



Final Report of the Investigation Committee
Wayne State University
November 30, 2011

RE: Investigation of research misconduct allegations—DIO 4414

Complainant: Christian A. Reynolds
Respondent: Christian W. Kreipke

I. NATURE OF ALLEGATIONS OF RESEARCH MISCONDUCT:

On February 10, 2011, the complainant met with Wayne State University's Research Integrity Officer (RIO) regarding several allegations of research misconduct that he provided in a letter dated February 8, 2010. The letter contained several allegations, including three for which he provided specific documentation involving figures in two publications and one NIH grant that the complainant believed were falsified and/or fabricated. During the initial assessment of these allegations, the RIO determined that three of the allegations were sufficiently credible and specific so that potential evidence could be identified. Additionally, the RIO determined that because the allegations involved NIH funding, the Office of Research Integrity would have jurisdiction. She convened an Inquiry. She also noted that one of the publications in questions referenced VA funding, so she informed the RIO at the John D. Dingell VAMC when she decided to convene an inquiry, and he provided a VA representative.

On March 9, 2011, the Inquiry Committee met and reviewed the letter containing the allegations along with the supporting documentation provided by the complainant. The material that the RIO sequestered from the respondent's laboratory was also made available to the Inquiry Committee. The committee concluded that there was sufficient supporting evidence for the allegations of research misconduct and that a full investigation was warranted. At some point before the investigation began, the VA's RIO informed WSU's RIO that he had determined that no VA funding or resources were involved in the alleged misconduct and therefore a VA representative would not be required for the investigation.

An Investigation Committee was convened and met initially on April 5, 2011. The RIO asked each member if he or she had any conflicts of interest with the complainant or the respondent or the Department of Anatomy and Cell Biology at WSU. They each stated that they had no conflicts. They were reminded that confidentiality was of the utmost importance.

The committee members were provided with the following information:

- The Inquiry Report
- The letter containing allegation(s) from the complainant
- The two publications and the NIH R01 application provided as supporting evidence by the complainant
- Access to the materials sequestered from the respondent's laboratory.
- Copies of WSU's Policy and Procedure Regarding Research Misconduct

The RIO charged the committee with conducting the investigation as prescribed in Section 7.5 of WSU's Policy 2010-01. They were directed to use diligent efforts to ensure that the investigation would be thorough, sufficiently documented, and included examination of all research records and evidence relevant to reaching a decision on each allegation. They were also directed to pursue diligently any evidence of any additional instances of possible research misconduct and any additional respondents. Initially, the committee pursued evidence of the three allegations described in the Report of the Inquiry Committee. During the course of the investigation, the committee added two more allegations for which they had multiple supporting documents. All allegations involved falsification and/or fabrication of figures in NIH grant applications, publications, and/or presentations (e.g. posters), as well as falsification and/or fabrication of a biosketch and letter of support contained in an NIH grant application. The specific allegations are described below.

II: PHS SUPPORT

The following provides a list of the NIH grants, and publications/presentations supported by these grants, that the committee identified as being directly involved in the alleged research misconduct:

Grant Proposals

Exhibit 1 1R01NS064976-01A1
Exhibit 2 1R01NS064976-01A2
Exhibit 3 2R01NS039860-09A2
Exhibit 18 1 R01 NS064976-01
Exhibit 20 1 R01 NS073603-01
Exhibit 21 1 R01 DK090549-01
Exhibit 24 1 R01 NS071101-01
Exhibit 25 1 R01 DK083977-01
Exhibit 26 1 R01 NS069651-01
Exhibit 27 1 R01 NS065824-01
Exhibit 28 1 R01 NS069937-01
Exhibit 30 U01 NS072045-01 2-2010
Exhibit 31 1 U01 NS072045-01A1
Exhibit 42 1R01NS064590-01

Papers:

Exhibit 4 Neurol Res, 33(2), 208-213, 2011
Exhibit 15 Neurol Res, 32(2), 209-214, 2010
Exhibit 41 Neurol Res, 33(2), 176-184, 2011
Exhibit 43 Neurol Res., 29, 375-381, 2007
Exhibit 44 Microvascular Res., 71, 197-204, 2006
Exhibit 46 Neurol. Res., 29, 348-355, 2007

III: SPECIFIC ALLEGATIONS OF RESEARCH MISCONDUCT

Allegation 1: The same image had been submitted as preliminary data in the R01 grant application (5R01NS064976, Fig. 8) and published in the 2011 paper (*Neurol Res.*, 33 (2), March 2011, pp. 208-213, Fig. 3), but representing different treatments. In the grant, the figure demonstrated that administration of an anti-calponin antibody was effective in reducing the extent of FJ labeling of neurons, while in the 2011 article the figure represented treatment with clazosentan.

Allegation 2: The same image had been submitted as preliminary data in the R01 grant application (5R01NS064976, Fig. 8) and published both in the 2010 article (*Neurol Res.* 32:209-214, 2010, Fig. 5c) and the 2011 paper (*Neurol Res.*, 33 (2), March 2011, pp. 208-213, Fig. 3). While the figure in the grant application and the 2011 paper represent the figures as TBI controls (in two different experiments), the 2010 article uses the figure to represent pre-treatment with BQ-788, resulting in an increase in FJ labeling.

Allegation 3: The same systolic blood pressure curve was included in the two publications (Fig. 4 in the *Neurol Res.* 32:209-214, 2010 paper and Fig. 2 in *Neurol Res.*, 33 (2), March 2011, pp. 208-213,) and as preliminary data for the R01 application (5R01NS064976, Fig. 13). These graphs are used to represent different experiments in the three documents.

Allegation 4: The respondent fabricated and/or falsified scientific data that were submitted in at least the following instances: (a) NIH grant proposals DK090549 Fig. 4; NS073603 Fig. 6; NS064976 Figs. 1, 5, 6, 7, 9 and 10; NS039860 Figs. 1 and 9; NS064976-01 Fig. 10; NS064976-01A1 Fig. 13; NS064976-01A2, Fig 13), published in at least the journal *Neurological Research* in 2010 (*Neurol Res.* 32:209-214, 2010; Figs. 2, 3 and 5) and 2011 (*Neurol Res.*, 33 (2), March 2011, pp. 208-213, Figs. 1 and 4) and (b) presented at, at least, four scientific meetings (see Winter Brain 2009 Poster-ETrA Antagonism, EtRA Poster VA 2009, VA Research Day 2010 Poster-ETrA Antagonism, World Congress poster (2010), in addition to the figures identified in the previous allegations.

Allegation 5: The respondent fabricated and/or falsified support documents submitted in at least the following (a) NIH R01 grant applications NS071101, DK083977, NS064976-01, NS069651-01, NS065824-01 NS069937 (see Kreipke Biographical Sketch, "Full Member of The Royal Society") and (b) NIH U01 grant applications (including U01 NS072045) (see Kreipke Biographical Sketch, "Full Member of The Royal Society") and Support Letter From Actelion.

Allegation 6: The respondent fabricated and/or falsified scientific data that were submitted in NIH grant proposals: 1 R01 NS064590-01 (Figs. 8), 1 R01 NS065824-01 (Figs. 1, 2, and 4) and published in at least: *Neurol Res.*, 33 (2), March 2011, pp. 176-186 (Fig. 6); *Microvasc Res.* 2006 May;71(3):197-204 (Fig. 4); and *Neurol Res.* 2007 Jun;29(4):348-55 (Fig. 2).

IV: INSTITUTIONAL POLICIES AND PROCEDURES

The WSU Policy 2010-01 was followed during the inquiry and investigation process. A copy of this policy was provided to ORI along with the Inquiry Report.

