

Additional evidence for Scientific Misconduct in the Division of Radiation Research in 1999 – 2001¹

You may know that the ORI has decided not to press the University to pursue the investigation of scientific misconduct that I reported to you in the spring of 2001. Shortly before the ORI staff met, Dr. Fields told me of a method that could be applied to data to determine the non-uniformity of numbers that should be uniform resulting from digital counters such as a scintillation counter or a Coulter counter. She asked me to send her my analysis; however, it arrived too late and was not considered by the ORI when they finally disposed of the case. You should know that Dr. Fields was so upset at the decision of her colleagues that she (by her description) stormed out of the room and was subsequently removed from the case. In the letters that I received from the ORI after their decision had been made, I was instructed to report my additional information to the University. It is my intention during this meeting to show you this analysis and to relate to you events that have occurred since your final decision in this case that strongly indicate that there has been cover-up by Dr. Howell of the misconduct and that this cover-up is supported by Dr. Azzam.

Re-analysis of Bishayee's data from the experiment in 1999

The analysis of the data in my possession is based on a paper that was recently published by James E. Mosimann, formerly a statistician at the ORI (Exhibit 1). Dr. Mosimann has retired and was not present at the ORI staff meeting. I was told that there were, in fact, no statisticians at this meeting. The premise of the paper is that when people make up numbers, they do not pick them randomly. Numbers that are generated by electronic instruments should be uniformly distributed if they are located in non-significant positions. In the paper, Mosimann, et al. present 4 cases in 2 of which numbers are reported that are discrepant as regards their expected uniform nature. In all 4 cases, when the originators of the numbers were confronted with the analyses, they admitted that the numbers had been fabricated.

I analyzed all the Coulter Counter records that I had in my notebook that were given to me by Dr. Bishayee and that I had obtained on my own (Exhibit 2). 198 Coulter digits were analyzed from Bishayee's Coulter counts and 160 were analyzed from my counts. The probability that Bishayee's counts are uniformly distributed is 1.76 times ten to the minus eleven (one chance in 57 billion), while the probability that my counts are uniform is 0.24 (one chance in 4.25), not statistically different from uniform. The probability that Bishayee's numbers were fabricated is extremely high, higher by orders of magnitude, in fact, than any of the chances resulting from the analyses in the Mosimann paper that were admittedly fabricated.

In order to convince myself of the validity of the method, I also analyzed digits from scintillation counts that were in my notebook (Exhibit 3). These numbers were taken from printouts so there is no possibility of fabrication. There were 194 digits in this analysis and the probability was 0.29 that they were uniform, again, a value that is not significantly different from the expectation of uniformity. In order to ascertain that the Coulter Counter was behaving in a manner similar to the scintillation counter, I analyzed counts that I received from Dr. Lenarczyk (Exhibit 4). In this case, 458 digits were analyzed and the probability that they were uniform was 0.43, i.e., not significantly different from uniform.

I do not have access to any more data from Dr. Howell's notebooks. He has, in fact, kept his notebooks locked up in his office since they were returned by the University. I believe that further analysis of data in these notebooks will strengthen the conclusion that data were fabricated. One of the experiments that I analyzed, dated 9/24, 9/27, 10/1 and 10/4/99 (Cf Exhibit 2), was used as preliminary data in Dr. Howell's successful grant application (Exhibit 5: Section C.2i, Figure 7, pages 29-30) I have already pointed out during the course of the initial investigation other discrepancies in the numbers in this experiment as well as observations that I made at the time that Dr. Bishayee had faked the mutation data because he reported numbers of mutants before he had processed the dishes (see my memo dated 5/22/01 to Dr. Raveché).

There is, in fact, an additional discrepancy in this experiment when it is compared to the preceding experiment which followed exactly the same protocol. I did the mutation arm of that first experiment. The purpose of the two experiments was to determine whether the clusters which Dr. Howell had designed were hypoxic (starved for oxygen) or not (Cf exhibit 5). To this end, the samples were divided into two parts. Both sets of samples were

¹ This document was prepared for Dr. Putterman to be given to her at our meeting on 10/24/02

incubated in clusters at 10.5° for 3 days. One set was then aerated while the cells in the other set remained compacted. The two sets were treated with graded doses of gamma rays. If hypoxia is present, the hypoxic cells will be resistant to the radiation. This is known as the oxygen effect, a well-known phenomenon in radiation biology. In the experiment that I did, there was essentially no increase in mutants in the cluster (compacted) set indicating that severe hypoxia was present. There are, apparently no survival data (done by Bishayee) from this experiment because they were lost due to contamination. In the experiment that Bishayee did (cf 9/24 – 10/4/99 above), the survival arm of the experiment indicates only a small amount of hypoxia and this is reflected again in the mutant arm. Dr. Howell used Bishayee's experiment to argue in his grant application (Figure 7) that hypoxia in clusters was minimal. I argue that it is probably substantial. Dr. Lenarczyk similarly found profound hypoxia in at least 2 experiments that he did but he says the data are in Poland whereas he is currently in Colorado.

