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Sunday, January 22, 2012

Editors, PLoS ONE

Dear Sirs/Mesdames,

I wish to submit for your consideration for publication in PLoS ONE a manuscript entitled “**Analysis of Key Experiments Obtained During Discovery in a Case for *Qui tam***” by myself and Dr Joel Pitt. *Qui tam* is a suit filed by a private individual – relator -- on behalf of the Federal Government charging violation of the False Claims Act (*cf* United States District Court District of New Jersey Case number 03-4837 DMC). I am that relator. During the course of the suit, copies of pertinent notebooks were made available to me in the form of over 20,000 Bates-stamped PDF files plus another approximately 10,000 paper documents. As a result, I was able, with the help of 2 expert witnesses, to extract and analyze over 200 experiments recorded by 2 of the defendants, Anupam Bishayee, a post-doctoral fellow, and Roger W Howell, the Principal Investigator of an R01 grant and its renewal, and by others in the Howell laboratory using the same counting instrument and carrying out similar experiments. The substance of the paper is the result of our analyses.

Our results demonstrate that experiments performed by Bishayee diverge markedly from expectations based on statistical considerations and when compared to the results of other workers in the laboratory. The experiments performed by Bishayee were recorded in 8 peer-reviewed publications and were cited as Preliminary Results in the grant application and its renewal. Furthermore, Howell and a second post-doctoral fellow, Marek Lenarczyk, were unable to replicate Bishayee’s results that were presented in 2 of the papers in spite of 22 attempts to do so. As scientists, most of us are taught early in our careers that reproducibility of experimental results is one of the canons of the scientific method. Indeed, in a recent editorial in *Science*, “Addressing Scientific Fraud”, Crocker and Cooper state that “replication is the cornerstone of a cumulative science”¹. This same issue of *Science* contains a Special Section with an introductory editorial and 5 articles on Data Replication and Reproducibility². The issue also includes a News Analysis about “intellectual Property”³ and a Retraction⁴.

You ask why this manuscript is suitable for publication in PLoS ONE: PLoS on-line journals do not shy away from controversy, nor do you adhere strictly to a standard format, *viz* the recent article by Lewis, *et al.* which challenged the premise of Stephen Jay

¹. Crocker J, Cooper ML (2011) Addressing scientific fraud. *Science* 334: 1182.

². Jasny BR, Chin G, Chong L, Vignieri S (2011) Again, and again, and again. *Science* 334: 1225.

³. Cohen J (2011) Dispute over lab notebooks lands researcher in jail. *Science* 334: 1189-1190.

⁴. Stapel DA, Lindenberg S (2011) Retraction. *Science* 334: 1202.

Gould regarding skulls⁵. This controversial article has been viewed more than 25,000 times as of this writing.

You ask how does our paper relate to previously published work? Recent publications in PLoS ONE indicate an interest in scientific misconduct and other concerns that may pressure researchers to stray from the beaten path, *viz* Fanelli, D: 2 reports in 2010^{6,7}. The first of these articles has been viewed more than 14,800 times, downloaded more than 2300 times, bookmarked 30 times and cited 41 times⁸. The second has been viewed more than 9400 times, downloaded more than 950 times, bookmarked 22 times and cited 11 times⁴. Her earlier paper (2009)⁹, asking more directly about research fabrication has been viewed more than 53,000 times, downloaded more than 6000 times, bookmarked 38 times, and cited 130 times⁴. These activities demonstrate the intense interest your readers have in questions pertaining to questionable scientific results.

The recent articles by Ginsparg¹⁰ and by Tenopir, *et al.*¹¹ deal with the importance of open access to scientific data that forms the background of publications, reports and grant applications. This is especially *a propos* of our report: had we not had access to the raw data that was made available to us for analysis during discovery in the *Qui tam* law suit, there would have been no way for us, or the scientific community, for that matter, to know of the questionable nature of the results reported in the 8 papers and the 2 grant applications.

You ask how does our paper provide a worthwhile addition to the scientific literature? We had access and were able to analyze several thousand bits of raw data from a single laboratory spanning a period of over 10 years and have been able to compare questioned data from a single individual to similarly generated data from 8 other individuals who worked at various times in the same laboratory and from 2 sets of data from outside laboratories. Furthermore, we have devised new ways to apply standard statistical methods for examining such data and our report emphasizes the importance for referees to know the scientific literature – those who passed on the various submissions apparently did not question results that were at variance with earlier reports of others.

