Case Number: ORI 2014-02 (formerly DIO5472)

SUBJECT: Investigation Committee Report Regarding the Allegation of Misconduct in Research

FROM: Alison Lakin, Ph.D., Research Integrity Officer (RIO) and Assistant Vice Chancellor for Regulatory Compliance

Respondent: [redacted]. (former doctoral student) - no legal counsel retained

Complainant: [redacted] no legal counsel retained

Original Allegations:

[redacted] This data had not been published.

Background:

[redacted] informed RIO Lakin that he had confronted [redacted] about some problems with data previously produced by [redacted]

[redacted]

RIO. Lakin was informed of these findings and in consultation with the Office of Research Integrity on December 3, 2013, agreed to treat the Honor Code Committee as the Inquiry Committee per 42 CFR part 93.

Dr. Traystman, Deciding Official for UCD, determined on December 27th, 2013 that an investigation was warranted.

A copy of the Inquiry Report and supporting documents was sent to the ORI on January 15, 2014.

Investigation Committee:

[redacted]

Conflict of Interest Screening:
Each member of the Investigation Committee stated that they were free of bias, conflicts of interest or conflicts of commitment that would impair their ability to render a fair and impartial judgment in this matter. RIO Lakin concurred in each instance.

The Investigation Committee was charged by RIO Lakin on January 27th, 2014 with Christopher Puckett, Associate General Counsel.

Investigation was conducted under the following regulations:
The applicable regulations are Public Health Service requirements contained in 42 C.F.R. 93 and University of Colorado Policy.

Applicable considerations:
When it considers that its task has been completed, the Investigation Committee shall determine by majority vote whether the allegations of misconduct are supported by a **preponderance of evidence**.
The Investigation Committee shall reach one of the following decisions as to each allegation of research misconduct:

1. A finding of research misconduct;
2. A finding of no culpable research misconduct, but serious research error; or
3. A finding of no misconduct and no serious research error.

Misconduct in research includes the following and means:

1. **Fabrication**, **falsification**, **plagiarism** and other forms of misrepresentation of ideas, and other serious deviations from accepted practices in proposing, carrying out, reviewing, or reporting results from research.

The following definitions apply:

Fabrication is making up data or results and recording or reporting them;
Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record;
Plagiarism is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit

2. Failure to comply with established standards regarding author names on publications;
3. Retaliation of any kind against a person who, in good faith, reported or provided information about suspected or alleged research misconduct.

Research misconduct does not include honest error or honest differences in interpretations or judgments of data. However, where a person's conduct otherwise constitutes research misconduct, the burden of proof lies with that person to establish by a preponderance of the evidence that his or her conduct represents honest error or differences in interpretation.

Standard for Determination:
A finding of research misconduct requires that the Investigation Committee makes the following determinations finding that:

1. There is a **significant departure** from accepted practices of the relevant research community; and
2. The misconduct be **committed intentionally, knowingly, or recklessly**; and
3. The allegation be proven by a **preponderance of the evidence**.

Investigation Process:

Documents and data sequestered:
On September 16th, [redacted] sequestered the following data:

1) [redacted]
[redacted] [redacted] V
[redacted] [redacted]
4) [redacted] bound thesis

On 12/13/13, RIO Lakin and Sean Clark, UCD IT security, sequestered the following additional documentation:

1) 7 folders belonging to [redacted] lab
2) 11 CD backups of [redacted] work stored in [redacted] office
3) 4 additional lab books belonging to [redacted] stored in [redacted] office.
4) Drive Array server for [redacted] laboratory
5) Mass spectrometer hard drive from room V20-4261
6) Hard drive from computer belonging to [redacted]

Interviews conducted by the Investigation Committee:

[redacted] PI of lab, Professor, department of Pharmaceutical Sciences
[redacted] Associate Professor, Department of Pharmaceutical Sciences
[redacted] Research Instructor in [redacted] lab
[redacted] Professor and Dean of the Graduate School
[redacted] doctoral student in [redacted] laboratory
[redacted] doctoral student in [redacted] laboratory
[redacted] doctoral student in [redacted] laboratory
[redacted] (by phone), respondent and former doctoral student in [redacted] lab

Data Analyzed:

From 2008 until 2012, [redacted] was the only person in [redacted] laboratory trained to use the API 3000 by Applied Biosystems LC-MS/MS machine. The committee reviewed all available LC-MS/MS and compared it to processed data available on discs that [redacted] had provided to [redacted] when he left the institution.

