NOOH].

Rule 56(c) of the Federal Rules of Civil Procedure states that summary judgment "shall be rendered if there is no genuine issue as to any material fact and the moving party is entitled to a judgment as a matter of law." The standard for administrative summary decision contained in 21 C.F.R. § 16.26(b) mirrors that contained in Rule 56(c). Therefore, the body of law developed under Rule 56 may serve as a guide in determining whether summary decision is warranted.[4]

In ruling on a summary judgment motion, the Presiding Officer, as decision-maker, must determine whether there are disputed issues of fact that need to be decided at a hearing.[5] The party requesting summary judgment bears the burden of establishing the absence of a genuine issue of material fact.[6] A party opposing a properly supported motion for summary decision has the burden of showing that a rational trier of fact could

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[2] Black's Law Dictionary at 426 (6th ed. 1990); *McLaughlin v. Richland Shoe Co.*, 486 U.S. 128, 133 (1988).
[3] 21 C.F.R. § 16.26(b).
[4] *Puerto Rico Aqueduct and Sewer Authority v. EPA*, 35 F.3d 600, 604-608 (1st Cir. 1994) (finding that "[f]rom its inception, the concept of administrative summary judgment has been linked inextricably to Fed. R.Civ.P. 56," and that "[m]any agencies habitually look to Rule 56 case law for guidance in respect to administrative summary judgments."); *John D. Copanos and Sons, Inc. v. FDA*, 854 F.2d 510, 523 (D.C. Cir. 1988) (finding that the principles of *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 247-248 (1986) "apply with equal force in the context of administrative judgment."). See also 53 Fed. Reg. 4613, 4614 (February 17, 1988)(stating that the standard for summary decision set forth in 21 C.F.R. § 16.26 "conforms to well-settled law.").
[5] *Celotex Corp. v. Catrett*, 477 U.S. 317 (1986).
[6] *Adickes v. S.H. Kress*, 398 U.S. 144, 157 (1970).

find in their favor and that there is a "genuine issue for trial."[7] To fulfill this burden, the nonmoving party "must set forth specific facts showing that there is a genuine issue for trial."[8] Any doubts are to be resolved in favor of the non-moving party, and the non-moving party is entitled to all justifiable inferences.[9]

The mere existence of a scintilla of evidence in support of the non-moving party's position will be insufficient to overcome a motion for summary judgment.[10] Further, the opposition to a properly supported motion for summary judgment "must do more than simply show that there is some metaphysical doubt as to the material facts,"[11] and cannot rest on mere allegations.[12]

III. Background

The following facts are undisputed. Dr. Carey Quarles conducted studies for the sponsor, American Cyanamid Company [ACC], at Dr. Quarles' research facility, Colorado Quality Research, Inc. [CQR].[13] Dr. Quarles, besides being the clinical investigator for these studies, was the President and Chief Executive Officer of CQR during the time that these four studies were conducted. All four studies were designed to test the efficacy of Cygro in combination with bacitracin zinc, an antibiotic, and other antibiotics in pen-reared turkeys.[14] Cygro is an approved animal drug for use in turkeys as a treatment for coccidiosis, a parasitic condition that forms in the intestinal tract. The

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[7] *Matsushita Electrical Indus. Co. v. Zenith Radio Corp.*, 475 U.S. 574, 586 (1986).
[8] Fed.R.Civ.P. 56(e); *Matsushita Electrical*, 475 U.S. at 586; *First Nat'l Bank v. Cities Service Co.*, 391 U.S. 253, 289 (1968).
[9] *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 255 (1986).
[10] *Anderson*, 477 U.S. at 252.
[11] *Matsushita Electrical*, 475 U.S. at 586.
[12] *First Nat'l Bank*, 391 U.S. at 289.
[13] CVM Motion for Summary Decision [MSD] at 4.
[14] CVM MSD at 4-5.

purpose of the studies was to determine whether Cygro in combination with antibiotics promoted growth and improved feed efficiency

The protocol for Dr. Quarles' studies required that turkeys be assigned to one of two treatment groups. Treatment Group 1 received Cygro alone mixed in the feed, whereas Treatment Group 2 received Cygro plus an antibiotic. The turkeys were separated by sex and housed in pens, with each pen containing between 7 to 21 turkeys. Eight to twelve pens were assigned to each treatment group. The turkeys started the study at the age of one day and stayed in the study for 105 days for females and 126 days for males.[15]

Turkeys' dietary requirements change as they grow, and so the feed mix was changed several times during the studies. The different types of feed used during the studies included starter feed, grower 1, grower 2, and grower 3 feed, and a withdrawal feed. The withdrawal feed contained neither Cygro nor any antibiotics. During each phase of the study, the investigator measured an amount of feed for each pen of turkeys by weighing the feed distributed to the pens at the start of the study phase and weighing the feed left at the end of the phase, called the "weighback" amount. The investigator calculated the feed consumed for each study phase by subtracting the "weighback" amount from the amount distributed. At the completion of the study, the investigator measured the final weight of the turkeys and recorded and weighed all mortalities and morbitities.[16]

[15] CVM MSD at 5.
[16] CVM MSD at 5-6.