V: SUMMARY OF RESEARCH RECORDS AND EVIDENCE REVIEWED AND NOT REVIEWED

All of the material listed in this section was reviewed by the Investigation Committee. Because it would be impossible to review every file on the sequestered computer hard drives, searches were performed using key words.

The RIO sequestered the following materials before the Inquiry Committee met, and these materials were provided to the Investigation Committee:

- The hard drives from 5 computers found in the laboratory rooms/offices of the respondent were copied by the IT Department of the Office of the Vice President for Research.
- The hard drive from the laptop of the complainant was copied by the IT Department of the Office of the Vice President for Research.
- Ten (10) laboratory notebooks

The committee obtained copies of all the grant proposals as well as publications relating to the investigation.

As mentioned above, the inquiry report along with Dr. Kreipke's response was reviewed.

The VA Merit grant on which the respondent is the PI, was not reviewed by the Investigation Committee because the RIO at the VA had determined that no VA funding or resources were involved with the allegations.

The committee also interviewed the following witnesses, including the complainant and respondent:

- Christian Reynolds (complainant), Graduate Research Assistant, 05/27/2011 – Exhibit #63; 08/19/2011 – Exhibit #68
- Michael Fronczak, Research Assistant, 05/27/2011 – Exhibit #64
- Dr. Yuchuan Ding, Department of Neurosurgery, 06/14/2011 – Exhibit #65
- Steven Schafer, former Research Assistant, 07/08/2011 – Exhibit #66
- Dr. Zheng Gang Zhang, Senior Staff Investigator to the Department of Neurology, Henry Ford Hospital, 07/19/2011 – Exhibit #67
- Dr. Christian Kreipke (respondent), Assistant Professor, Department of Anatomy and Cell Biology, WSU School of Medicine 08/12/2011 – Exhibit #13
- Dr. Glen Kaatz, Director of Research and ACOS, John Dingel Veterans Administration Medical Center, August 15, Exhibit #50
- Dr. Linda Hazlett, Chair, Department of Anatomy and Cell Biology, WSU School of Medicine, August 19, 2011-Exhibit #49
- Justin Graves, Kreipke Laboratory Technician, Department of Anatomy and Cell Biology, WSU School of Medicine, August 23, 2011-Exhibit #48
- Anthony Kropinski, Kreipke Laboratory Technician, Department of Anatomy and Cell Biology, WSU School of Medicine, August 23, 2011-Exhibit #48
- Brandon Cantazaro, Potential MD/Ph.D. student, Department of Anatomy and Cell Biology, WSU School of Medicine, August 23, 2011-Exhibit #48

These interviews were recorded and transcribed by a court reporter. Relevant information from these interviews is described in the analysis section below. The full transcripts of the interviews are included with this draft report.

Allegation 1: The same image had been submitted as preliminary data in the R01 grant application (5R01NS064976, Fig. 8) and published in the 2011 paper (*Neurol Res.*, 33 (2), March 2011, pp. 208-213, Fig. 3), but representing different treatments. In the grant, the figure demonstrated that administration of an anti-calponin antibody was effective in reducing the extent of FJ labeling of neurons, while in the 2011 article the figure represented treatment with clazosentan.

Allegation 2: The same image had been submitted as preliminary data in the R01 grant application (5R01NS064976, Fig. 8) and published both in the 2010 article (*Neurol Res.* 32:209-214, 2010, Fig. 5c) and the 2011 paper (*Neurol Res.*, 33 (2), March 2011, pp. 208-213, Fig. 3). While the figure in the grant application and the 2011 paper represent the figures as TBI controls (in two different experiments), the 2010 article uses the figure to represent pre-treatment with BQ-788, resulting in an increase in FJ labeling.

Allegation 3: The same systolic blood pressure curve was included in the two publications (Fig. 4 in the *Neurol Res.* 32:209-214, 2010 paper and Fig. 2 in *Neurol Res.*, 33 (2), March 2011, pp. 208-213,) and as preliminary data for the R01 application (5R01NS064976, Fig. 13). These graphs are used to represent different experiments in the three documents.

Allegation 4: The respondent fabricated and/or falsified scientific data that were submitted in at least the following instances: (a) NIH grant proposals DK090549 Fig. 4; NS073603 Fig. 6; NS064976 Figs. 1, 5, 6, 7, 9 and 10; NS039860 Figs. 1 and 9; NS064976-01 Fig. 10; NS064976-01A1 Fig. 13; NS064976-01A2, Fig 13), published in at least the journal *Neurological Research* in 2010 (*Neurol Res.* 32:209-214, 2010; Figs. 2, 3 and 5) and 2011 (*Neurol Res.*, 33 (2), March 2011, pp. 208-213, Figs. 1 and 4) and (b) presented at, at least, four scientific meetings (see Winter Brain 2009 Poster-ETrA Antagonism, EtRA Poster VA 2009, VA Research Day 2010 Poster-ETrA Antagonism, World Congress poster (2010), in addition to the figures identified in the previous allegations.

Allegation 5: The respondent fabricated and/or falsified support documents submitted in at least the following (a) NIH R01 grant applications NS071101, DK083977, NS064976-01, NS069651-01, NS065824-01 NS069937 (see Kreipke Biographical Sketch, "Full Member of The Royal Society") and (b) NIH U01 grant applications (including U01 NS072045) (see Kreipke Biographical Sketch, "Full Member of The Royal Society") and Support Letter From Actelion.

Allegation 6: The respondent fabricated and/or falsified scientific data that were submitted in NIH grant proposals: 1 R01 NS064590-01 (Figs. 8), 1 R01 NS065824-01 (Figs. 1, 2, and 4) and published in at least: *Neurol Res.*, 33 (2), March 2011, pp. 176-186 (Fig. 6); *Microvasc Res.* 2006 May;71(3):197-204 (Fig. 4); and *Neurol Res.* 2007 Jun;29(4):348-55 (Fig. 2).

Allegation 1:

The same image was submitted as preliminary data in R01 grant application, 5R01NS064976 (Fig. 8), and published in *Neurol Res.*, 33 (2), March 2011, pp. 208-213, (Fig. 3), but representing different treatments. In the grant proposal, the figure was provided as evidence that administration of an anti-calponin antibody reduced the extent of fluorojade (FJ) labeling of neurons in rats subjected to traumatic brain injury (TBI), while in the 2011 article the same figure was provided as evidence that treatment with the drug clazosentan reduced the extent of FJ labeling of neurons in rats subjected to TBI.

Analysis: All publications, presentations, and NIH grant proposals with which the respondent was affiliated were examined to identify any additional instances where the figure in question was used. Image files from the laboratory computers and the respondent's computer were searched to identify files containing the image. The sequestered laboratory notebooks of the respondent were also examined in an effort to identify the experimental protocol used to prepare the animal, tissue and image. Each of the images was examined for evidence of intentional misrepresentation. Finally, based on these analyses, the committee considered whether the preponderance of the evidence suggested that the mislabeling of the figure was done deliberately by the Respondent or whether it could have been accidental.

A. Presence of the figure in grant proposals, publications and presentations.

NIH grant proposals: The image was used to represent the effects of *anti-calponin* antibody administration on the effects of TBI in two of the respondent's NIH grant proposals (Exhibit 1, 1R01NS064976-01A1 Fig. 8, "TBI + anti-Cp", and Exhibit 2, 1R01NS064976-01A2, Fig. 8-B, "TBI + anti-Cp") and in an NIH grant proposal in which Dr. Jose Rafols is the P.I. and the respondent is key personnel (Exhibit 3, 2R01NS039860-09A2, Fig. 8-B, "TBI + anti-Cp").

Publications: The image is used to represent the effects of *clazosentan* administration on the effects of TBI in one published paper in which the respondent is the corresponding author and which acknowledges "support from National Institutes of Health (no. NINDS NS064976) and a Department of Veterans Affairs Rehabilitation Research & Development Merit Award (no. RX000224) to Christian Kreipke." See Exhibit 4, *Neurol Res*, 33(2):208-213, 2011, Fig. 3.