Reproducibility of the bystander effect for ³H:

It should be noted that the so-called bystander effect for radiation is a robust phenomenon that has been demonstrated a number of times and in several different systems. However, Dr. Howell is the only one who has reported a bystander effect for tritium (³H). At Dr. Fields' request, I documented this statement by searching PubMed for 'bystander 3H-thymidine' and found 8 citations none of which were relevant, for 'bystander 3H' I found 18 citations, none of which were relevant. For 'bystander tritium', I found 5 citations, 3 of which were not relevant; the other two were Dr. Howell's papers.

When Dr. Howell and I first went to Dr. Raveché's office to report Dr. Bishayee's scientific misconduct, Dr. Howell was told to repeat the key experiments. During the next few weeks, the experiment purporting to demonstrate a bystander effect for ³H was repeated a number of times. These trials were related to me by Dr. Lenarczyk, who participated in several of them. Dr. Lenarczyk sent me the data from his bystander experiments and I have summarized them on a graph (Exhibit 6). This graph summarizes data from 8 of Dr. Lenarczyk's experiments (filled circles) and compares them to the plot drawn from Dr. Howell's paper (Bishayee, et al., Radiation Research 155: 335-344, 2001: Figure 2, panel A, open circles; these data are similar to those plotted in Figures 3 and 6 in Bishayee, et al. Radiation Research 152: 88-97, 1999), red line and circles. In all of these experiments, 50% of the cells incubated in clusters for 3 days have been pre-labeled with ³H-thymidine. The other 50% were randomly mixed with the ³H-labeled cells but were themselves unlabeled. Dr. Howell reported in the two papers that the unlabeled cells (bystanders) were killed by their close proximity to the ³H-labeled cells (red line and circles). Dr. Lenarczyk's experiments show that this is clearly not the case. Dr. Lenarczyk's data show essentially no killing of the bystander cells.

I understand that Dr. Howell has said that he believes that the cells changed over the time since the original experiments were done, or that the bystander effect that he purported to have observed was dependent on serum which is a component of the growth medium. These are possible but unlikely explanations for the non-reproducibility of the data. Furthermore, when I spoke to Dr. Bishayee on August 1, 2001, he told me that sometimes in these early experiments there was bystander killing and sometimes there was none. This indicates that somewhere in the notebooks there will be early experiments that show no bystander effect, thus indicating that cell or serum changes are unlikely explanations for the discrepancies.

I conclude from the data that are available to me for analysis:

- 1.) The experiment reported on pages 29-30 and in Figure 7 of Dr. Howell's successful grant application was fabricated.
 - a. Coulter counter analysis indicates extreme departure from uniform for digits that should be uniformly distributed, a strong indication that these numbers were invented.
 - b. As pointed out during the course of the 2001 investigation, at high gamma ray doses, the reported data show significant cell death in the survival arm of the experiment. This should have been reflected in lower cell counts at higher doses for the first Coulter counts on day 3. However, the counts on day 3 were approximately the same for all samples. There were lower counts in the preceding experiment in which I performed the counts.
 - c. I observed at the time of the experiment that the dishes from that experiment had not been processed at a time when Dr. Bishayee had already given me the results.

Scientific Misconduct
Page 3

d. The mutagenesis arm of the experiment that I did indicated that the cells that were irradiated while in clusters were hypoxic. This was not consistent with the results reported for the same experiment performed by Bishayee.

2.) The bystander effect for tritium as reported in two papers is not reproducible.