IV. Procedural History

Between October 1988 through March 1989, Dr. Quarles conducted twelve studies involving Cygro.[17] In September 1990 and November 1991, investigators from CVM visited Dr. Quarles' facility and reviewed his studies. Around this same time, CVM conducted a criminal investigation of ACC and Dr. David Sharkey, who was ACC's principal study monitor for all Cygro studies.[18] In February and April of 1994, Dr. Sharkey and ACC pleaded guilty to the failure to establish and maintain records required to be kept under the Federal Food, Drug, and Cosmetic Act relating to the investigational use of the new animal drug Cygro.[19] Dr. Quarles was not implicated in the plea agreements.[20]

In September 1995, CVM issued a Warning Letter to Dr. Quarles for four of his twelve Cygro studies. The Warning Letter alleges that Dr. Quarles submitted false data to ACC and violated regulations governing the proper conduct of the studies.[21] In January 1996, Dr. Quarles offered his written response to the Warning Letter.[22] On August 13, 1998, FDA issued an NOOH to Dr. Quarles.[23] The NOOH alleges that Dr. Quarles submitted false data to the study sponsor in connection with four studies: Study A-88-29, Study A-88-37, Study A-88-41, and Study A-89-8. Subsequent to the issuance of the NOOH, Dr. Quarles and CVM participated in informal settlement negotiations and mediation, but the parties were unable to reach an agreement.[24]

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[17] Quarles MSD at 1-2.
[18] CVM MSD, Exhibit B at 15.
[19] CVM MSD, Exhibit H at 12-15 [Sharkey plea agreement], and 21-24 [ACC plea agreement].
[20] Quarles MSD at 2; CVM MSD, Exhibit H at 12-15 [Sharkey plea agreement], and 21-24 [ACC plea agreement].
[21] Quarles MSD at 2; CVM MSD, Exhibit A [Warning Letter].
[22] CVM MSD, Exhibit B; Quarles, Exhibit 3.
[23] CVM MSD, Exhibit E [NOOH].
[24] Quarles MSD at 2, citing Exhibit 4.

V. Dr. Quarles' Overarching Arguments

As noted above and discussed in more detail below, find that Dr. Quarles submitted false information to ACC three times. Specifically, find that in Studies A-88-37 and A-88-41, Dr. Quarles reported that he prepared certain feed for distribution to the turkeys, but discarded it without ever distributing it. The evidence shows that if the feed had been discarded as Dr. Quarles claims, there would not have been enough feed to distribute to the turkeys to keep them alive and healthy. Regarding a third allegation, I find that Dr. Quarles, rather than submitting data actually collected during the study, submitted false data for Study A-89-8 because he discarded raw data and used a standardized chart to calculate the amount of feed that the turkeys ate during part of the study.

Before addressing CVM's allegations and Dr. Quarles' response in detail, note that Dr. Quarles raises a number of overarching arguments in response to CVM's motion for summary decision and in support of his own motion for summary decision. He first argues that CVM's failure to issue notice of the allegations underlying this disqualification proceeding until more than six years after the studies were completed or to issue the NOOH until nine years had passed has prejudiced his ability to refute CVM's allegations.[25]

I agree that a disturbing length of time has passed since the studies were completed. However, as CVM points out, 21 CFR § 511.1 contains no time limitations for the initiation of disqualification proceedings. In any event, Dr. Quarles admits that he altered the feed weighback data in Study A-89-8, and so a more timely disqualification

proceeding would not have placed Dr. Quarles in any better position to refute CVM's allegations with respect to this allegation With respect to the two allegations connected with Studies A-88-37 and A-89-41 for which I find CVM is entitled to summary decision, Dr. Quarles states that he does not remember why the feed batches were discarded, and cannot explain how he would have had enough feed to complete the study after the batches were discarded. This failure of memory does not raise a genuine and substantial issue of fact The records of a clinical investigation should be complete and accurate, and should not depend on the uncertain memory of individuals. Inasmuch as Dr. Quarles is unable to produce evidence sufficient to identify genuine and substantial issues of fact, CVM is entitled to summary decision on these two allegations

Dr. Quarles also argues that the purpose of disqualifying investigators is supposed to be remedial rather than punitive, but that the purpose of this disqualification proceeding against him appears punitive. In support of this argument, Dr. Quarles points to CVM's delay in initiating these proceedings and the severity of disqualification. Dr. Quarles also argues that this proceeding is punitive because he has not acted in the capacity of a clinical investigator for several years -- [ ] [ ] C].[26]

The circumstances enumerated by Dr. Quarles present no independent evidence that CVM has proposed disqualification for an improper purpose. Section 51 1(c) clearly authorizes disqualification when an investigator has repeatedly or deliberately submitted false information to a sponsor. Dr. Quarles' disagreement with the scope of the remedial measures used by the agency to protect the public health does not, in my

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[25] Quarles MSD at 19-20.
[26] Quarles MSD at 21- 22.

view, demonstrate a punitive purpose. Nevertheless, it should be noted that a decision not to disqualify an investigator who has repeatedly or deliberately submitted false information to a sponsor is committed to the Commissioner's discretion.

now turn to a detailed discussion of the allegations made with respect to each of the four studies.

VI. Study A-88-29

In Study A-88-29, CVM alleges that Dr. Quarles falsified feed preparation records and drug inventory records by reporting that he mixed two batches of 7000 pounds of feed each for Treatment Groups and 2 on January 19, 1989. CVM alleges that, in fact, Dr. Quarles mixed two batches of 4000 pounds each for the two treatment groups and submitted false records regarding these batches to the sponsor with the final report of the study.

To support this allegation, CVM first compares Dr. Quarles' handwritten drug inventory records from Study A-88-29 with his drug inventory records for Study A-89- Both parties agree that the handwritten drug inventory records for Study A-89-1 were supposed to have carried over inventory data of drugs used during Study A-88-29 on January 19, 1989. However, the inventory records for Study A-88-29 are inconsistent with those for Study A-89- Specifically, the drug inventory records for A-88-29 report that more Cygro and bacitracin methylene disalicyclate (BMD-50) was used on that date in Study A-88-29 than is reflected in the carry-over data reported in the inventory records for Study A-89-1. Cygro in the amount reported in the drug inventory records for A-88-29 on January 19, 1989, is sufficient for the mixing of two batches of feed weighing 7000

pounds each. This recorded amount is consistent with the amount of Cygro reported in Dr. Quarles' feed preparation records for Study A-88-29.[27] By contrast, the amount of Cygro reflected in the carry-over data reported in the inventory records for Study A-89- is sufficient only for the mixing of two batches of feed weighing 4000 pounds each. Comparable discrepancies are found in the amount of BMD-50 recorded in the drug inventory records of A-88-29 and A-89- CVM also presents evidence that Dr. Quarles' mixer had a mixing capacity of 4,000 pounds, and so CVM argues that Dr. Quarles could not have mixed batches of 7,000 pounds as he says he did.[28]