Presentations: The image was used to represent the effects of *clazosentan* administration on the effects of TBI in at least four poster presentations from the respondent's laboratory in which NIH was acknowledged for support. See Exhibit 5 (Winter Brain 2009), Fig. 6; Exhibit 6 (VA Research Day 2009), Fig. 6; Exhibit 7 (VA Research Day 2010), Fig. 6 and Exhibit 8 (World Congress 2010), Fig. 5. NIH support cited for the research presented in Exhibits 5 and 6 is NS39860 (Dr. Jose Rafols, PI). Support cited for Exhibit 7 is NIH NS064976 (Dr. Christian Kreipke, PI), VA RX000224 (Dr. Christian Kreipke, PI) and NS39860 (Dr. Jose Rafols, P.I.).

B. *Primary data:*

Laboratory notebooks: None of the sequestered laboratory notebooks contained experimental protocols corresponding to the data described in these allegations. A section of laboratory notebook 3 contained experiments involving clazosentan but these experiments were not those under investigation.

Image files: A tiff file from which the figure in question was derived entitled “FJ Hipp 20x 48h TBI.tif” with a creation date of Oct. 31, 2008 was identified during an examination of the image files on the respondent’s computer (Exhibit 9). Increasing the exposure and contrast and rotating the tiff file image (see Exhibit 10) transformed the image shown in Exhibit 9 into the image shown in Exhibits 1-8.

A second tiff file containing the image, labeled TBI_anti Cp.tif, with a creation date of November 6, 2008 (Exhibit 11) was also identified on the respondent’s computer. This file is a composite of two FJ images that is identical to the anti-calponin antibody images in Exhibits 1-3.

Examination of the poster file, Winter_Brain_2009_Poster_-_ETrA_Antagonism.ppt (Exhibit 5), revealed that the label on Figure 6 (TBI + Clazo) was a text box that had been placed on top of the original label of the figure, TBI + anti-Cp (see Exhibit 12, Fig. 6). The labels in the corresponding figures in the other posters (Exhibits 6-8), were similarly altered.

Evidence of misconduct.

- A. Was the same image used in published papers, NIH grant proposals, and presentations to represent different experiments/treatments?

Allegation 1 claimed that a single micrograph was used to represent two different TBI treatment protocols. One treatment was with anti-calponin antibody and the other was with clazosentan. Subsequently, we identified several other instances where the same image was used to represent each of these treatments. In each instance, the image is identified as sensory-motor cortex (smCx) and the time of animal sacrifice from which the section was obtained following TBI varies from 4 hours to 48 hours, depending on the document in which the image is located.

The conclusion of the committee is that the same image was used in each of the instances cited in Allegation 1 to represent different experimental treatments and that the image also appeared in several other documents, as discussed above.

- B. Does the preponderance of the evidence suggest that the figures were falsified by the intentional, knowing, or reckless act of the respondent?

During our investigation, the committee identified what we believe is the original micrograph from which all of these figures were derived (Exhibit 9). When Dr. Kreipke

was asked to explain the label for the tiff file (Exhibit 9), he stated that the sample represented a FJ-stained section from the hippocampus of an animal that had been subjected to TBI but with *no treatment* and that the animal was sacrificed 48 hours post TBI (see Exhibit 13, pp. 25-33). This is consistent with the label on the tiff image file (FJ Hipp 20x 48h TBI.tif). Thus, in none of the instances where this image was used in publications, NIH grant submissions or presentations is it correctly attributed, because each of them identify the tissue source as smCx, the times at which the animals were sacrificed varies, and in each instance the slide is used to represent treatment with either clazosantan or anti-calponin antibody. Furthermore, in the instances where the label on the FJ image is TBI + Clazo in the upper left corner of the image (Exhibits 5-8), we determined that the TBI + Clazo label was created as a text box and then placed on top of the label TBI + anti-Cp in an effort to intentionally cover the original label (see Exhibit 12, Fig. 6).

The tiff file containing what appears to be the original micrograph (FJ HIpp 20x 48h TBI, Exhibit 9) was created on 10/31/08. The tiff file containing the two micrographs used in the grant proposals, publications, and presentations (TBI_anti Cp.tif, Exhibit 11) was created one week later, on 11/6/08. The first instance in which the image appeared in an official document was 11 days after that, in an NIH grant proposal submitted to the WSU Sponsored Programs Administration (SPA) by Dr. Kreipke on November 17, 2008 (1R01NS064976-01A1, Exhibit 1, Fig. 8). The same figure appears in the resubmission of this proposal on 3/13/09, 1R01NS064976-01A2 (Exhibit 2, Fig. 8-B). In these two grant proposals the image is labeled “TBI + anti-Cp”.

The earliest use of the textbox, “TBI + Clazo” to cover the “TBI + anti-Cp” label in Exhibit 5 is in a PowerPoint poster file labeled “Winter Brain 2009 Poster - ETrA Antagonism.ppt”, created on 1/14/2009. Nearly identical posters were presented in two VA conferences in 2009 (Exhibit 6) and 2010 (Exhibit 7) and a World Conference Poster in 2010 (Exhibit 8). In each of these posters, Dr. Kreipke was the first author and the original label was covered by the “TBI + Clazo” text box.

Kreipke et al. *Neurological Research*, 33(2):208-213,2011, (Exhibit 4, Fig. 3) also contains what appears to be the same over layered TBI + Clazo figure used in the posters but in Figure 3 the word “Clazo” is shifted to the second line. When the figure was copied from one of the posters and pasted into a Word document, we observed the same shift of “Clazo” to the second line, which occurs when the figure size is automatically reduced to fit in the Word document.

Exhibits 9, 11 and 1 were created within a period of three weeks in October and November of 2008. Thus, the composite tiff file image in which the original micrograph (Exhibit 9) is incorrectly labeled as “TBI + anti-Cp” was created six days after the original micrograph was created and submitted 11 days later in Dr. Kreipke’s NIH proposal where it was used to illustrate the effect of anti-calponin antibody treatment on neuronal damage following TBI (Exhibit 1, 1R01NS064976, Fig. 8). The earliest use of the “TBI + Clazo” text box to hide the label “TBI + anti-Cp” discovered by the investigation committee was in the PowerPoint poster file entitled “Winter Brain 2009

Poster - ETrA Antagonism.ppt” (Exhibit 5, Figure 6), which was created on January 14, 2009, two months after the Dr. Kreipke’s NIH proposal as submitted.

The members of the Investigation Committee find it highly unlikely that the original micrograph, which was labeled “TBI”, could have been mislabeled “TBI + anti-Cp” and submitted in an NIH grant proposal 17 days later, and then unintentionally used to illustrate the effects of clazosentan treatment on neuronal damage in TBI damaged animals by pasting a text box with “TBI + Clazo” on top of the already mislabeled “TBI + anti-Cp” label used in Dr. Kreipke’s NIH grant proposal.

In his testimony (Exhibit 13, pp. 18-19), and in his written response to the allegations (Exhibit 14, p. 1) provided to the Investigation Committee immediately before his interview on August 12, 2011, Dr. Kreipke states that the complainant, Christian Reynolds, was solely responsible for the 2011 *Neurological Research* paper (Exhibit 4) including the selection of all figures and suggests that Mr. Reynolds is therefore responsible for the misrepresentation described in Allegation 1. Given that the original figure and the majority of the subsequent misrepresentations of the figure occurred well before Mr. Reynolds joined the lab, the committee finds that this accusation by Dr. Kreipke is not credible.