Some of the original LC-MS/MS data had been deleted from the machine (LC-MS/MS instrument) and could not be recovered by IT. IT security determined that the files had been deleted on August 3, 2013 and August 4, 2013. This time period coincided with [redacted] visit to the laboratory at the request of [redacted] to explain the data discrepancies after he had obtained his PhD and left the institution for another position. The room at that time did not require badge access. It is not possible to verify who deleted the data.

The process to determine whether data was falsified occurred by first reviewing whatever original data was available. As noted, some original data was available directly from the LC-MS/MS, while other raw data had been provided to [redacted] from [redacted] as data saved CDs by [redacted] at the time he left [redacted] lab. These CDs had been kept

in [redacted] office since [redacted] had graduated and left the institution. After identifying this data, the processed data or data used for publication/graphing was reviewed. In comparing these two data sets, it became very clear where data had been falsified.

E-mail Review:
University IT Services captured snapshots of [redacted] Outlook email inbox, outbox, saved drafts, and deleted files. There is no evidence contained in the emails that [redacted] any of [redacted] original raw or processed data files. Any type of lab data transmitted between [redacted] and [redacted] was a quick email regarding a lab finding, a plotted chart or diagram contained in a Word file, or data that was to be included in a manuscript or final paper. There were one or two instances where [redacted] suggests an urgency or tight timeline for publication. There were also email exchanges between Dr. [redacted] and [redacted] regarding how to answer a question posed by external researchers based on published papers where [redacted] were co-authors, or journals reviewing submitted manuscripts. In these instances, [redacted] and [redacted] exchange information, then [redacted] would respond to the external individual or entity, and copy [redacted] on the response containing an explanation of the finding or data. There is no information to suggest that [redacted] should have been "on notice" to question any of [redacted] data or that the data should have been investigated further.

In addition, there is email evidence that [redacted] who was co-author with [redacted] on one of the questioned publications, was contacted by outside researchers stating that the outcome that he and [redacted] reached in a published paper was not possible. When this occurred, [redacted] contacted [redacted] to ask about these discrepancies. This is when [redacted] and [redacted] began to examine [redacted] data for discrepancies.

Review of Grants:
FDA U01FD004929 (2013-2014) cited the following two publications in which falsified data was used:

- [redacted]. Influence of choroidal neovascularization and biodegradable polymeric particle size on transscleral sustained delivery of triamcinolone acetonide. Int J Pharm. 2012 Sep 15;434(1-2):140-7.
- [redacted]. Hybrid dendrimer hydrogel/PLGA nanoparticle platform sustains drug delivery for one week and antiglaucoma effects for four days following one- time topical administration. ACS Nano. 2012 Sep 25;6(9):7595-606

These papers were used to indicate [redacted] laboratory's ability to perform drug delivery system preparation, drug analysis and pharmacokinetic studies.

FDA U01FD004719 (2012-2013; no cost extension 2013-2014) – Figures 1 and Table 1 used published data from:

[redacted]. Ocular pharmacokinetics of dorzolamide and brinzolamide after single and multiple topical dosing: implications for effects on ocular blood flow. Drug Metab Dispos. 2011 Sep;39(9):1529-37.

The data from this publication has been verified as accurate.

NIH R01EY022097 (2013-2017): one LC-MS/MS plot used data on three beta-blockers in Figure 6. To date, the committee has not been able to verify this data.

2 publications cited the following two publications in which falsified data was used:

- [redacted] Influence of lipophilicity on drug partitioning into sclera, choroid-retinal pigment epithelium, retina, trabecular meshwork, and optic nerve. J Pharmacol Exp Ther. 2010 Mar;332(3):1107-20.
- [redacted]. Sclera-choroid-RPE transport of eight β-blockers in human, bovine, porcine, rabbit, and rat models. Invest Ophthalmol Vis Sci. 2011 Jul 23;52(8):5387-99.

These papers were used to indicate [redacted] laboratory's ability to perform drug delivery system preparation, drug analysis and pharmacokinetic studies.

NIH R01EY018940 (2010-2015) Preliminary LC-MS/MS data provided by [redacted] for figure 4. To date, the committee has not been able to verify this data.
NIH R01HL119533 (pending) cited one publication in which falsified data was used:

- [redacted]. Influence of choroidal neovascularization and biodegradable polymeric particle size on transscleral sustained delivery of triamcinolone acetonide. Int J Pharm. 2012 Sep 15;434(1-2):140-7

This paper was used to indicate the ability of [redacted]s laboratory to assess particulate delivery systems in animal models.