In response, Dr. Quarles acknowledges that the cited drug inventory records for the two studies contain conflicting information. However, he submits an affidavit of [ ] [ ], a member of Dr. Quarles' staff, indicating that the inconsistencies between the two studies with respect to the drug amounts used on January 19, 1989 reflect a transcription error in transferring data from the drug inventory records for Study A-88-29 to the drug inventory records for Study A-89- .[29] Dr. Quarles further argues that there would be no purpose or benefit for him to falsify the inventory records in this manner and that the inconsistencies must be an error rather than a falsification. As for CVM's allegation that Dr. Quarles' mixer had only a 4,000 pound capacity, Dr. Quarles

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[27] The drug inventory records from Study A-88-29 indicate that on June 19, 1989, Dr. Quarles used 3180 grams of Cygro, which is the amount of Cygro needed to mix two batches of feed of 7000 pounds each. (CVM MSD at 6; Id., Exhibit E [NOOH] at 32.) However, the drug inventory records found with the files of Study A-89-1 report that on January 19, 1989, Dr. Quarles used only 1816 grams of Cygro for Study A-88-29, which is the amount of Cygro needed to mix two batches of 4000 pounds each. (CVM MSD, Exhibit I.) The inventory records for Study A-88-29 also indicate that on January 19, 1989, Dr. Quarles used 1590 grams of BMD-50, which is the approved concentration for one batch of 7,000 pounds. (CVM MSD at 8, citing Exhibit M.) As for the inventory of BMD-50, according to the protocol for Study A-88-29, Treatment Group 1 was not to be given any BMD-50 in the feed mixed on January 19, 1989, and thus BMD-50 would have been needed for only the one batch of 7,000 pounds of feed mixed for Treatment Group 2. In a conflicting report, drug inventory records for Study A-89-1 state that on January 19, 1989, Dr. Quarles used only 908 grams of BMD-50 for Study A-88-29, which is the approved concentration for one batch of 4,000 pounds. (CVM MSD at 8, citing Exhibit N.)

[28] CVM MSD at 8, citing Exhibit L.

responds by offering evidence that he had a California Pellet Mill, which enabled him to make a continuous mix for production of a variety of batch sizes exceeding 4,000 pounds.[30]

In reviewing the records, I find that CVM has pointed to actual discrepancies between the records for the two studies. The records for the two studies are obviously in conflict, and both cannot be correct. Moreover, Dr. Quarles appears to concede that the records for at least one of the studies must be incorrect because he does acknowledge that there was an error. Nevertheless, to grant a motion for summary decision in favor of CVM on this allegation, I must find that there are no genuine and substantial issues of fact as to the submission of false information in Study A-88-29. In considering CVM's allegations, find that CVM has failed to support its allegation that the inconsistencies stem from falsification of data in Study A-88-29. While it is undisputed that the records for one of the two studies contain false information, it is not clear whether it is the records from Study A-88-29 that are incorrect or whether it is the records from A-89-1 that are incorrect. Although CVM argues that it is Study A-88-29 which contains incorrect, and allegedly falsified, drug inventory data and that the proportions of the differences in the drug amounts suggest that the falsification was deliberate, it is equally plausible, based on the evidence, that it is the drug inventory records from Study A-89-1

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[29] Quarles MSD, Exhibit 9 at 3, ¶ 12 [affidavit of

[30] Quarles MSD at 15, citing Exhibits 6 and 8.

In its opposition to Dr. Quarles' motion for summary decision, CVM argues that if Dr. Quarles had used a continuous mixing method, current good manufacturing practice requirements would have required him to include this information in his reports to the sponsor. (Memorandum in Support of CVM's Request for Summary Decision and in Opposition to Dr. Quarles' Initial request for Summary Decision [CVM's Reply Brief] at 6-7, citing 21 C.F.R. § 225.102.) However, CVM does not argue that his failure to include this information in the report to the sponsor amounts to a falsification, nor has CVM charged Dr. Quarles with falsification on these grounds. Furthermore, insofar as CVM attempts to discredit Dr. Quarles by referring to his failure to include this information in the report to the sponsor or by questioning why he would not have combined two of the 5,000 pound batches if he were using a continuous mixing method,

that are incorrect. However, there are no allegations against Dr. Quarles for Study A-89-1.

As for CVM's allegation that Dr. Quarles could not have mixed batches of feed larger than 4,000 pounds, Dr. Quarles has offered evidence that he could mix larger batches with his California Pellet Mill. I find that this issue cannot be resolved based on the evidence before me.

Therefore, a genuine and substantial issue of fact remains as to whether Dr. Quarles repeatedly or deliberately falsified data in Study A-88-29. Accordingly, I cannot grant summary decision in favor of either CVM or Dr. Quarles with respect to these allegations.

VII. Study A-88-37

Regarding Study A-88-37, CVM alleges that Dr. Quarles falsified feed preparation records to conceal his failure to obtain assays for several batches of feed used during this study. Dr. Quarles submitted these feed preparation records to the sponsor with the final report of the study.[31] CVM, to substantiate its allegations, submits copies of Dr. Quarles' feed preparation records[32] and compares these to a handwritten chart prepared by Dr. Sharkey, which was found in Dr. Sharkey's files at ACC. This handwritten chart appears to be a compilation of the feed preparation information for Study A-88-37.[33] For each of the feed batches, the chart lists the percent of protein, the amount mixed, the date the samples were submitted for assay, a check if the assay was

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such attempts at impeachment go to the weight of the evidence, not the sufficiency of the evidence submitted by Dr. Quarles in response to a motion for summary decision.