Conclusions for Allegation 1: By a preponderance of the evidence, the Investigation Committee finds that the images in question were intentionally and knowingly misrepresented and mislabeled in NIH grant proposals, published papers and scientific presentations by the respondent, Dr. Christian Kreipke. These acts constitute falsification as described in the WSU Policy and Procedure Regarding Research Misconduct 2010-01 and 42 CFR Part 93.103.

Allegation 2:

The same image had been submitted as preliminary data in the R01 grant application (1R01NS064976, Fig. 8) and published both in the 2010 article (*Neurol Res.* 32:209-214, 2010, Fig. 5c) and the 2011 paper (*Neurol Res.*, 33(2):208-213, 2011, Fig. 3). While the image in the grant application and the 2011 paper is described as TBI controls (in two different experiments), the 2010 article uses the figure to represent pre-treatment with BQ-788, resulting in an increase in FJ labeling.

Analysis: All publications, presentations, and NIH grant proposals with which the respondent was affiliated were examined to identify any additional instances where the figure in question was used. Image files from the laboratory computers and the respondent’s computer were searched to identify files containing the image. The sequestered laboratory notebooks of the respondent were also examined in an effort to identify the experimental protocol used to prepare the animal, tissue and image. Each of the images was examined for evidence of intentional misrepresentation. Finally, based on these analyses, the committee asked whether the preponderance of the evidence suggested that the mislabeling of the figure was done deliberately by the Respondent or whether it could have been accidental.

A. *Presence of the figure in grant proposals, publications and presentations.*

NIH grant proposals: The image was used to represent the effects of “*only TBI*” in two of the respondent’s NIH grant proposals (Exhibit 1, 1R01NS064976-01A1, Fig. 8, and Exhibit 2, 1R01NS064976-01A2, Fig. 8-B) and in an NIH grant proposal in which Dr. Jose Rafols is the P.I. and the respondent is key personnel (Exhibit 3, 2R01NS039860-09A2, Fig. 8-B).

Publications: The image is used to represent the effects of *BQ-788* administration on the effects of TBI in *Neurol Res.* 32(2):209-214, 2010 (Exhibit 15, Fig. 5c), in which Dr. Jose Rafols is the corresponding author and which acknowledges “support from the National Institute of Health (grant no. NS039860).” The image is also used to represent “*TBI*” in *Neurol Res.*, 33(2):208-213, 2011, in which the respondent is the corresponding author and in which “support from National Institutes of Health (no. NINDS NS064976) and a Department of Veterans Affairs Rehabilitation Research & Development Merit Award (no. RX000224) to Christian Kreipke” is acknowledged (See Exhibit 4, Fig. 3).

Presentations: The image was used to represent the effects of “*only TBI*” in at least four poster presentations from the respondent’s laboratory in which NIH was acknowledged as support. See Exhibit 5 (World Congress 2009), Fig. 6; Exhibit 6 (VA Research Day 2009), Fig. 6; Exhibit 7 (VA Research Day 2010), Fig. 6 and Exhibit 8 (World Congress 2010), Fig. 5.

B. *Primary data:*

Laboratory notebooks: None of the sequestered laboratory notebooks contained experimental protocols corresponding to the data described in these allegations.

Image files: A tiff file from which the figure in question was derived, entitled “FJ 20X 48TBI Hipp n2 higher exposure.tif”, with a creation date of Oct. 31, 2008, was identified during an examination of the image files on the respondent’s computer (Exhibit 16). Increasing the exposure and contrast of the tiff image (see Exhibit 17) transformed the image shown in Exhibit 16 into the image shown in Exhibits 1-8, and 15.

The previously identified tiff file entitled *TBI_anti Cp.tif* with a creation date of November 6, 2008 (Exhibit 11) also contains this figure with the label “TBI”.

Examination of the poster file, *Winter_Brain_2009_Poster_-_ETrA_Antagonism.ppt* (Exhibit 5), revealed that the label on the left panel of Figure 6 (“TBI”) is a text file placed on top of the original label of the figure, which is also labeled “TBI” (see Exhibit 12). The labels in the corresponding figures in other posters, Exhibits 6-8, were similarly altered.

Evidence of misconduct.

- A. Was the same figure used in published papers, NIH grant proposals, and presentations incorrectly labeled?

Allegation 2 claimed that a single micrograph was used by the respondent to represent two different TBI experimental protocols. In *Neurol Res.* 32(2):209-214, 2010 the image is purported to represent the effects of BQ-788 administration following TBI (see Exhibit 15, Fig. 5c). In every other instance in which the image is used, the image represents the effect of TBI only. In each instance, the image is identified as sensory motor cortex (smCx) and the time of animal sacrifice from which the section was obtained following TBI varies from 4 hours to 48 hours, depending on the document in which the image is located.

The conclusion of the committee is that the same image was used in each of the instances cited in Allegation 2 to represent different experimental treatments and/or time courses and that the image also appeared in several other documents, as discussed above.

- B. Does the preponderance of the evidence suggest that the figures were falsified by intentional, knowing, or reckless acts of the Respondent?

During our investigation, the committee identified what we believe is the original micrograph from which all of these figures were derived (Exhibit 16). When Dr. Kreipke was asked to explain the file label on Exhibit 16 (FJ 20X 48TBI Hipp n2 higher exposure.tif), he stated that the sample represented a FJ stained section from the hippocampus of an animal that had been subjected to TBI but with no therapeutic treatment and that the animal was sacrificed 48 hours post TBI (see Exhibit 13, pp. 69-81). Thus, in none of the instances where this image was used in publications, NIH grant submissions or presentations is this image correctly attributed. Each of them incorrectly states that the tissue source is smCx, the times at which the animals were sacrificed varies, and in one instance the image is used to represent treatment with BQ-788.

The tiff file containing what appears to be the original micrograph (Exhibit 16, FJ 20X 48TBI Hipp n2 higher exposure.tif) was created on 10/31/08. The tiff file containing the two micrographs used in the grant proposals, publications and presentations (TBI_anti Cp.tif, Exhibit 11) was created seven days later, on 11/6/08. The first instance in which the image appeared in an official document was in an NIH grant proposal submitted to the WSU Sponsored Programs Administration (SPA) by Dr. Kreipke on November 17, 2008 (1R01NS064976-01A1, Exhibit 1, Fig. 8). The same figure appears in a resubmission of this proposal on 3/13/09, 1R01NS064976-01A2 (Exhibit 2, Fig 8-B). In these two grant proposals, the image is labeled "TBI". The *Neurol Res.* 32(2):209-214, 2010 paper where the image is used to represent BQ-788 (Exhibit 15, Fig. 5c), was published in March of 2010 and was therefore presumably submitted for publication less than a year after the grant proposal (Exhibit 2) was resubmitted.

The members of the Investigation Committee find it highly unlikely that the original 2008 tiff file (“FJ 20X 48TBI Hipp n2 higher exposure.tif”, Exhibit 16), located on Dr. Kreipke’s computer and clearly labeled as having been prepared from the hippocampus of an animal that was sacrificed 48 hours after TBI, could be accidentally attributed to smCx tissue in animals sacrificed at various times following TBI, within three weeks of its creation. Similarly, the members of the committee do not understand how the same image could then be accidentally mislabeled as BQ-788 and published a short time thereafter.

Conclusions for Allegation 2: By a preponderance of the evidence, the Investigation Committee finds that the image in question was misrepresented in NIH grant proposals, publications and presentations by intentional and knowing acts of the respondent and constitutes falsification as described in the WSU Policy and Procedure Regarding Research Misconduct 2010-01 and 42 CFR Part 93.103.

Allegation 3:

The same systolic blood pressure curve was included in two publications (Fig. 4 in the *Neurol Res.* 32:209-214, 2010 paper and Fig. 2 in *Neurol Res.*,33(2): 208-213, 2011) and as preliminary data for the R01 application (1R01NS064976, Fig. 13). These graphs are used to represent different experiments in the three documents.