The cover-up:

Dr. Bishayee lived in an apartment in Ivy Hill that I was holding for my son from some time in late 1999 until May of 2002. I met with him on August 1, 2001. At that time, he told me 1.) that he was sorry for anything that he might have done to hurt me, 2.) Dr. Howell had handed him a letter of resignation and told him to sign it, 3.) Dr. Howell told him he was not to come on to this campus, 4.) Dr. Howell told him he was not to look for or take any positions in research on this campus, 5.) Dr. Howell told him he was not to apply for any jobs in Radiation Biology at any other institution, 6.) he was changing his visa status from H to Visitors which would be good for 3 months, renewable for an additional – final – period of 3 months, 7.) he requested that I allow him to continue to live in my son's apartment – the rent was very cheap, he had no income and he had nowhere else to go. I agreed to let him stay there. Items no. 3 through 5 were confirmed in conversations with Dr. Azzam who also told me that he, Dr. Azzam, was the one that persuaded Dr. Howell to get rid of Dr. Bishayee. Dr. Azzam also told me that he advised Dr. Bishayee to 'get out of research'.

Dr. Bishayee came to pay me for the apartment every month. He wanted to avoid being seen by Dr. Howell so he would call me late in the day and ask me 'how is the weather?'. If Dr. Howell had gone home, he would come to see me. In November, he was running out of money and he told me that he could no longer pay me. I allowed him to continue living in the apartment without paying. He resumed paying in March. He did not pay any attention to Dr. Howell's injunctions. He continued to come to the campus nearly every day and worked in the Academic Computing facility looking for jobs. I asked him how he had managed to retain his ID and he said that he was friendly with the folks in security. I know for a fact that he applied for a job in one of the other departments in this medical school and that when Dr. Howell was asked for a recommendation his response was 'keep looking'. He also went for an interview for a job in Radiation Biology at the University of Iowa but did not get it although I do not know why. I understand that Dr. Pain in the Pharmacology-Physiology Department moved to this campus from Penn in October. He permitted Dr. Bishayee to work in his lab as a volunteer to learn Molecular Biology for several months. He promised Dr. Bishayee a position which would take effect after Dr. Bishayee returned from a trip to India to get married in February. I assume that Dr. Pain arranged for his sponsorship and that he was again salaried in March. He resumed paying for the apartment at that time.

I understand that the current position is that Dr. Bishayee resigned from Dr. Howell's lab in order to 'learn Molecular Biology'. This is not logical. Dr. Bishayee came to the UMDNJ sponsored by Dr. Subal Bishayee (no relation) in the Pathology Department. I assume he was on a J visa at the time. Things did not work out with Dr. S. Bishayee and he was let go after 6 months. Dr. Howell then hired him as a part-time Post-Doctoral Fellow for, I believe, about \$19,000 with minimal fringe benefits. Dr. Bishayee wanted very much to be able to apply for a green card. When Dr. Howell's grant was funded on July 1, 2000, Dr. Bishayee was promoted to Research Associate with a salary that must have been close to double what he had been making and with full fringe benefits. Dr. Bishayee immediately changed his visa to an H and initiated an application for a green card. Once he had 'resigned' from the Laboratory of Radiation Research, he lost his salary and his H visa. This all within a month after termination of the investigation by the Committee on Research Integrity. It is not logical that he would have done this voluntarily. His 'lessons in Molecular Biology' cannot have started until October because Dr. Pain was not here before that time. Dr. Bishayee now works in the Office of Radiation Safety Services. His visa history can be confirmed through the University Visa Office or by contacting the INS.

The whistle-blower

In 1999, my grant monies had run out and I had been moved to the F-level to share laboratory space with Dr. Howell who was also without grant support. Both of us were applying for grants that were reviewed by the Radiation Study Section. My application was triaged but Dr. Howell's had a reasonable score. I thought we could be more productive if we teamed up together so I offered to join forces with him. He agreed. I helped him with his resubmission and it was funded. In the spring of 2000, Dr. Edouard Azzam joined the Division of Radiation

Scientific Misconduct
Page 4

Research. His wife, Dr. Sonia de Toledo, remained in Boston so their children could finish the school year. For 3 months, Dr. Azzam was a guest in our house, in our small efficiency apartment in our basement. Dr. de Toledo joined us in July and they moved into their own house. Dr. Lenarczyk came in the fall as a Post-Doc with Dr. Howell and took Dr. Azzam's place in our basement. At this time, I thought I could never be happier. We were now a lively, interactive, productive group. We often met for coffee and lunch and shared information about our research. The only sour note was my suspicion that Dr. Bishayee made up data and that Dr. Howell refused to admit it. Dr. Lenarczyk was assigned to work closely with Dr. Bishayee and it was not long before he was voicing his suspicions about Dr. Bishayee as well. Dr. Lenarczyk and I also worked closely together on another project of Dr. Howell's. The happy period ended when Dr. Lenarczyk showed me what Dr. Bishayee was up to at the end of March, 2001 and I became a reluctant whistle blower. I made my report to Drs. Howell, Baker and Raveché on April 10, 2001. As you know, the committee ruled that there was not enough evidence to proceed onto the next phase. I disagreed and after much soul-searching, at the end of August, I submitted anonymously what information I had to the ORI.