[31] CVM MSD at 9.

[32] CVM MSD, Exhibits O, P, and Q.

completed, and the assay number. On the basis of comparisons between Dr. Quarles' records and Dr. Sharkey's chart, CVM makes four separate sets of allegations regarding distinct instances of falsification.

a. Batches of Feed Allegedly Combined

The first two allegations CVM makes are that Dr. Quarles falsified the feed preparation records to report that he mixed a large batch of feed on one day, but that he actually mixed smaller batches over the course of several days. According to CVM, Dr Quarles' purpose for the alleged falsification was to conceal the fact that he had obtained an assay for only the first of these smaller batches of feed.

Dr. Quarles' feed mixing records report that he mixed 20,000 pounds of grower 3 feed on January 11, 1989, and 12,000 pounds of withdrawal feed on February 7, 1989.[34] CVM, relying on Dr. Sharkey's chart, argues that contrary to Dr. Quarles' feed preparation records, Dr. Quarles mixed 20,000 pounds of grower 3 feed over three days (January 11, January 24, and February 6, 1989). Similarly, CVM alleges that Dr. Quarles mixed 12,000 pounds of withdrawal feed over two days (February 7 and March 2, 1989).[35] On Dr. Sharkey's chart, batches of grower 3 feed from the three separate dates in January and February total 20,000 pounds, and batches of withdrawal feed from the two separate dates in February and March total 12,000 pounds.[36] For both the grower 3 feed and the withdrawal feed, the separate dates are circled, with a line connecting the dates and the word "combine" or, in the case of the withdrawal feed, "combine 2

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[33] CVM MSD, Exhibit R.
[34] CVM MSD at 9, citing Exhibits O and P.
[35] CVM MSD at 9-10, citing Exhibit R.
[36] CVM MSD, Exhibit R.

withdrawals" is written next to the connecting line.[37] No dates of assay submission are included on Dr. Sharkey's chart for the grower 3 batches mixed on January 24 or February 6 or the withdrawal feed mixed on March 2, nor are checkmarks for assay completion or assay numbers included for these batches.

Additionally, CVM argues that the mixer available to Dr. Quarles had a mixing capacity of 4,000 pounds and would not have accommodated the four batches of 5,000 pounds reported by Dr. Quarles in the feed preparation records.[38] In response, Dr. Quarles offers evidence that he had a California Pellet Mill, which enabled him to produce a continuous mix so that a 4,000 pound mixer could produce batches that were larger than the capacity of the mixer and that were not equally divisible by 4,000 pounds (as would be the case if separate 4,000 pound batches were combined).[39]

I have reviewed all of the evidence and I find that there are genuine and substantial issues of fact regarding CVM's allegations. While CVM argues that, contrary to the report in the feed preparation records, Dr. Sharkey's chart demonstrates conclusively that Dr. Quarles mixed batches of feed over several days, Dr. Quarles argues that Dr. Sharkey's chart was merely Dr. Sharkey's mixing plan -- a plan that was not followed by Dr. Quarles -- and was not a report of the feed actually mixed by Dr. Quarles in Study A-88-37. While CVM puts forward the plausible argument that Dr. Sharkey's handwritten chart proves that the feed was actually mixed on separate days, I find Dr. Quarles' explanation for the discrepancies between Dr. Sharkey's chart and Dr. Quarles' feed preparation records to be equally plausible.

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[37] CVM MSD, Exhibit R.
[38] CVM MSD at 12, citing Exhibit O.
[39] Quarles MSD at 15, citing Exhibits 6 and 8.

As for CVM's allegation that Dr. Quarles could not have mixed batches of feed larger than 4,000 pounds on January , 1989, Dr. Quarles has offered evidence that he could mix larger batches with his California Pellet Mill.[40] As I said in my discussion of this same issue in Study A-88-29, I find that this allegation cannot be resolved based on the evidence before me.

Based on the conflicting evidence, I find that genuine and substantial issues of fact remain, and thus I cannot grant summary decision in favor of either party on this issue.

b. Batches of Feed that were Represented as Discarded

The third and fourth allegations CVM makes are that Dr. Quarles falsely reported in his feed preparation records that four batches of feed were "mixed but not used."[41] Specifically, CVM maintains that the feed preparation records report that two batches of starter feed prepared on November 9, 1988, and two batches of grower 1 feed prepared on February 28, 1989, were discarded.[42] CVM claims that Dr. Quarles actually used this feed but reported in the feed preparation record that these batches of feed were discarded to conceal his failure to obtain assays for these batches.[43]

According to Dr. Quarles' feed preparation records, two batches of starter feed, each weighing 2,000 pounds, were mixed for Treatment Groups 1 and 2 on November 9, 1988. The feed preparation records contain a notation at the bottom of the page that these

[40] Quarles MSD at 15, citing Exhibits 6 and 8.
[41] CVM MSD at 11-12, citing Exhibit Q.
[42] CVM MSD at 9, citing Exhibit Q.
[43] CVM MSD at 9, 11-12.

batches were "mixed but not used."[44] Consistent with this notation, the word "Toss" is written next to the entries for these batches of feed on Dr. Sharkey's chart.[45] CVM argues that if Dr. Quarles discarded this feed as he says, Dr. Quarles would not have had enough feed to distribute to the turkeys in Treatment Groups and 2.[46]