Analysis: All publications, presentations, and NIH grant proposals with which the respondent was affiliated were examined to identify any additional instances where the figure in question was used. Excel and image files from the laboratory computers and the respondent’s computer were searched to identify files containing the source data for the figure and additional copies of the image. The sequestered laboratory notebooks of the respondent were also examined in an effort to identify the experimental protocol used to prepare the animal, tissue and image. Each of the images was examined for evidence of intentional misrepresentation. Finally, based on these analyses, the committee asked whether the preponderance of the evidence suggested that the mislabeling of the figure was done deliberately by the Respondent or whether it could have been accidental.

A. *Presence of the figure in grant proposals, publications and presentations.*

NIH grant proposals: The image was used to represent the effects of clazosentan injection on systolic blood pressure following TBI in the respondent’s 2008 NIH grant proposal (1R01NS064976-01, Exhibit 18, Fig. 10) and two resubmissions (Exhibit 1, 1R01NS064976-01A1, Fig. 13 and Exhibit 2, 1R01NS064976-01A2, Fig. 13).

Publications: The two panels of the image are used to represent the effects of *BQ-123* and *BQ-788* administration on the effects of “endothelin receptor A and B antagonism on cerebral hypoperfusion” following TBI in *Neurol Res.* 32(2):209-214, 2010 (Exhibit 15, Fig. 4), in which Dr. Jose Rafols is the corresponding author and which acknowledges “support from the National Institute of Health (grant no. NS039860).” The right (Exhibits 1, 2, and 18) or lower (Exhibit 15) panel of the figure is also used to represent the effects of clazosentan injection on systolic blood pressure when administered 30 minutes following TBI in *Neurol Res.*, 33(2):208-213,2011 (Exhibit 4, Fig. 2), in which

the respondent is the corresponding author and in which “support from National Institutes of Health (no. NINDS NS064976) and a Department of Veterans Affairs Rehabilitation Research & Development Merit Award (no. RX000224) to Christian Kreipke” is acknowledged.

Presentations: The right panel of the image was used to represent the effects of clazosentan injection on systolic blood pressure when administered 30 minutes following TBI in three posters in which NIH was acknowledged as providing financial support. See Exhibit 5, World Congress 2009, Fig. 4; Exhibit 6, VA Research Day 2009, Fig. 4; and VA Research Day 2010, Exhibit 7, Fig. 4.

B. *Primary data*:

Laboratory notebooks: The members of the committee were unable to identify experimental protocols corresponding to the data described in these allegations among the sequestered laboratory notebooks.

Data files: An Excel file containing the data points and the figures in question entitled “BQ-123 systolic blood pressure.xls” with a creation date of Jan. 6, 2009 was identified during an examination of files on the respondent’s computer (Exhibit 19). No other Excel files containing systolic blood pressure data were discovered.

Evidence of misconduct.

A. Was the same figure used in published papers, NIH grant proposals, and presentations incorrectly attributed?

Allegation 3 claimed that a single pair of systolic blood pressure curves was used to represent different experimental treatments in two published papers and in a grant proposal. In *Neurol Res.* 32(2):209-214, 2010 the figure is purported to represent the effects of *BQ-123* and *BQ-788* administration on the effects of “endothelin receptor A and B antagonism on cerebral hypoperfusion” (Exhibit 15, Fig. 4). The figure is also used to represent the effects of *clazosentan* injection on systolic blood pressure following TBI in *Neurol Res.*, 33(2):208-213, 2011 (Exhibit 4, Fig. 2) and in the respondent’s 2008 NIH grant proposal (1R01NS064976-01, Exhibit 18, Fig. 10) and two resubmissions (1R01NS064976-01A1, Exhibit 1, Fig. 13 and 1R01NS064976-01A2, Exhibit 2, Fig. 13). Three PowerPoint poster presentations were identified on the respondent’s computer that contain one of the systolic blood pressure panels in question, which were attributed to the effects of clazosentan treatment (Exhibit 5, World Congress 2009, Fig. 4; Exhibit 6, VA Research Day 2009, Fig. 4; and Exhibit 7, VA Research Day 2010, Fig. 4.)

The conclusion of the committee is that the same figure was used in each of the instances cited in Allegation 3 to represent different experimental treatments and that the image also appeared in several other documents, as discussed above.

- B. Does the preponderance of the evidence suggest that the figures/data were falsified by intentional, knowing, or reckless acts of the Respondent?

The earliest appearance of the graphs in question is in the respondent's initial submission of his NIH R01 proposal, 1R01NS064976 (Exhibit 18, figure 10) which was received by the WSU SPA on June 2, 2008 and the first and second resubmissions of the proposal (Exhibit 1, 1R01NS064976-01A1, Fig. 13 and Exhibit 2, 1R01NS064976-01A2, Fig. 13) were received by WSU SPA on November 17, 2008 and March 13, 2009, respectively. The Excel file containing the numerical data and the graphs (BQ-123 systolic blood pressure.xls, Exhibit 19) was created on Jan. 6, 2009. The paper in which the same graphs were used to represent BQ-123 and BQ-788 treatments for TBI was published in March 2010 (Exhibit 15, *Neurol Res.*, 32(2):209-214, 2010, Fig. 4) and the figure was published in another paper, in March of 2011 (Exhibit 4, *Neurol Res.*, 33(2):208-213, 2011, Fig. 2) in which it is purported to represent the effects of clazosentan treatment on systolic blood pressure. Thus, the data used to produce the systolic blood pressure figures attributed to clazosentan treatment in all three grant submissions were incorporated in an Excel file labeled BQ-123 that was created between the times of the second and third grant submissions, published one year later as the effects of BQ-123 and BQ-788 treatment and published again one year after that as the effects of clazosentan treatment on systolic blood pressure.

The members of the Investigation Committee find it highly unlikely that the graphs presented in three of Dr. Kreipke's grant proposals as clazosentan treatment could have been incorporated into an Excel spreadsheet and accidentally labeled BQ-123, then published as BQ-123 and BQ-788 treatments and then published again as clazosentan treatment all by accident or through carelessness.

Conclusions for Allegation 3: By a preponderance of the evidence, the Investigation Committee finds that the images and data in question were intentionally and knowingly misrepresented and mislabeled in NIH grant proposals, published papers and scientific presentations by the respondent, Dr. Christian Kreipke and constitute falsification and fabrication as described in the WSU Policy and Procedure Regarding Research Misconduct 2010-01 and 42 CFR Part 93.103.

Allegation 4:

The respondent fabricated and/or falsified scientific data that were submitted in at least the following instances: (a) NIH grant proposals DK090549 Fig. 4; NS073603 Fig. 6; NS064976 Figs. 1, 5, 6, 7, 9 and 10; NS039860 Figs. 1 and 9; NS064976-01 Fig. 10; NS064976-01A1 Fig. 13; NS064976-01A2, Fig 13), published in at least the journal *Neurological Research* in 2010 (*Neurol Res.* 32:209-214, 2010; Figs. 2, 3 and 5) and 2011 (*Neurol Res.*, 33 (2), March 2011, pp. 208-213, Figs. 1 and 4 and (b) presented in at least four scientific meetings (see Winter Brain 2009 Poster-ETrA Antagonism, ETrA Poster VA 2009, VA Research Day 2010 Poster-ETrA Antagonism, World Congress poster (2010), in addition to the figures identified in the previous allegations.¹

Analysis: All publications, presentations, and NIH grant proposals with which the respondent was affiliated were examined to identify any additional instances where the data in question were

used. Image and data files from the laboratory computers and the respondent's computer were searched to identify files containing the images or data used to construct the figures. The sequestered laboratory notebooks of the respondent were also examined in an effort to identify the experimental protocol used to prepare the animal, tissue and image. Each of the images and figures was examined for evidence of intentional misrepresentation. Finally, based on these analyses, the committee asked whether the preponderance of the evidence suggested that the mislabeling of the figure was done deliberately by the Respondent or whether it could have been accidental.