1 R01 EY024072-01A1 (pending) – figure 2 and 8 used LC-MS/MS data
2 publications cited the following two publications in which falsified data was used:

- [redacted]. Hybrid dendrimer hydrogel/PLGA nanoparticle platform sustains drug delivery for one week and antiglaucoma effects for four days following one- time topical administration. ACS Nano. 2012 Sep 25;6(9):7595-606
- [redacted]. Influence of choroidal neovascularization and biodegradable polymeric particle size on transscleral sustained delivery of triamcinolone acetonide. Int J Pharm. 2012 Sep 15;434(1-2):140-7.

Review of Patents: The Investigation Committee is aware that [redacted] was a co-inventor on at least one patent that involved the use of LC-MS/MS machine data. The Committee recommends that the Tech Transfer Officer review all available material involving this patent and any others that relied on or utilized work by [redacted] and/or LC-MS/MS data.

Timeline for the Committee Review:

The Investigation Committee was scheduled to complete its work by May 27th, 2014. RIO Lakin requested an extension to the investigation due to the significant number of publications requiring review. A 90 day extension was granted by ORI, which changed the due date for the Investigation Committee report to August 25th, 2014.

Conclusions:

[redacted] is an author on 29 publications. His role in each of these publications was evaluated by the Investigation Committee.
In 6 papers, LC-MS/MS data was not used and [redacted] role was determined to not present a risk to the integrity of the paper;
For 2 papers, the raw LC-MS/MS data was not available; and
For 6 papers, the processed data utilized in the publication was not available

The Investigation Committee, in collaboration with and using [redacted] as an expert, reviewed/compared the raw data with the processed data utilized in the manuscript for 15 papers.
In 5 papers, the raw data and processed data appeared to match;
Significant discrepancies were identified in 10 papers involving raw and processed LC-MS/MS data used in the manuscripts. The identified discrepancies were then verified by [redacted] in [redacted] laboratory.

No evidence was found to suggest that any other students, faculty or employees in the laboratory of [redacted] knew that data from the LC-MS/MS machine was being falsified.

Findings of Scientific Misconduct

[redacted]

Specifically:

1. [redacted]

[redacted]

[redacted]

B. [redacted] knowingly and intentionally falsified and/or fabricated results by manipulating LC-MS/MS/MS peak area data to smooth kinetics and/or alter statistical significance for one figure in [redacted] Self-assembled phenylalanine-α,β- dehydrophenylalanine nanotubes for sustained intravitreal delivery of a multi-targeted tyrosine kinase inhibitor. J Control Release. 2013 Dec 28;172(3):1151-60.

> Figure 6: The standard curve for the drug pazopanib was falsified to make it appear linear. In fact, the raw data for the standard curves were highly scattered and non-linear, resulting in an unusable standard curve. As a result, the pazopanib values calculated from the fabricated curve are completely unreliable.

C. [redacted] knowingly and intentionally falsified or fabricated results by manipulating LC-MS/MS/MS peak area data to smooth kinetics and/or alter statistical significance for two figures in [redacted]. Suprachoroidal delivery in a rabbit ex vivo eye model: influence of drug properties, regional differences in delivery, and comparison with intravitreal and intracameral routes. Mol Vis. 2013 May 30;19:1198-210.

> Figure 6: The transport data for 4 beta blockers was found to be falsified The effect of these changes was to make the uptake curves for these drugs appear less variable and more monotonic.
> Figure 7: This figure used the data of Figure 6 to analyze the effect of physicochemical properties of these drugs on their distribution in various compartments of the eye. Thus these analyses are contaminated by fabricated data.

D. [redacted] knowingly and intentionally falsified or fabricated results by manipulating LC-MS/MS/MS peak area data to smooth kinetics and/or alter statistical significance for one figure in [redacted]. Hybrid dendrimer hydrogel/PLGA nanoparticle platform sustains drug delivery for one week and antiglaucoma effects for four days following one- time topical administration. ACS Nano. 2012 Sep 25;6(9):7595-606.

> Figure 6: Nearly all data for the uptake of brimonidine were falsified, including the standard curve. Thus the claimed correlation between the uptake of this drug and its anti-glaucoma action appears to be false.