CVM says that according to the pen cards, 2405.9 pounds of starter feed was distributed to Treatment Group 1 between the dates of November 7 and December 8, 1988.[47] CVM argues that if the feed prepared on November 9 was discarded as Dr. Quarles says, then according to the feed preparation records, there would have been only ,000 pounds of starter feed for Treatment Group for this part of the study.[48] Specifically, only the 1,000 pound batch mixed on October 10, 1988, would have remained, notwithstanding the fact that 2405.9 pounds of feed were distributed to Treatment Group 1, leaving a deficit of 1405.9 pounds.[49]

Similarly, the amount of starter feed mixed for Treatment Group 2 also fell short compared with the feed distributed. If the feed mixed on November 9 was discarded, only the 2,000 pound batch of starter feed mixed on October 7 was available for distribution to the pens between November 7 and December 8, 1988.[50] However, according to the pen cards, the turkeys in these pens received 2466.7 pounds of feed during this time, leaving a 466.7 pound deficit.[51]

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[44] CVM MSD, Exhibit Q.
[45] CVM MSD, Exhibit R.
[46] CVM MSD at 11-12.
[47] CVM has submitted a chart purporting to record data from the pen cards themselves. (CVM MSD, Exhibit T.) Copies of the pen cards are not in the record before me. Dr. Quarles does not dispute the information in the chart submitted by CVM.
[48] CVM MSD at 11, citing Exhibit S.
[49] CVM MSD, Exhibit T at 1.
[50] CVM MSD, Exhibit S.
[51] CVM MSD, Exhibit T at 2.

As for the feed mixed on February 28, 1989, CVM makes no allegations that Dr. Quarles would have run out of feed if he had discarded this batch. The only allegation that CVM makes about this batch is to say that it was listed on Dr. Sharkey's chart, albeit with the word "tossed" written next to it.[52]

Dr. Quarles responds by stating that he has no reason to believe that the two batches of feed prepared on November 9, 1988, were not discarded as reported.[53] He states that he does not remember why these batches were discarded and cannot explain how he would have had enough feed after this feed was discarded. Dr. Quarles offers the affidavit of [ ] who states that she does not specifically remember why the feed was discarded, but that feed was discarded for one of three reasons: (1) the feed was mixed incorrectly, (2) extra feed was made at ACC's request as backup feed in case the first batch proved to be out of compliance by assay, or (3) feed was mixed in excess of what was needed to feed the birds in the study.[54]

I have reviewed the record as a whole, and I find that CVM has established that Dr. Quarles falsely reported in his feed preparation records that the feed mixed on November 9, 1988, was discarded. Dr. Quarles does not dispute that the amount of feed distributed to Treatment Groups 1 and 2 exceeded the amount of feed mixed for that phase of the study. Dr. Quarles has no explanation for this anomaly. Although Dr. Quarles submits an affidavit from [ ], who proffers three reasons why these batches might have been discarded, these reasons do not explain the discrepancies between the feed preparation records and the pen cards. Given that the amount of recorded feed distributed exceeded the amount of recorded feed mixed, it is clear that

[52] CVM MSD at 9, citing Exhibit Q.
[53] Quarles MSD, Exhibit 3 at 11 [Quarles response to Warning Letter].

either the feed preparation records or the pen cards showing the amount of feed distributed are inaccurate and thus false. Because there is no evidence that the pen cards contain false information regarding the amount of feed distributed therefore conclude that Dr. Quarles has not raised a genuine and substantial issue of fact with respect to CVM's allegation that the feed preparation records falsely reported that the feed prepared on November 9, 1989, was discarded.[55] Accordingly, grant summary decision for CVM as to these allegations.

However, regarding the records of feed discarded on February 28, 1989, find that there are genuine and substantial issues of fact. Unlike the feed allegedly discarded on November 9, the feed discarded on February 28 does not raise the question of an apparent shortage of feed for the study, nor does CVM make such an allegation. It is possible that this feed could have been discarded while the study continued as Dr. Quarles described in the final report Therefore, find that there are genuine and substantial issues of fact that preclude a summary decision on the issue of feed discarded on February 28, 1989.

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[54] Quarles MSD, Exhibit C at 3, ¶ 11.

[55] Dr. Quarles does argue in his response to CVM's motion for summary decision that his failure to provide an alternative explanation for the discrepancies between the feed preparation records and pen cards does not mean that CVM has excluded other possible explanations. (Quarles' Response to CVM's Request for Summary Decision at 4.) I agree. Nonetheless, Dr. Quarles' failure to provide any explanation whatsoever for these discrepancies reduces his response to a mere denial of CVM's evidence, which does not suffice to overcome a motion for summary decision. (See *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 255 (1986).) CVM need not exclude all conceivable explanations for clear discrepancies in a report submitted to the sponsor. (See *Matsushita Electrical Indus. Co. v. Zenith Radio Corp.*, 475 U.S. 574, 586 (1986).) While CVM might have made an even stronger case if it had alleged in the alternative that the pen cards were falsified, I cannot deny CVM's motion for summary decision on the basis of Dr. Quarles' mere denial. The only reasonable conclusion to be drawn from the evidence before me is that Dr. Quarles' report to the sponsor contained genuine discrepancies. CVM has provided a reasonable and supportable explanation for these discrepancies. Despite the serious implications of these discrepancies, i.e., the clear existence of false data in the report submitted to the sponsor, Dr. Quarles provides no explanation for them.

VIII. Study A-88-41

The allegations that CVM makes for Study A-88-41 are identical to those it makes for Study A-88-37, right down to the size of the batches and the dates on which they were mixed. Because the issues are identical will not repeat these allegations in detail. [*See* Study A-88-37, above In summary, as with Study A-88-37, CVM alleges that Dr. Quarles failed to obtain assays for some batches of feed and tried to conceal this failure by falsely indicating that he combined some of these batches and discarded others To prove its allegations, CVM again cites to a handwritten chart prepared by Dr Sharkey. As with Study A-88-37, the essence of CVM's allegations for Study A-88-41 is that Dr. Quarles allegedly falsified feed preparation records to hide the fact that he failed to obtain assays for batches of feed. These records were submitted to the sponsor with the final report.[56]

The only difference between the issues for the two studies is the referenced documents.[57] The charts for Studies A-88-37 and A-88-41 contain the same information, but there are enough minor differences between the charts to show that these are not identical copies of the same document but are separate, handwritten documents.[58]

Dr. Sharkey's chart indicates that Dr. Quarles was to follow the identical mixing schedule for Studies A-88-37 and A-88-41 The same amounts of feed were mixed on the same dates for both studies. According to the final reports for these two studies, the

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[56] CVM MSD at 12-13.