Once the original investigation was over, on or about June 22, 2001, Dr. Howell called me into his office and told me that he did not want to have anything more to do with me, saying 'it was not what was done, it was how it was done'. He also told me that both Dr. Bishayee and Dr. Lenarczyk would be leaving at the end of the month.

As you know, this was followed by a memo from my Department Chairman to my whole Department that was obviously designed to demean me and that gave Dr. Howell carte blanche to retaliate against me by taking away my administrative duties and putting me under Dr. Howell's jurisdiction. The next step was to lock me out of the laboratory which we all shared. I complained to the AAUP and on their advice reported the retaliation to you after which my key to the laboratory was restored. Given Dr. Howell's dictum regarding not wanting to have anything to do with me, I could no longer work with him and Dr. Azzam said he would be pleased to have me work with him. I realize that this 'shunning' by Dr. Howell constituted continuing retaliation but, just as he did not want to have anything to do with me, I did not want to associate with him since I knew that he was refusing to face the fact that there had been misconduct. To associate with him would align me with the cover-up. The happy days were certainly gone. During this time, Dr. de Toledo and I worked together and became friends. We frequently lunched together and she would help me with the bench work that I was doing for her and her husband. However, there was no longer a happy, cohesive research group. I felt isolated and somehow dirty and ashamed even though I knew that I had done the right thing. The whistle-blower is clearly the lowest form of human life. While Dr. Azzam acknowledged that the spurious papers should be withdrawn, he defended Dr. Howell's inability to withdraw them. My work at the bench saved my sanity, although it was upsetting to see myself excluded from joint interactions with Drs. Azzam, de Toledo and Howell. I was the outsider – closed out.

Things went along this way until April, 2002. The Radiation Research Society met in Reno, NV at the end of the month and Dr. Howell left on the train about a week before. On April 18, Dr. Azzam told me that I would have to move my equipment and supplies out of the big shared lab to make room for a new Post-Doc who was coming to work with Dr. Howell. I didn't feel that this was unreasonable and I still had room in another small lab in which to work. However, the timing was bad because I had other things that I wanted to do. When I came in on April 19, Dr. Azzam accosted me and accused me of being angry by telling me that he could 'read my mind'. He asked me 'when is it going to end?', meaning, of course, the investigation by the ORI. I replied that I did not know. He followed me to my office and demanded that I give him all of the experiments that I had done for him and his wife, the work of the past 8 months. I was stunned but I complied.

I then called Dr. Fields because I suspected that she had been in touch with you and that you had interrogated Dr. Howell about things that I had told her. This was confirmed by Dr. Fields. She advised me to open up to Dr. Azzam about my report to the ORI and that his harassment of me constituted further retaliation. He returned to my office and I told him these things. He was very agitated and told me 'I am an Arab! I am an Arab!'. I can only assume that he said this to intimidate me. He told me that 'if those people come on this campus, I will leave'. It was apparent that he – and Dr. Howell – believed that the 'NIH' would come on to this campus to investigate and that they feared that Dr. Howell would lose his grant. He told me that I 'would be responsible if Dr. Howell's children found out that he had done something shameful' and furthermore, I 'would be responsible if Dr. Howell's post-doctoral fellows lost their jobs'. He said that it was his responsibility to prevent this from happening. I was so overcome that I was shaking. Dr. Azzam returned again sometime later and apologized. He returned the experiments that I had done and said that I could still work with him. After he went away, I thought everything over

Scientific Misconduct
Page 5

and realized that I could not work with him anymore. I could forgive him for his temper tantrum but it was clear that he now was participating in the cover-up. I bundled up the experiments and put them on Dr. de Toledo's desk.