Allegation 4-1

In an NIH grant proposal, R01 NS073603-01, in which Dr. Jose Rafols is P.I. and Dr. Kreipke is listed as key personnel, the third panel of Figure 6 contains a FJ image purported to be smCx tissue from animals treated with clazosentan 30 minutes following TBI and sacrificed 24 hours post TBI. The same image occurs in other grant proposals, publications and posters by the respondent but it is labeled TBI + BQ123 and the times the animals were sacrificed post TBI varies.

A. Presence of the figure in grant proposals, publications and presentations.

NIH grant proposals: The image was used to represent the results of *clazosentan* administration on the effects of TBI in smCx from animals sacrificed 24 hours post TBI in NIH proposal 1R01NS073603-01 in which Dr. Jose Rafols is P.I. and Dr. Kreipke is listed as key personnel (Exhibit 20, Fig. 6, panel 3). The same image appears in three other NIH proposals where it is used to represent the effects of BQ-123 treatment on animals sacrificed four hours following TBI (Exhibit 21, 1R01DK090549-01, Fig. 4, Dr. Anders Adolph Fredrik Sima, P.I.; Exhibit 1, 1R01NS064976-01A1, Fig. 7, Dr. Christian Kreipke, P.I.; and Exhibit 2, 1R01NS064976-01A2, Fig. 7, Dr. Christian Kreipke, P.I.).

Publications: The image is used to represent the effects of BQ-123 administration on the effects of TBI in one published paper in which Dr. Rafols is the corresponding author and which acknowledges support from NIH (NS039860), (Exhibit 15, *Neurol Res*, 32(2):209-214, 2010, Fig. 5B).

Presentations: The image was used to represent the effects of BQ-123 administration on the effects of TBI in at least three poster presentations from the respondent's laboratory in which NIH was acknowledged as support (Exhibit 5, World Congress 2009, Fig. 3; Exhibit 6, VA Research Day 2009, Fig. 3; and Exhibit 7, VA Research Day 2010, Fig. 3).

B. Primary data:

Laboratory notebooks: The members of the committee were unable to identify experimental protocols corresponding to the data described in these allegations among the sequestered laboratory notebooks.

Image files: A tiff file from which the figure in question was derived, entitled "FJ SmCx 20x 24hr+BQ123 TBI.tif" with a creation date of Oct. 31, 2008, was identified during an

examination of the image files on the respondent's computer (Exhibit 22). Increasing the exposure and contrast of the tiff file image (see Exhibit 23) transformed the image shown in Exhibit 22 into the image present in the grant proposals, publications and presentations described above (Exhibits 1-2, 4-7).

Evidence of misconduct.

- A. Was the same figure used in published papers, NIH grant proposals, and presentations incorrectly labeled?

The allegation claims that the respondent used a single micrograph to represent two different TBI treatment protocols. One treatment was with BQ-123 and the other was with clazosentan. Subsequently, we identified several other instances where the same image was used to represent BQ-123. In each instance, the image is identified as sensory-motor cortex (smCx) and the time of animal sacrifice from which the section was obtained following TBI varies from 4 hours to 48 hours, depending on the document in which the image is located.

The conclusion of the committee is that the same image was used in each of the instances cited to represent different experimental treatments and that the image also appeared in several other documents, as discussed above.

- B. Does the preponderance of the evidence suggest that the figures were falsified by the intentional, knowing, or reckless act of the Respondent?

During our investigation, the committee also identified a tiff file that we believe is the original micrograph from which all of the figures were derived (Exhibit 22, FJ SmCx 20x 24hr+BQ123 TBI.tif). When Dr. Kreipke was asked to explain the label for the tiff file, he stated that the sample represented a FJ stained section of the sensorimotor cortex with a magnification of 20X obtained 24 hours post- BQ-123 treatment (see Exhibit 13, p. 92). This is consistent with the label on the tiff image file. Thus, the tissue type, and treatment appear to be correctly identified as smCx and BQ-123 in all of the instances in which the image is used with the exception of the image in Dr. Rafols' grant proposal, in which the image is used to represent treatment with clazosentan (Exhibit 20, 1R01NS073603-01, Fig. 6, panel 3). In each use of the images, however, the times at which the animals were purportedly sacrificed following TBI appear to be incorrect. The original tiff image is labeled "24 hrs" but in each of the instances where the figures were used, the sacrifice times are either 4 or 48 hours post TBI.

Conclusions: The image in question was incorrectly labeled and submitted in R01NS073603-01 in which Dr. Rafols is the P.I. and Dr. Kreipke is listed as key personnel (Exhibit 20, Fig. 6, panel 3). We repeatedly requested that Dr. Rafols meet with the committee to help clarify this and other questions regarding his interactions with Dr. Kreipke, but he never confirmed his attendance at any of the five dates and times offered to him. He did request that all of the committee's questions be submitted to him in written form so that he could answer all questions

posed to him in writing. The Investigation Committee declined his request in keeping with WSU Policy and Procedure Regarding Research Misconduct 2010-01:7.5.1c. As noted, in no instance is the time interval between TBI and sacrifice of the injured animals consistent with the label on the original tiff image; however, because the mislabeling of the image in the instances other than that in Dr. Rafols' grant involved only the times between TBI and sacrifice of the animal, we cannot exclude the possibility that this was due to what appears to be a worrisome lack of organization and record keeping in the space shared by Dr. Kreipke and Dr. Rafols.

Allegation 4-2

The same data were used to illustrate the effects of treatments with bosentan on TBI damaged animals in an NIH grant proposal (R01NS064976-01) and treatment with BQ-788 on TBI damaged animals in a scientific research article (*Neurol Res.* 32:209-214, 2010).

A. Presence of the figure in grant proposals, publications and presentations.

NIH grant proposal: In a 2008 NIH grant proposal 1R01NS064976-01 in which Dr. Kreipke is P.I., Figure 9 purportedly illustrates the "Effect of various doses of Bosentan on CBF in the smCx" (Exhibit 18, Fig. 9).

Publication: In *Neurol Res.*, 32(2):209-214, 2010, Figure 3A purportedly illustrates the effects of BQ-788 on CBF in smCx (Exhibit 15, Fig. 3A).

B. Primary data:

Laboratory notebooks and computer files: Examination of the sequestered laboratory notebooks for experimental protocols corresponding to the data described for this image and attempts to locate the data from which the figures were constructed were unsuccessful.

Evidence of misconduct.

A. Were the same data used to illustrate the effects of two different experimental treatments?

Analysis of the graphs in the two figures revealed that the data from which each of the graphs was constructed are identical, with the exception of the data set labeled "Pre-TBI" in Exhibit 15, *Neurol Res.*, 32(2):209-214, 2010, Fig. 3A. These data are not present in Exhibit 18, 1R01NS064976-01, Fig. 9.

The conclusion of the committee is that the same data were used in both of the instances cited to represent different experimental treatments.

B. Does the preponderance of the evidence suggest that the data were falsified by the intentional, knowing, or reckless act of the Respondent?

When presented with the evidence during his testimony, Dr. Kreipke did not deny that the data in the two figures are identical. Instead, he explained that BQ-788 and Bosentan

were different compounds but with similar mechanisms of action and that there would be no reason to suspect that either of the graphs were not what they were reported to be, because similar results would be expected from either treatment: “I do recognize though, that there's absolutely no reason why we would question either of the graphs. That is to say that BQ-788 we know from multiple, multiple times causes a no change in hypoperfusion as versus to TBI. BQ-788 doesn't either. So when we saw the printed out graph, we had no reason to question that that was the exact same graph.” (Exhibit 13, pp. 96-99).