We believe that it is imperative for cases like this to be published in the scientific literature in order that scientists not be misled by results that are based on doubtful

⁵ Lewis JE, DeGusta D, Meyer MR, Monge JM, Mann AE, et al. (2011) The Mismeasure of Science: Stephen Jay Gould versus Samuel George Morton on Skulls and Bias. PLoS Biol 9(6): e1001071. doi:10.1371/journal.pbio.1001071.

⁶ Fanelli, D. Do Pressures to Publish Increase Scientists' Bias? An Empirical Support from US States Data. PLoS ONE 5(4): e10271. doi:10.1371/journal.pone.0010271,

⁷ Fanelli, D. "Positive" Results Increase Down the Hierarchy of the Sciences. PLoS ONE 5(4): e10068. doi:10.1371/journal.pone.0010068

⁸http://apps.webofknowledge.com.libproxy3.umdj.edu/summary.do?product=WOS&search_mode=GeneralSearch&qid=1&SID=X17ao3lckp31Af3kKjf&page=1&action=changePageSize&pageSize=50

⁹ Fanelli, D. How Many Scientists Fabricate and Falsify Research? A Systematic Review and Meta-Analysis of Survey Data. PLoS ONE 4(5): e5738. doi:10.1371/journal.pone.0005738

¹⁰ Ginsparg, G. ArXiv at 20. Nature 476: 145-147, 2011.

¹¹ Tenopir C, Allard S, Douglass K, Aydinoglu AU, Wu L, et al. (2011) Data Sharing by Scientists: Practices and Perceptions. PLoS ONE 6(6): e21101. doi:10.1371/journal.pone.0021101

science. Not only do Bishayee's papers contain questionable data, the original grant application and its renewal were similarly compromised. As David V. Kirby, the US attorney for Vermont said in commenting on the Poehlman case "This ... siphoned millions of dollars from the pool of resources available for valid scientific research proposals"¹². Funds for Howell's grant and its renewal totaled approximately \$2,500,000.

You ask which types of scientists do we believe will be most interested in our study? All scientists, indeed, the general public as well, should see our report as a signal of what can happen if one lets down one's guard. We also show that there can be several ways to analyze and confirm or refute numerical data.

Although we would not have had the opportunity to examine the volumes of data had it not been for the *Qui tam* suit, we want other scientists to know that the legal route is probably not the best one. The original charges were made in October of 2003. The judge made a ruling in September of 2010 in favor of the defendants. His ruling was based on technicalities and vagaries of the law which were independent of the analyses we present in our paper. The Appeals Court upheld the District Court's decision and the case is now closed, at least in the courts. We, however, stand firm behind the analyses presented in this paper, we believe that it is scientists that should be judging science and we sincerely hope that PLoS ONE will support us and allow the paper to be published.

We address the concerns regarding competing interests as follows:

I do not believe that any competing interests exist at this time. There are no financial competing interests involved in the submission or projected publication of this paper. Both Dr Pitt and I have academic appointments at our respective institutions and will receive no compensation should the paper be published. It is important to note, however, that Dr Pitt did serve as an Expert Witness for the Plaintiff in the *Qui tam* case. He was compensated by me for his report (which is submitted as supporting material) and by the defense for his testimony at his deposition.

Much of the data presented in the paper have nothing to do with the *Qui tam* case and were not presented as evidence. This includes but is not limited to experiments on isotopes other than tritium. Much of the information that we have analyzed only became known to us because it was provided after subpoena. Since all of this material is contained in Discovery and/or court documents, it is in the public domain and should be freely accessible to the public.

Neither Dr Pitt nor I have any current personal relationship with Dr Howell or Dr Bishayee¹³, although they were defendants in the *Qui tam* case. However, since they and the University were co-defendants in the case, you may consider that we have an adversarial relationship with them. You may wish to give them an opportunity to comment on the paper and we would encourage you to do so.