[57] The relevant documents in evidence include the following exhibits: CVM MSD, Exhibit U [feed mix of 20,000 pounds], Exhibit V [feed mix of 12,000 pounds], Exhibit W [record of feed tossed], Exhibit X [record of feed tossed], Exhibit Y [record of feed tossed], Exhibit Z [Sharkey's chart], Exhibit AA [CVM's summary of pen card totals].

[58] CVM MSD, Exhibit R [Study A-88-37], and Exhibit Z [Study A-88-41]. One other difference that I noticed between the studies was that for Study A-88-41, Dr. Sharkey's chart lists one more batch of feed as having been mixed but not used. However, this batch was not mentioned as an issue by either party, and so I draw no conclusion from this.

only difference between the feed mixed for each study is that different drugs were mixed in the feed lots, depending upon the requirements of the study.[59]

Because the issues for Study A-88-41 are identical to those for A-88-37, my decision on these issues is the same. I find that there remain genuine and substantial issues of fact concerning the batches of feed that Dr. Quarles asserts were combined.

As for the feed that was discarded during Study A-88-41 on November 9, 1988, reach the same conclusion as I did with Study A-88-37. find that for Study A-88-41, Dr. Quarles has failed to demonstrate the existence of a genuine and substantial issue of fact requiring a hearing. According to the undisputed record before me, Dr. Quarles distributed 2,420.2 pounds of feed to Treatment Group between November 7 and December 8, 1988.[60] However, if the batch of feed mixed November 9 was discarded, there was only ,000 pounds of feed available for distribution to Treatment Group [61] Similarly, for Treatment Group 2, the uncontroverted evidence before me indicates that 2,445.3 pounds of starter feed was distributed for Treatment Group 2, but that, excluding the feed mixed on November 9, only 2,000 pounds of starter feed was mixed for this time period.[62] Therefore, for the same reasons as discussed with these comparable allegations under Study A-88-37, I find that a summary decision for CVM is warranted as to its allegations that Dr. Quarles falsified data in Study A-88-41 by reporting in a feed preparation record that starter feed for two different treatment groups was discarded.

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[59] CVM MSD attachment "Final Reports" [no exhibit number], Final Report for A-88-37 and Final Report for A-88-41.
[60] CVM again submits a chart purporting to document the data in the pen cards involved. (CVM MSD, Exhibit AA.) Dr. Quarles does not dispute the accuracy of this chart.
[61] CVM MSD, Exhibit AA at 1.
[62] CVM MSD, Exhibit AA at 2.

As for the feed reported to have been discarded for Study A-88-41 on February 28 989, find that there are genuine and substantial issues of fact remaining As was the case for the feed discarded in connection with Study A-88-37, it is not impossible for this feed to have been discarded while the study continued as described in Dr. Quarles final report. Therefore, find there are genuine and substantial issues of fact that preclude summary decision for either party as to CVM's allegations regarding the feed discarded on February 28, 1989.

IX. Study A-89-8

The Center presents two separate allegations regarding Study A-89-8 will discuss each of these allegations in turn.

a. Retention Samples

CVM first alleges that Dr. Quarles submitted false feed samples for assay Some of the assay records obtained from Dr. Sharkey's files indicate that three feed samples were found to be subpotent or at the low end of the acceptable assay range for bacitracin zinc.[63] CVM argues that to correct these poor assay results, Dr. Quarles mixed 500 pounds of feed at the end of the study, sent samples from this batch of feed to the analytical laboratory on January 16, 1990, and represented these samples as retention samples from the batches of feed for which there were poor assay results

As support for these allegations, CVM points to an unsigned, handwritten note found in Dr. Sharkey's files. The note lists three of the feed assays for bacitracin zinc

[63] CVM MSD at 16, citing Exhibit BB.

that tested as subpotent.[64] CVM maintains that Dr. Sharkey wrote this note. At the bottom of this handwritten note is a comment that, according to CVM, reads, "Will mix 500 lbs for 3 bac zn assays." CVM says that this notation demonstrates that Dr. Quarles mixed new feed for additional assays of bacitracin zinc at the request of Dr. Sharkey.

In response, Dr. Quarles denies that he mixed additional feed samples.[65] Dr. Quarles says that Dr. Sharkey consistently asked for additional feed samples for analysis during the studies he oversaw, and so Dr. Quarles issued a standard order to his staff to take large amounts of feed samples to satisfy Dr. Sharkey's repeated requests.[66] Dr. Quarles maintains that he did not know why Dr. Sharkey requested that multiple feed samples be sent for analysis. Dr. Quarles says that during the study, he believed that either Dr. Sharkey or the assaying laboratory lost the originally submitted samples.[67] Dr. Quarles further states that he believes that the repeated samples were needed because the assaying procedure for bacitracin and Cygro was difficult to conduct and that reproducible assay results were difficult to obtain due to the fatty composition of turkey feed. [ ] states in her affidavit that Dr. Sharkey frequently asked for multiple retention samples, and that it became standard practice during the study to take a large sample of each mixed batch to have sufficient retention samples for repeated submissions of samples for assay.[68]

Dr. Quarles further states that although he was responsible for submitting all feed samples for assay to the independent laboratory, the assay results from the laboratory did not go to him but were sent directly to Dr. Sharkey. Dr. Quarles says that after his staff