When asked to clarify what the data in the two graphs actually represent Dr. Kreipke stated, “That particular graph, to my knowledge, actually represents the BQ-788” (see Exhibit 13, p. 99). The use of the data to represent BQ-788 occurred in Dr. Kreipke’s 2010 paper (Exhibit 15, *Neurol Res.*, 32(2):209-214, 2010, Fig. 3A) but the first use of these data was in 2008 in Dr. Kreipke’s NIH R01 application where it was used to represent treatment with Bosantan (Exhibit 18, 1R01NS064976-01, Fig. 9).

In considering the evidence, the members of the Investigation Committee find it highly unlikely that the graph used to illustrate the effects of Bosantan in 2008 might have been mistakenly constructed from data that actually represented BQ-788 treatment but correctly labeled as such in a paper published two years later, assuming that the original data were used to generate the figure in the paper. Similarly, if instead of the primary data, only the figure itself were used in writing the 2010 paper, the labels associated with the figure should have identified it as being from the first usage of the figure, in 2008 (Exhibit 18, 1R01NS064976-01, Fig. 9) in which it was used to illustrate the effects of Bosantan treatment on TBI.

Conclusions: By a preponderance of the evidence, the Investigation Committee finds that the images and data in question were intentionally and knowingly misrepresented and mislabeled in an NIH grant proposal and a published paper by the respondent, Dr. Christian Kreipke and constitutes falsification as described in the WSU Policy and Procedure Regarding Research Misconduct 2010-01 and 42 CFR Part 93.103.

Allegation 4-3

The same data were used to represent two different experimental protocols in NIH grant proposal and in a published paper.

A. Presence of the figure in grant proposals, publications and presentations.

NIH grant proposal: Figure 6 (left panel) in Dr. Kreipke’s NIH grant proposal, 1R01NS064976-01, purportedly shows the effect of BQ-123 treatment on cerebral blood flow (CBF) following TBI (Exhibit 18, Fig. 6). The protocol states that “CBF was measured in 4 rats (Pre) using ASL-MRI imaging. TBI was induced in the same animals 4 hours later. 1 hour following injury, the same animals were given an ICV injection of 40 nmol BQ-123, an ETrA antagonist. 4 hours after injury and again at 24 and 48 hours post injury animals were re-scanned for CBF.”

Publication: In *Neurol Res.* 32:209-214, 2010, Figure 2 also purportedly shows the effects of BQ-123 on CBF (Exhibit 15, Fig. 2). In this protocol, however, “MRI was used to detect CBF both before (pre-injection) and after injury (pre-TBI) in six rats given bilateral i.c.v. injections of 40 nmol BQ-123 (20 nmol per side), a selective ETrA antagonist, 24 hours before injury. CBF measurements were then repeated in the same animals at 4, 24 and 48 hours after impact.”

B. *Primary data:*

Laboratory notebooks and computer files: Examination of the sequestered laboratory notebooks for experimental protocols corresponding to the data described for this image and attempts to locate the data from which the figures were constructed were unsuccessful.

Evidence of misconduct.

A. Were the same data used to illustrate the effects of two different experimental protocols?

Analysis of the data points in the two figures revealed that the data used to generate the figures are identical with the exception of the points labeled “Pre-injection” in Exhibit 15, *Neurol Res.*, 32(2):209-214, 2010, Fig. 2. These data are not present in Exhibit 18, 1R01NS064976-01, Fig. 6.

The protocol described in the grant proposal involves *four* rats that received BQ-123 *one hour after TBI*. In the paper, however, *six* rats are used and they are injected with BQ-123 *24 hours before TBI*:

The conclusion of the committee is that the same data were used in both of the instances cited to represent different experimental treatments.

B. Does the preponderance of the evidence suggest that the data were falsified by the intentional, knowing, or reckless act of the Respondent?

Although the two protocols each describe the effects of BQ-123 treatment on CBF following TBI, they differ significantly in that in one protocol the BQ-123 is given *24 hours before* inducing TBI and in the other protocol BQ-123 is given *one hour after* TBI is induced. Furthermore, the paper was published in March of 2010, three months before Dr. Kreipke’s NIH grant was submitted to WSU SPA. The members of the Investigation Committee find it highly unlikely that the experiments described in the grant proposal, which was submitted after the paper was published, could have fewer animals, one less control (pre-injection), a different treatment protocol and yet produce identical data.

Conclusions: By a preponderance of the evidence, the Investigation Committee finds that the images and data in question were intentionally and knowingly misrepresented in NIH grant proposals, published papers and scientific presentations by the respondent, Dr. Christian Kreipke

and constitute falsification as described in the WSU Policy and Procedure Regarding Research Misconduct 2010-01 and 42 CFR Part 93.103.

Allegation 5:

The respondent fabricated and/or falsified support documents submitted in at least the following (a) NIH R01 grant applications NS071101, DK083977, NS064976-01, NS069651-01, NS065824-01 NS069937 (see Kreipke Biographical Sketch, “Full Member of The Royal Society”) and (b) NIH U01 grant applications (including U01 NS072045) (see Kreipke Biographical Sketch, “Full Member of The Royal Society” and Support Letter From Actelion).

Analysis: All publications, presentations, and NIH grant proposals with which the respondent was affiliated were examined to identify any additional instances where the documents in question or similar documents were used. Computer files from the laboratory computers and the respondent’s computer were searched to identify documents containing information regarding The Royal Society or Actelion. The files were examined and assessed for relevance to the allegations and, where appropriate, evidence of misrepresentation. Finally, based on these analyses, the committee asked whether the preponderance of the evidence suggested that documents were deliberately falsified or fabricated by the Respondent.

Allegation 5-1

During the investigation, members of the committee noticed that Dr. Kreipke reported that he was a Full Member of the Royal Society in most of his NIH biosketches submitted in support of grant proposals in which he is the P.I. or is listed as key personnel (see Exhibits 1, p. 14; 2, p. 14; 18, p. 14; 21, p. 18; 24, p. 17; 25, p. 21; 26, p. 21; 27, p. 15; 28, p 21; and 31, p. 14).

Evidence of misconduct.

- A. Do the NIH Biosketches in question inaccurately state that the respondent is a Full Member of The Royal Society?

Membership in the Royal Society: During his interview, Dr. Kreipke stated that he is a member of the Royal Society of Chemistry (RSC) and that the RSC is a subsidiary of The Royal Society. He also stated that he was asked to correct this during a recent grant review and that he subsequently submitted the correction with supplemental data (Exhibit 13, pp. 57-66 and Exhibit 14, p. 2).

The RSC is clearly not a subsidiary of The Royal Society. The investigation committee contacted the RSC who confirmed that they are not affiliated with The Royal Society. In addition, Dr. Kreipke did state that he was a member of *both* the Royal Society of Chemistry *and* the Royal Society on his 2010 official WSU Curriculum Vitae (CV) (Exhibit 32, p. 2) though he lists only membership in the Royal Society of Chemistry in his 2011 CV.

The conclusion of the committee is that the NIH biosketches in question incorrectly state that Dr. Kreipke is a Full Member of The Royal Society.

- B. Does the preponderance of the evidence suggest that the respondent fabricated and/or falsified material in his NIH Biosketches?

The respondent's claim that he did not understand the difference between the Royal Society of Chemistry and the Royal Society is worrisome. There are, however, little data, to support the allegation that he intentionally misrepresented his biographical information on his Biosketches, other than his 2010 WSU C.V. in which he reported his membership in both organizations.

Conclusions: There is insufficient evidence to support allegation 5-1 of intentional falsification of the material in the respondent's NIH Biosketches pertaining to his membership in The Royal Society.