E. [redacted] knowingly and intentionally falsified or fabricated results by manipulating LC-MS/MS/MS peak area data to smooth kinetics and/or alter statistical significance for one figure in [redacted]. Influence of choroidal neovascularization and biodegradable polymeric particle size on transscleral sustained delivery of triamcinolone acetonide. Int J Pharm. 2012 Sep 15;434(1-2):140-7.

> Figure 3: Data on sustained delivery of triamcinolone acetate were extensively falsified to reduce variability in the results. This appears to falsely support the conclusions regarding the influences on drug delivery reported in the paper.

F. [redacted] knowingly and intentionally falsified and/or fabricated results by manipulating LC-MS/MS/MS peak area data to smooth kinetics and/or alter statistical significance for four figures in [redacted] Hydrophilic prodrug approach for reduced pigment binding and enhanced transscleral retinal delivery of celecoxib. Mol Pharm. 2012 Mar 5;9(3):605-14.

> Figure 3: Data were extensively falsified. The effect was to make smooth monotonic uptake curves for prodrug CSA which otherwise would have been very scattered without a clear trend.
> Figure 5, 6, 7: Data for tissue distribution of celecoxib and CSA prodrug and effects of metabolic inhibitors were significantly falsified. Result was to reduce variability in measurements, creating statistical differences among the tissue distributions of the drugs.

G. [redacted] knowingly and intentionally falsified and/or fabricated results by manipulating LC-MS/MS/MS peak area data to smooth kinetics and/or alter statistical significance for five figures in [redacted]. Sclera-choroid-RPE transport of eight β-blockers in human, bovine, porcine, rabbit, and rat models. Invest Ophthalmol Vis Sci. 2011 Jul 23;52(8):5387-99.

> Figure 1. This figure compares the transport of 8 different beta blockers across the sclera of rabbit, pig, human, and cow. The raw data files for human , cow, or for albino rabbit were not available for these species.

Pigmented rabbit sclera uptake:

(1) Sotolol: Uptake time points in two of 4 replicates were altered; Chamber 1 to replace all transport time points (which were measured in the raw data as up to 6x higher than the means reported in Fig. 1 "Sotolol") to those close to the mean reported; Chamber 2 replaced the 3-6 hour time points with data that were increased to the reported means.
(2) Atenolol: Uptake time points in Chamber1 and Chamber 3 replicates were altered to conform to expected means. All Chamber 1 raw data was actually ~10x higher than other replicates, whereas Chamber 3 3,4,5 hr time points were replaced with falsified values that conformed to the montonically increasing transport pattern reported in Fig 1.
(3) Nadolol: No comparison between raw and reported data available.
(4) Pindolol: No comparison between raw and reported data available

(5) Metopralol: All data points in Chamber 1 and Chamber 3 fabricated. 1 point in Chamber 2 falsified. Effect was to make all replicates appear close to one another, thus reducing variability of individual points and creating a monotonic transport curve.
(6) Timolol: No comparison between raw and reported data available.
(7) Betaxolol: Data from all four replicates falsified to varying degrees (Chamber 1- all 6 points reduced by a factor of ~10; Chamber 2-3 pts falsified; Chamber 3- 5 points falsified; Chamber 4- 3 points falsified). Effect was to create a smooth, monotonic transport curve from highly disparate and scattered data.
(8) Propranolol: No comparison between raw and reported data available.

Porcine Sclera beta blocker uptake:
Similar to the situation with rabbit experiments above, data for all beta blockers (except sotolol, for which no comparison between raw and reported data was available) contained significant numbers of falsified time points. The effect of these changes was to create smooth monotonic transport curves with smaller error bars.

Figure 3. Was as Figure 1, except done on the SCRPE tissues of these species (again, no data available on human, cow or albino rabbit)
Pigmented rabbit SCRPE uptake: Data for 6 replicates for each of the 8 beta blockers contained numerous time points that were changed from the raw measurements. The affect points appeared to have been replaced to reduce mean variability and to create a smooth, monotonically rising uptake curve.

Porcine SCRPE uptake: Data for atenolol appeared unaltered, while no raw data for comparison to publish sotolol results was available. The other 6 beta blockers all had altered time points, ranging from 1 change (Nadolol) to 28 changes (propranolol) out of 30 time points total for each.

Tables 2, 3; Figs 2,3,4,5,7,8 and 10: All use the primary transport data from curves in Fig 1 and 3, hence the analyses reported will all be contaminated by falsifieddata from Fig 1 and/or Fig 3.