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[64] CVM MSD, Exhibit CC.
[65] Quarles MSD at 10.
[66] Quarles MSD at 5.
[67] Quarles MDS, Exhibit 3 at 5 [Quarles response to Warning Letter]

sent the feed samples to the independent laboratory, the staff had no idea whether the samples were received by the laboratory, whether the laboratory conducted the assay, whether the results were reported to Dr. Sharkey, or whether the results were within specification or out of specification.[69] As for the note purportedly written by Dr. Sharkey, Dr. Quarles says that he has no independent information from which he can draw to explain the comment at the bottom of this note and can only differ with the conclusions that CVM draws from this comment. Dr. Quarles argues that Dr. Sharkey's note is not part of the data submitted by Dr. Quarles to the sponsor and cannot constitute a basis for charging falsification.[70] Dr. Quarles further argues that none of Dr. Sharkey's notes catalogs the actions of Dr. Quarles.[71]

Based upon my review of the evidence, I find that CVM raises valid questions about these feed assays. The fact that documents introduced by CVM show that feed samples sent for assay had less than the required potency of bacitracin zinc, but in later tests appeared to have acceptable potency, does warrant concern. However, I find that Dr. Quarles raises genuine and substantial issues of fact that preclude my granting a summary decision. As CVM concedes, feed mixing records from Dr. Quarles' files do not show the use of any additional bacitracin zinc beyond what was needed for the study. Although CVM notes that Dr. Quarles could have bought bacitracin zinc over-the-counter, CVM offers no evidence in support of this allegation.[72] Moreover, Dr. Quarles introduces the affidavit of [ ], who denies that there were new feed samples mixed after the fact.

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[68] Quarles MSD, Exhibit C at 2, ¶ 9.
[69] Quarles MSD at 11.
[70] Quarles MSD at 11.
[71] Quarles MSD at 11.

find that there are genuine and substantial issues of fact on the allegation that Dr. Quarles mixed additional feed samples after the completion of the study. Therefore, I find that a summary decision is not appropriate on this issue

b. Feed Weighback Data

In its second allegation for Study A-89-8, CVM maintains that Dr. Quarles falsified data for weighback amounts for pens 8, 12, 13, and 27 for two kinds of feed -- grower 3 feed and withdrawal feed -- and submitted this falsified data to the study sponsor.[73] CVM argues that a comparison between Dr. Quarles' study files and a facsimile sent by Dr. Sharkey to [ ], one of the staff members who worked with Dr. Quarles, shows that Dr. Quarles' falsified data for pens 8, 12, 13, and 27.[74]

Dr. Sharkey's facsimile, dated March 1, 1990, appears to have been written after Dr. Quarles completed his final report for Study A-89-8. In the facsimile, Dr. Sharkey comments on items in Dr. Quarles' final report The last page of Dr. Sharkey's facsimile lists the final feed weighbacks for pens 8, 13, and 27, and shows Dr. Sharkey's calculations for the feed consumed by the birds in these three pens during the withdrawal phase. Written next to Dr. Sharkey's calculations is the notation, "Will talk to CQ."[75] CVM reasonably says that "CQ" is Carey Quarles. CVM also submits a letter written by [ ], dated March 30, 1990. The letter contains responses to the several questions and corrections identified by Dr. Sharkey in his facsimile. Regarding final feed

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[72] CVM Reply Brief at 3.
[73] CVM MSD at 18.
[74] CVM MSD, Exhibit GG.
[75] CVM MSD, Exhibit GG at p. R024085

weighback data, [ ] writes, "Pens 8, 12, 13, and 27 -- feed weighback before withdrawal feed added were incorrect. Figures were corrected."[76]

Relying on this evidence, CVM suggests that Dr. Quarles made two types of changes to the study data. First, CVM argues that Dr. Quarles crossed-out final feed weighback data for these four pens on the "Weight Data Sheets," i.e., the records reporting the total amount of feed used in each pen, and wrote new data above the original data.[77] Second, CVM states that Dr. Quarles changed grower 3 feed weighback data on the pen cards by erasing the original entries and writing new entries in their place.[78] CVM argues that Dr. Quarles made these alterations to ensure that the originally reported amount of total feed consumed by pens 8, 12 3, and 27 remained unchanged. CVM states that this alteration of data was favorable to the study results.[79]

Dr. Quarles responds by admitting that he made the changes described by CVM. Dr. Quarles suggests that errors in the raw data occurred when leftover feed from the grower 3 phase was mistakenly recorded as leftover feed from the withdrawal phase. According to Dr. Quarles, this error made it appear that the turkeys ate a lot of grower 3 feed but an insufficient amount of withdrawal feed to sustain them.[80] Dr. Quarles states that his original data could not be correct because if the turkeys had eaten so little feed during the withdrawal phase, they would most likely have died, or at a minimum become very sick. Dr. Quarles states that the turkeys in pens 8, 12, 13, and 27 were healthy and of a similar size and weight to turkeys in the other pens, so Dr. Quarles concluded that

[76] CVM MSD, Exhibit HH at p. R024050.
[77] CVM MSD, Exhibit II.
[78] CVM MSD at 20, citing Exhibit JJ.
[79] CVM MSD at 20.
[80] Quarles MSD at 12.

the weight data sheets were incorrect.[81] Dr. Quarles states that when this apparent error was brought to his attention, he corrected the data consistent with the good health of the turkeys. To make this correction, Dr. Quarles states that he used a feed guide "to determine how much grower 3 and withdrawal feed the birds in pens 8, 12, 13, and 27 would have eaten at the relevant stages of development."[82] Dr. Quarles argues that his alteration of the data is not a falsification because he was attempting to present a reasonable approximation of the amount of feed consumed by the turkeys in the pens at issue.[83]