After this, at the Radiation Research meeting, Dr. Azzam was very solicitous and urged me several times to have coffee or to go to dinner. Since then, he has apologized again and offered to support any research project that I want to do. I believe that this turn of events results from his fear of what I will do next and that his offer is for hush money. Since my return from the meeting at the end of April, Dr. de Toledo has hardly spoken to me. My isolation is greater than ever. I realize that this is partly my fault. I cannot bring myself to have anything to do with people who knowingly cover up misconduct. I would be most happy to see things go back to the way they were before but only if there is a clean sweep and the papers that contain falsified data are withdrawn. I feel now like a person without a country. I have the small lab in which to work but I contributed several thousand dollars to the lab in supplies and I don't know where they are and what is mine and what is not mine. I am alienated and alone. Happily, a former post-doctoral fellow of mine is now an Associate Professor at CCNY and wants to collaborate with me on a project so I will be able to divorce myself from the research that I had been doing here and which I found exciting and interesting. Through the Foundation I have contributed money to support my own research and take care of my own needs.

The responsibility of the University

I believe that you – and I – have a responsibility to the scientific community to set the literature right. Researchers interested in bystander effects caused by tritium will waste countless months trying to repeat experiments that are not true and are not repeatable. I believe that we also have a responsibility to the United States Government to acknowledge that preliminary data in a funded R01 grant were false. Because Dr. Howell's grant was funded, someone else in that Study Section was not funded. This is not right. However, Dr. Fields assures me that the NIH is very reluctant to withdraw grants and that their likely response will be to request Dr. Howell to outline his proposed course of action in the light of the falsifications.

Data that were used for Preliminary Results and in the 8 publications in which Dr. Bishayee participated must be closely analyzed. The Mosimann technique must be applied where applicable. The publications that are not true should then be withdrawn. There are two ways to do this, but first, the notebooks must be sequestered again:

1.) Confront Dr. Bishayee with the Mosimann analysis, but assure him that if he tells all, he will not lose his job. The thing that frightens him the most is being deported. In Dr. Mosimann's paper, all 4 of the miscreants when confronted with the analyses broke down and confessed. Once Dr. Bishayee has confessed, then he could cooperate with Dr. Howell and a third – objective -- individual, to go over the papers and the grant to show which data were falsified.

or

2.) Re-initiate the investigation by the Committee. However, if this is done, it must be done properly. There must be a Microbiologist involved to reexamine the original misconduct of March-April, 2001, and there must be a Statistician. Radiation research is esoteric and obscure. It would be desirable for a Radiation Biologist from outside the University to sit on the Committee or be consulted. Dr. Raveché must recuse herself from the Committee. She is President of the Faculty Organization and this would represent a conflict of interest. Furthermore, she expressed her antagonism to me in a confrontation we had in March of 2001. I have reason to believe that she does not like whistle-blowers.

I will not take further action until I have received a complete and detailed report from you. This I expect to receive in approximately 2 months. In your previous investigation, I never had a chance to respond to statements made that I might well have known to be false. I would appreciate having the opportunity to review claims made by others. If I am not satisfied with your decision, I may proceed to file a *Qui Tam* suit. I have been told that I have a strong case and that the penalty to the University if you lose -- which you surely will -- is three times the government's loss or, in this case, 4.2 million dollars. I have also been told that presentation of falsified data in a grant application is a violation of the US False Claims Act and could lead to criminal proceedings.

There are two additional things that I wish to bring to your attention:

Scientific Misconduct
Page 6

1.) I am a co-author on one of the papers that contains fraudulent information. I wish to withdraw my name from that publication. I will not do this until I have heard from you in 2 months or less, but after that time, I will do it with or without your approval.

2.) Dr. Lenarczyk and I are preparing a paper based on data that were generated while he was here. Data that will have to be included (see exhibit 6) are in direct opposition to the key findings in the two publications by Bishayee, *et al.* (Exhibit 6). Thus to publish our paper requires some explanation of those original findings, presumably by way of retraction. We will continue to prepare this paper but will not submit it for publication until I have heard from you in 2 months or less.

This has been the worst year of my scientific career. I have spent many sleepless nights agonizing over what I should do. I am ashamed of Drs. Howell and Azzam for their behavior and I am ashamed of my Chairman for not having the wisdom to sit down with me and listen to what I had to say when this all began. Nonetheless, I am not insensitive to the pain that the necessary admissions will bring to Dr. Howell. I truly do not want his children to have to know what has happened. But we all have to take responsibility for our own actions and I say it again as I said it before: there is no place in science for dishonesty and that honesty, honor and integrity should be above all else in everything that we do.