[redacted]

H. [redacted] knowingly and intentionally falsified and/or fabricated results by manipulating LC-MS/MS peak area data to smooth kinetics and/or alter statistical significance for one figure in [redacted] Synthetic LXR agonist suppresses endogenous cholesterol biosynthesis and efficiently lowers plasma cholesterol. Curr Pharm Biotechnol. 2011 Feb 1;12(2):285-92. PubMed PMID: 21190543; PubMed Central PMCID: PMC3163291.

Figure 6C: data for brain levels of LXR agonist were falsified. The data for the internal standards were altered to lower the drug values for brain, making it appear that very little drug entered the brain when in fact uptake was 10-30 times higher.

I. [redacted] knowingly and intentionally falsified and/or fabricated results by manipulating LC-MS/MS peak area data to smooth kinetics and/or alter statistical significance for two tables and four figures in [redacted]. Influence of lipophilicity on drug partitioning into sclera, choroid-retinal pigment epithelium, retina, trabecular meshwork, and optic nerve. J Pharmacol Exp Ther. 2010 Mar;332(3):1107-20.

Tables 3,4,5; Figures 1,2,3,4,5. These were all based on falsified data for the partitioning of 8 different beta blockers into eye tissues. Data were altered from that obtained directly from the LC-MS/MS apparatus. In nearly all cases the data were altered by changing the internal standard values to produce less variable and more consistent partition value patterns. The extent of data falsified involved about 30% of the points overall, and was apparently done to create smoothed, less variable, and in some cases enhanced or reduced partition data.

Response from Respondent:
The Investigation Committee noted that initially [redacted] admitted to falsification of data impacting [redacted] At a later date when confronted by the Inquiry Panel, he admitted to falsification of data in [redacted] When questioned by the Investigation Committee, [redacted] suggested that the only data manipulated was in his [redacted] He refused to admit that any other papers were impacted although he did admit to "gross scientific negligence" (see e-mail dated 6.4.14) when asked to review data relating to Figures 6 and 7 in *Molecular Vision* 2013: 19:1198-1210 and Figures 2 and 3 in *International Journal of Pharmaceutics* 434 (2012) 140 -147. [redacted] did not allege that anyone else was aware of or involved in his falsification activities. The Investigation Committee specifically asked [redacted] on numerous occasions about whether he was directed or asked to falsify data. [redacted] was clear that he acted on his own to falsify data.

Additional Considerations and Findings:
The Investigation Committee noted that when he learned of it, [redacted] is the one who brought forward the allegation regarding [redacted] He took the correct step in reporting this matter to the RIO and he is commended for doing so. As principal investigator, [redacted] the Director of a busy, productive laboratory. The Investigation Committee is also aware that there is an inherent pressure in any research laboratory to publish manuscripts and obtain research funding for it to be successful.

It is also important to note that [redacted] has been in India since mid-December and did not meet with the Investigation Committee in person. He has, however, been pleasant, cooperative and usually responsive to specific questions by e-mail or by phone. He has not, however, admitted to any falsification and/or fabrication of data that has not been specifically brought to his attention. He has not cooperated with the committee to identify which of the other articles that use LC-MS/MS data have been impacted. Despite being advised on several occasions to retain a lawyer, [redacted] has declined to do so.

On several occasions, the Investigation Committee heard from [redacted] who expressed that he felt pressure from his mentor, [redacted] to produce quality results. However, other students in the laboratory at the same time attested that they were under much more pressure than [redacted] because by comparison to [redacted] productivity, they were not considered by [redacted] to be meeting expectations. Several individuals interviewed described [redacted] as the "Golden Boy". The Investigation Committee concluded that his elevated status resulted in him being an author on numerous manuscripts (29 in total) and repeatedly receiving kudos for producing positive data. The consensus is that maintaining this status created additional pressure for [redacted] Other students in the laboratory at the time are to be commended for not falsifying data and ultimately for bringing forward concerns that led to this investigation.

A complicating factor in the laboratory was that there was no one else in the laboratory who could produce data from the liquid chromatography-mass spectroscopy (LC-MS/MS) instrument. Consequently, [redacted] was the only person in the lab who could use and produce data from this machine. There was no direct, first-hand oversight of [redacted] work using the LC-MS/MS.