Both CVM and Dr. Quarles agree that the original raw data were inconsistent with the good health of the turkeys and that it is likely that an error occurred in collecting and recording the raw data. Dr. Quarles responds by offering an explanation for the error. However, CVM's allegations are not based on the alleged error itself, but on Dr. Quarles changing of the data and submitting it as true study data to the sponsor. Dr. Quarles concedes that he used a standardized feed chart to calculate the amount of feed that the turkeys should have eaten. do not find Dr. Quarles' use of a feed chart to compute data to be a correction. It is simply inventing data to suit the desired outcome of a study. Dr. Quarles attempts to justify his changing of the data by pointing to apparent problems with the raw data and arguing that his changing of the data was merely a "correction." However, it is important to note that the data submitted to the sponsor do not contain an accompanying explanation or any indication whatsoever -- other than cross-outs and eraser-marks -- that the numbers reported were not the raw data from the study. Regardless of whether the sponsor was aware of the alterations to the raw data made by

[81] Quarles MSD at 12-13.
[82] CVM MSD, Exhibit B at 8 [letter from Quarles to FDA, January 5, 1996].

Dr. Quarles, Dr. Quarles' failure to document these alterations of the data by itself renders the submission of data "false information" under 21 C.F.R. § 51 and compromises the integrity of the study, regardless of Dr. Quarles' underlying motivation. In fact, Dr. Quarles' admission that in a report submitted to the sponsor he purposely altered numerous data points to conform to a standardized feed chart amounts to an admission that he repeatedly and deliberately submitted false information to the sponsor.

It should not be necessary to state that a keystone of clinical trials is that the data reported must be the data actually collected during the study. If it were acceptable to submit data derived from a standardized chart, particularly without an accompanying explanation, there would be no need to measure carefully the amount of feed distributed during each phase of the study. Dr. Quarles' use of a standardized feed chart to calculate data and report it as true study data is a violation of 21 C.F.R. § 51 Accordingly, grant summary decision in CVM's favor with respect to these allegations.

X. Conclusion

After reviewing the evidence presented by both parties, I find that genuine and substantial issues of fact remain as to the following allegations:

In Study A-88-29, the allegation that Dr. Quarles falsified feed preparation records and drug inventory records for January 19, 1989;

2. In Study A-88-37, the allegation that Dr. Quarles falsely reported that he mixed a 20,000 pound batch of grower 3 feed on January , 1989;
3. In Study A-88-37, the allegation that Dr. Quarles falsely reported that he mixed a 12,000 pound batch of withdrawal feed on February 7, 1989;

[83] Quarles MSD at 13-14.

4 In Study A-88-37, the allegation that Dr. Quarles falsely reported that he discarded feed mixed on February 28, 1989;

5. In Study A-88-41, the allegation that Dr. Quarles falsely reported that he mixed a 20,000 pound batch of grower 3 feed on January , 1989;

6. In Study A-88-41, the allegation that Dr. Quarles falsely reported that he mixed a 12,000 pound batch of withdrawal feed on February 7, 1989;

7. In Study A-88-41, the allegation that Dr. Quarles falsely reported that he discarded feed mixed on February 28, 1989; and

8. In Study A-89-8, the allegation that Dr. Quarles submitted false feed retention samples for assay.

I find that there are no genuine and substantial issues of fact regarding the following allegations, and for this reason, find that CVM is entitled to summary decision on these allegations:

In Study A-88-37, Dr. Quarles falsely reported that he discarded feed mixed on November 9, 1988;

2 In Study A-88-41, Dr. Quarles falsely reported that he discarded feed mixed on November 9, 1988; and

3 In Study A-89-8, Dr. Quarles falsified data for weighback amounts for pens 8, 12, 13, and 27 for grower 3 feed and withdrawal feed.

Because I find that there are multiple violations of the regulations, find that Dr. Quarles' actions were done "repeatedly" within the meaning of 21 C.F.R. § 51 1(c). I

also find that, at least for Dr. Quarles' falsification of weighback amounts for Study A-89-8, Dr. Quarles actions were also done "deliberately." Because my findings as to these three allegations are sufficient to warrant a recommendation under 21 C.F.R. § 5 to disqualify Dr. Quarles, a hearing is not needed on any of the issues for which a genuine and substantial issue of material fact remains.

XI. Recommendation

The drug-approval process at FDA is founded on the accurate and reliable conduct of scientific studies. Failure to maintain the integrity of the data compiled in these studies undermines this process. For reasons outlined in previous sections, I have concluded that Dr. Quarles has failed to raise genuine and substantial issues of fact concerning CVM's evidence that he violated the regulations by repeatedly and deliberately submitting false data. These violations are significant in that they involve a disregard for maintaining the integrity of data collected during a scientific study. Dr. Quarles has admitted to deliberately submitting false data by utilizing a standardized chart to calculate the amount of feed consumed during part of the study and representing this data as actual data collected from the study. This violation was repeated four times during Study A-89-9. Dr. Quarles also submitted false data by stating feed was discarded when such could not have been the case. This manipulation occurred in Studies A-88-37 and A-88-41

Based upon these findings, I recommend that the Commissioner disqualify Carey L. Quarles, Ph.D., from being eligible to receive investigational new drugs. Nonetheless, I believe that circumstances exist that should be brought to the attention of the

Commissioner. [ ] [ ] It is my understanding that investigator disqualifications are not intended to serve a punitive function, but that investigator disqualifications serve to protect the integrity of scientific studies performed in the future. In my opinion, [ ] should thus play a role in evaluating the need for disqualification, [ ] Although I have found that there remain no genuine and substantial issues of fact as to the allegations before me, I believe that [ ] warrant some consideration in the Commissioner's decision as to whether Dr. Quarles should be disqualified.

Date 10/23/01

Henry H. Startzman III, M.D.
Presiding Officer