¹² Goldberg, Carey and Allen, Scott. "Researcher admits fraud in grant data - Ex-Vermont scientist won nearly \$3M from US." The Boston Globe: March 18, 2005, p. A1.

¹³ From July, 2000 for a period of about 1.5 years, I sublet an apartment in Newark to Dr Bishayee

We also wish to inform you that Dr Paul Driscoll who is on your Board of Academic Editors has read an earlier draft of our manuscript.

The following Academic Editors would appear to have the expertise necessary to review this paper:

Research Integrity/Publication ethics: Cameron Neylon and Erick Turner

Biology/Radiobiology: Kerstin Borgmann, Nils Cordes and Marianne Koritzinsky

For Statistics, we recommend: Keith A Baggerly and Kevin R Coombes, Department of Breast Medical Oncology, The University of Texas MD Anderson Cancer Center, BO Box 301439, Houston, TX 77030-1439, USA.

The Supporting Material includes 1.) the 3 expert reports associated with the *qui tam* case; 2.) Lenarczyk's experiments (experiments presented during Dr Lenarczyk's deposition some of which were not provided in PDF form); 3.) PDF files from Discovery (extraneous and irrelevant files have been removed); 4.) Tritiated thymidine survivals with and without deoxycytidine (6 experiments not included in the original PDF files submitted by the defense); 5.) Colony and Coulter counts by Bates number and Date (an Excel file that aids in locating files analyzed in the expert reports and in the paper); and 6.) R routines used in the paper. Items 1 through 4 all come from Discovery and are in the public domain.

The manuscript was reviewed and edited by the American Journal Experts (Editorial Certificate Verification Key DBFD-0979-287A-DD09-FACA).

Sincerely yours,

A handwritten signature in black ink that reads "Helene Z Hill, PhD". The signature is written in a cursive, slightly slanted style.

Helene Z Hill, PhD
Professor of Radiology
NJ Medical School

Subject: PLoS ONE Decision: PONE-D-12-03472
From: "PLOS ONE" <plosone@plos.org>
Date: 2/10/2012 6:41 PM
To: "Helene Z Hill" <hzhill@verizon.net>

PONE-D-12-03472
Analysis of Key Experiments Obtained in Discovery in a Qui Tam Case
PLOS ONE

Dear Dr Hill,

Thank you for submitting your manuscript to PLoS ONE. Following careful consideration by the Editorial team, we have decided that we cannot consider your submission for publication in PLoS ONE and are returning it to you.

We recognise that this paper addresses a controversial topic. PLoS ONE is not averse to publishing original research studies which are critical, or controversial, with respect to previous research studies. However, in this case we feel your manuscript does not address a specific research question or describe a research study per se. In addition, we are concerned that the analyses reported imply misconduct in relation to previous articles published elsewhere. In the light of this, and in accordance with accepted procedures in publishing ethics, we feel it is more appropriate for the journals that published the original articles to pursue this matter.

I am sorry we cannot be more positive on this occasion. We hope you appreciate the reasons for this decision.

Yours sincerely,

Anne Tran
Publications Manager
PLOS ONE

on behalf of

Elizabeth Silva
Associate Editor
PLOS ONE

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Monday, February 20, 2012

Elizabeth Silva
Associate Editor
PLOS ONE

Re: Appeal regarding your decision on PONE-D-12-03472
Analysis of Key Experiments Obtained in Discovery in a Qui Tam Case

Dear Ms Silva,

I respectfully appeal your editorial decision not to publish the above named paper.

First, you state that our manuscript does not address a specific research question or describe a research study per se.

1. The first research question that we explore is "do the numerical results of Bishayee's Coulter and colony counts conform to the null hypothesis for randomness or uniformity?" We clearly conclude that they do not, whereas similar results of others do so conform.
2. The second research question that we explore is "are Bishayee's radiation biology results consistent with those reported in the literature for similar experimental conditions?" We conclude that they are not, whereas results obtained by Howell and Lenarczyk are so consistent.

We could rewrite our paper to address these questions more succinctly. However, we chose to let the reader draw his/her own conclusions, in order to avoid making any direct accusations of research misconduct.