At laboratory meetings, many of the students stated that [redacted] students were encouraged to bring forward analyzed data, moving towards publication. Even when other students asked to learn how to use the LC-MS/MS, [redacted] did not train them and was not required to do. Consequently, valuable cross-checks and the ability to provide meaningful oversight were missing.

Based on the testimonies of the other students, the Investigation Committee has significant concerns about the quality of the mentoring of students and post-doctoral fellows in the [redacted] laboratory and the lack of engagement of [redacted] in the activities within the laboratory.

In conclusion, the Investigation Committee, however, finds that [redacted] was solely responsible for his conduct and it is his conduct that led to the findings of Scientific Misconduct detailed above. The committee found no evidence that either [redacted] or any other students or employees were aware of and/or participated in any activity amounting to Scientific Misconduct.

Recommendations based on the findings of the Investigation Committee:

Recommendations specific to [redacted]

1. [redacted]

[redacted]

[redacted]

Recommendations relating to publications:

4. The Investigation Committee recommends that correspondence be sent by the University of Colorado RIO to the relevant journals and co-authors to inform them that based on the significant falsification of data in the following 10 manuscripts, the following articles should be retracted:
   i. [redacted]. Self-assembled phenylalanine-α,β- dehydrophenylalanine nanotubes for sustained intravitreal delivery of a multi-targeted tyrosine kinase inhibitor. J Control Release. 2013 Dec 28;172(3):1151-60
   ii. [redacted]. Suprachoroidal delivery in a rabbit ex vivo eye model: influence of drug properties, regional differences in delivery, and comparison with intravitreal and intracameral routes. Mol Vis. 2013 May 30;19:1198-210
   iii. [redacted] Hypoxia alters ocular drug transporter expression and activity in rat and calf models: implications for drug delivery. Mol Pharm. 2013 Jun 3;10(6):2350-61.
   iv. [redacted] Immunohistochemical and functional characterization of peptide, organic cation, neutral and basic amino acid, and monocarboxylate drug transporters in human ocular tissues. Drug Metab Dispos. 2013 Feb;41(2):466-74
   v. [redacted] Hybrid dendrimer hydrogel/PLGA nanoparticle platform sustains drug delivery for one week and antiglaucoma effects for four days following one- time topical administration. ACS Nano. 2012 Sep 25;6(9):7595-606.
   vi. [redacted] Influence of choroidal neovascularization and biodegradable polymeric particle size on transscleral sustained delivery of triamcinolone acetonide. Int J Pharm. 2012 Sep 15;434(1-2):140-7.
   vii. [redacted] Hydrophilic prodrug approach for reduced pigment binding and enhanced transscleral retinal delivery of celecoxib. Mol Pharm. 2012 Mar 5;9(3):605-14.
   viii. [redacted] Sclera-choroid-RPE transport of eight β-blockers in human, bovine, porcine, rabbit, and rat models. Invest Ophthalmol Vis Sci. 2011 Jul 23;52(8):5387-99.
   ix. [redacted]

[redacted] Synthetic LXR agonist suppresses endogenous cholesterol biosynthesis and efficiently lowers plasma cholesterol. Curr Pharm Biotechnol. 2011 Feb 1;12(2):285-92

x. [redacted] Influence of lipophilicity on drug partitioning into sclera, choroid-retinal pigment epithelium, retina, trabecular meshwork, and optic nerve. J Pharmacol Exp Ther. 2010 Mar;332(3):1107-20.

5. Because it was not possible for the Investigation Committee to validate the LC-MS/MS data used in the following 8 manuscripts, the committee recommends that correspondence be sent to the relevant journals and co-authors stating that based on the findings of Scientific Misconduct against [redacted] including the falsification of data in 10 other publications, that the University of Colorado Denver has concerns as to the scientific validity and integrity of the following papers:

i. [redacted] Pigmented-MDCK (P-MDCK) cell line with tunable melanin expression: an in vitro model for the outer blood-retinal barrier. Mol Pharm. 2012 Nov 5;9(11):3228-35.

ii. [redacted] Transporter targeted gatifloxacin prodrugs: synthesis, permeability, and topical ocular delivery. Mol Pharm. 2012 Nov 5;9(11):3136-46.

iii. [redacted] Polyamidoamine dendrimer hydrogel for enhanced delivery of antiglaucoma drugs. Nanomedicine. 2012 Jul;8(5):776-83.