Next, You raise questions regarding "accepted procedures in publishing ethics" without, in fact, specifying what these are. PLoS ONE is a member of COPE. Editors under the COPE Code of Conduct are exhorted to

1. Strive to meet the needs of readers and authors: we hold that this paper is needed by your readers as it demonstrates processes that underlie data presented in papers that are entirely opaque and that, if known, would completely change the conclusions to be drawn. It further emphasizes the need for raw data to be made available so that readers can verify for themselves the conclusions that are drawn.
2. Champion freedom of expression.
3. Maintain the integrity of the academic record. This is clearly a role that our paper plays.
4. Preclude business needs from compromising intellectual standards. We must ask whether this is the reason you have chosen to reject our paper?

5. Base their decisions only on **the paper's importance, originality and clarity.**
6. Editors have a duty to encourage debate. "Cogent criticisms of published work should be published unless Editors have convincing reasons why they cannot be."
7. "Editors have a duty to act if they suspect misconduct. This duty extends to both published and unpublished papers. Editors should not simply reject papers that raise concerns about possible misconduct. They are ethically obliged to pursue alleged cases."
8. Ensure the integrity of the academic record. "Whenever it is recognized that a significant inaccuracy, misleading statement or distorted report has been published, it must be corrected promptly and with due prominence."

In addition, the following items are listed under your Guideline for Authors, item 2: Criteria for Publication:

1. **The study presents the results of primary scientific research.** We argue that this applies to our paper. Our study involves an analysis of data that were obtained through legal means and are publicly available. We posit that such an analysis represents primary analytical scientific research just as do interpretations of gels or quantification of numerical data in case-control studies. As Louis Agassiz famously said "look at your fish", we have applied a microscope to data that supported as many as 8 publications in peer reviewed journals. This is primary scientific research.
2. **Results have not been published elsewhere.** This is true.
3. **Experiments, statistics, and other analyses are performed to a high technical standard and are described in sufficient detail.** This statement applies to our study, *cf* the **Methods** section of our paper.
4. **Conclusions are presented in an appropriate fashion and are supported by the data.** This statement applies to our study, *cf* the **Summary and Conclusions** sections of our paper.
5. **The article is presented in an intelligible fashion and is written in standard English.** This applies to our paper which has been certified by American Journal Experts (certificate verification key: DBFD-0979-287A-DD09-FACA).
6. **The research meets all applicable standards for the ethics of experimentation and research integrity.** Our paper is about the ethics of experimentation and research integrity.
7. **The article adheres to appropriate reporting guidelines and community standards for data availability.** All of the data that we analyzed were made available to us during Discovery in the *qui tam* case and all are intended to be posted as supporting material so that any other researcher/statistician can verify the integrity of our results.

We urge and fervently hope that you will reconsider your decision and submit our paper for review. We firmly believe that your reviewers will see the importance of our analysis and that public interest in the subject matter will become evident once the paper has been published and the scientific community has an opportunity to weigh in regarding its impact.

Sincerely yours,

Helene Z Hill, PhD

Helene Z Hill, PhD
Professor of Radiology
NJ Medical School

Subject: PLoS ONE manuscript PONE-D-12-03472
From: "Iratxe Puebla" <ipuebla@plos.org>
Date: 3/12/2012 5:28 PM
To: "Helene Z Hill" <hzhill@verizon.net>

Analysis of Key Experiments Obtained in Discovery in a Qui Tam Case
PONE-D-12-03472

Dear Dr Hill,

Thank you for your email in response to the decision to reject your manuscript 'Analysis of Key Experiments Obtained in Discovery in a Qui Tam Case'.

As indicated in the decision letter, your submission was considered by different members of the editorial team. We have also considered your request for reconsideration and regret to say that our original concerns in relation to the manuscript remain. Our decision to decline consideration was mainly based on concerns over the suitability of the piece for the journal's scope rather than specific issues related to the specific criteria for publication. The decision we have reached regarding your article is consistent with others we have made about the limits of the journal.

We take note about COPE's Code of Conduct, PLoS ONE is a member of COPE and we abide by their recommendations. However, we consider that in this case, the duty to correct any inaccuracies in relation to the published articles you have evaluated falls within the responsibility of the editors where the articles were published.

I am sorry to disappoint you further but I hope that this provides some clarification for our decision.

Sincerely,

Iratxe Puebla
Consulting Editor, PLoS ONE