iv. [redacted]. Trabecular meshwork and lens partitioning of corticosteroids: implications for elevated intraocular pressure and cataracts. Arch Ophthalmol. 2011 Jul;129(7):914-20.

v. [redacted]. Influence of drug solubility and lipophilicity on transscleral retinal delivery of six corticosteroids. Drug Metab Dispos. 2011 May;39(5):771-81

[redacted] Poly(L-lactide) Microparticles Sustain Retinal and Choroidal Delivery of TG-0054, a Hydrophilic Drug Intended for Neovascular Diseases. Drug Deliv Transl Res. 2011 Feb;1(1):76-90.

vii. [redacted]. Human scleral diffusion of anticancer drugs from solution and nanoparticle formulation. Pharm Res. 2009 May;26(5):1155-61.

viii. [redacted]. Cassette analysis of eight beta-blockers in bovine eye sclera, choroid- RPE, retina, and vitreous by liquid hromatography- tandem mass spectrometry. J Chromatogr B Analyt Technol Biomed Life Sci. 2009 Jan 15;877(3):253-60.

6. The Investigation Committee did not obtain any evidence that the following papers contain compromised datas currently written and, accordingly, did not conclude that these papers are impacted by findings of scientific misconduct. [redacted] has also provided assurance and data review to establish that these papers are not impacted by findings of scientific misconduct:

i. [redacted] Effect of Cytochrome P450 2C8*3 on the Population Pharmacokinetics of Pioglitazone in Healthy

Caucasian Volunteers. Biol Pharm Bull. 2013;36(2):245-51.

ii. [redacted]. Comparison of suprachoroidal drug delivery with subconjunctival and intravitreal routes using noninvasive fluorophotometry. PLoS One. 2012;7(10):e48188.

iii. [redacted] S. Impact of the CYP2C8 *3 polymorphism on the drug-drug interaction between gemfibrozil and pioglitazone. Br J Clin Pharmacol. 2013 Jan;75(1):217-26.

iv. [redacted]. Nano-advantage in enhanced drug delivery with biodegradable nanoparticles: contribution of reduced clearance. Drug Metab Dispos. 2012 Jul;40(7):1380-8.

v. [redacted]. Recent advances in ophthalmic drug delivery. Ther Deliv. 2010 Sep;1(3):435-56.

vi. [redacted] mitochondrial drug delivery: influence of drug physicochemical properties. Pharm Res. 2011 Nov;28(11):2833-47

vii. [redacted] Rescue of photoreceptor degeneration by curcumin in transgenic rats with P23H rhodopsin mutation. PLoS One. 2011;6(6):e21193.

viii. [redacted]. Ocular pharmacokinetics of dorzolamide and brinzolamide after single and multiple topical dosing: implications for effects on ocular blood flow. Drug Metab Dispos. 2011 Sep;39(9):1529-37

ix. [redacted] Nanosized dendritic polyguanidilyated translocators for enhanced solubility, permeability, and delivery of gatifloxacin. Invest Ophthalmol Vis Sci. 2010 Nov;51(11):5804-16.

x. [redacted]. Luteinizing hormone-releasing hormone receptor-targeted deslorelin-docetaxel conjugate enhances efficacy of docetaxel in prostate cancer therapy. Mol Cancer Ther. 2009 Jun;8(6):1655-65.

xi. [redacted]. Synthetic LXR agonist attenuates plaque formation in apoE-/- mice without inducing liver steatosis and hypertriglyceridemia. J Lipid Res. 2009 Feb;50(2):312-26.

Recommendations relating to grants:

The Investigation Committee recommends that the University of Colorado Denver notify the FDA and NIH about the findings of this investigation so that these agencies can determine if any additional action should be taken at this time regarding the grants cited below,:

- FDA U01FD004929 (2013-2014)

- FDA U01FD004719 (2012-2013; no cost extension 2013-2014)
- NIH R01EY022097 (2013-2017)
- NIH R01HL119533 (pending)

Also, the Principal Investigator should be notified by the University of Colorado Denver of the findings of this investigation with the recommendation that proposal 1 R01 EY024072-01A1 (pending) not be resubmitted without independent verification of the LC-MS/MS data.

Recommendations relating to patents:

7. The Investigation Committee recommends that the University of Colorado Denver notify the Technology Transfer Office, and any co-investigators named on the patents as to the findings of this investigation so that appropriate action can be taken related to any current or pending patents.

Signed by:

[redacted] Date: July 21, 2014

[redacted]

Signed by:

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