Allegation 5-2

During the investigation, members of the committee encountered a PowerPoint document entitled "Letter from Actelion.ppt" among the files sequestered from Dr. Kreipke's computer. The document was created on January 12, 2010 and contained a letter of support, purportedly from Dr. Marc Iglarz, Pharmacology and Preclinical Development, Actelion Pharmaceuticals, Ltd (Exhibit 29). This letter was identical to the Actelion letters of support that were submitted with Dr. Kreipke's NIH applications, 1U01NS072045-01 (Exhibit 30, p. 69) and the resubmission, 1U01NS072045-01A1 (Exhibit 31, p. 83). Further examination of the PowerPoint document revealed that the letter was assembled by combining a text box containing the body of the letter, the Actelion letterhead, the Actelion footer and a signature that was digitally copied (scanned) from another document. The scanned Iglarz signature also contained the closing and the typed signature identification of the scanned letter. Two white boxes were created in PowerPoint and placed over the closing and signature identification of the scanned signature image in the PowerPoint document (see Exhibit 33).

Evidence of misconduct.

- A. Did the respondent fabricate and/or falsify the Actelion support letter submitted in his NIH U01 grant applications?

Immediately prior to his testimony before the investigation committee, Dr. Kreipke distributed a written response to the revised allegations stating, "I cannot respond to the unspecified accusation that the support letter from Actelion [is] somehow defective. I have no idea what is supposedly falsified or fabricated with respect to that letter" (Exhibit 14, p. 2).

After the committee showed Dr. Kreipke the Actelion PowerPoint document from his computer and explained why it appeared to have been fabricated from other documents, including what appeared to be a forged/scanned signature, Dr. Kreipke acknowledged that he did assemble the letter in PowerPoint (Exhibit 13, pp. 47-48). Dr. Kreipke explained that the letter originally provided by Marc

Iglarz contained the phrase "in your rat model of TBI," and because his research involves both mice and rats, Dr. Kreipke asked Actelion to change the letter (Exhibit 13, pp. 47-49). Dr. Kreipke stated that there was insufficient time for Actelion to change the letter before the submission deadline and that in a phone conversation with the Actelion legal department, he was instructed to change the word "rats" to "animals" (Exhibit 13, pp. 47-48). Because he was unable to change the word "rats" to "animals" in the original letter, Dr. Kreipke stated that he assembled the letter in PowerPoint and that the only difference between the original letter and the one submitted with the grant proposal was substitution of the word "animals" for "rats" (Exhibit 13, pp. 48-51).

The respondent's U01 proposal was first submitted on February 2, 2010 (Exhibit 30, U01NS072045-01) and resubmitted nine months later on November 3, 2010 (Exhibit 31, 1U01NS072045-01A1). Both proposals contained letters of support from Dr. Linda Hazlett, Dr. Dan Walz and Dr. Mark Iglarz of Actelion. For the November submission, the respondent obtained new letters of support from Drs. Hazlett and Walz, but he used the same letter from Dr. Iglarz in both submissions. If, as stated by the respondent (see Exhibit 13, pp 48-52), there was insufficient time to obtain a modified letter from Actelion for the first submission, it is difficult to understand why the letter used in the second submission, nine months later, was identical to the letter used in the first submission, especially when new letters of support from Drs. Hazlett and Walz were obtained during this nine-month period.

A letter was written to Dr. Marian Borovsky in the Actelion legal department by The WSU RIO at that time, Dr. Dorothy Nelson, asking Actelion to "verify whether the attached letter is the letter signed by Dr Iglarz" and whether Actelion instructed Dr. Kreipke to modify the Actelion support letter (see Exhibit 34). A copy of the support letter from the U01 applications (Exhibit 35) was included. An email response was received from Dr. Iglarz in which he stated "The letter attached is indeed the one I signed and corresponds to the language approved by Actelion. I recall we had a phone conversation with Dr. Kreipke regarding this letter as the main point to clarify was the status of existing safety + tox preclinical package (that is mentioned in the letter)" (see Exhibit 36). Because Dr. Iglarz' comments did not address the respondent's rationale for constructing the letter used in his grant proposal and appeared to be inconsistent with the statement of the respondent that "upon consultation with their [the Actelion] legal team, they said just change "rat" to "animals"" (see Exhibit 13, p. 47), the investigation committee requested clarification on these issues and a second letter was mailed to the Actelion legal department from WSU General Counsel asking for additional information regarding the construction of the letter in PowerPoint and confirmation that Actelion did in fact instruct Dr. Kreipke to alter their letter of support (see Exhibit 37). The second letter also contained the version of the support letter from the U01 proposals (Exhibit 35) as well as an illustration showing the deconstruction of the PowerPoint version of the letter (see Exhibit 33).

A response from Nathalie Gutenstein, Associate Director, Senior Legal Counsel, Actelion Pharmaceuticals, Ltd. was received on 10-26-11 (see Exhibit 38). In the letter, Ms. Gutenstein apologizes “..for Dr. Iglarz’s erroneous e-mail of 6 September 2011 to Dr. Nelson where he confirmed that the letter referring to “animal models” was the version signed by Actelion.” She also provided the original letter signed by Dr. Iglarz in which the use of clazosentan for rat studies is mentioned and she further explained that “...Dr. Iglarz seems to remember that there was a telephone conversation where Dr. Kreipke asked whether Actelion would agree if the study was done on animal models rather [than] only on rats as referred to in the letter and he was told that Actelion would not have a problem if animal models rather than rats were used.” Ms. Gutenstein also states that “The letter itself was never revised and reissued.”

By his own admission, Dr. Kreipke constructed the support letter contained in both of his U01 grant submissions.

B. Does the preponderance of the evidence suggest that the respondent fabricated and/or falsified support documents?

The Investigation Committee is concerned that Dr. Kreipke stated in his written response to the allegations “I cannot respond to the unspecified accusation that the support letter from Actelion [is] somehow defective. I have no idea what is supposedly falsified or fabricated with respect to that letter” (Exhibit 14, p. 2) and then, when presented with the evidence (Exhibit 33), admitted that he did assemble the letter but stated that he was advised to do so by the Actelion legal department (see Exhibit 13, pp. 47-48).

Dr. Kreipke stated that he believed the original letter from Actelion arrived as a pdf (see Exhibit 13, p. 56). This is consistent with his testimony that he was unable to easily modify the letter, though the Investigation Committee was unable to locate the “original letter” among the files sequestered from Dr. Kreipke’s computer. The Investigation Committee found it highly unlikely that the members of the legal department at Actelion would advise Dr. Kreipke to change the content of an official company letter of support instead of simply changing the letter themselves and emailing the letter to him (see Exhibit 13 pp. 48-49). During his interview, Dr. Kreipke stated that for the legal department to change the document it would have to undergo further review and that there was insufficient time for the review process, so the legal department simply advised him to make the changes himself (see Exhibit 13, p. 48). In addition, the evidence does not explain why an updated and properly signed letter was not obtained within the nine months prior to resubmission of the U01, when updated letters were obtained from others who submitted letters of support.

Through the RIO and WSU General Counsel, we asked the legal department at Actelion for clarification regarding the explanation provided by Dr. Kreipke, and

Dr. Iglarz responded that the letter in the grant is the one he signed and that he and the legal department had a phone conversation regarding “the status of existing safety + tox preclinical package.” As shown in Exhibit 33, the letter in the grant proposal could not have been the letter signed by Dr. Iglarz because it was constructed by Dr. Kreipke. In his testimony regarding the Actelion letter, Dr. Kreipke never mentioned the safety + tox issue (see Exhibit 13, pp. 45-57). In fact, in her response to our follow-up letter Ms. Gutenstein confirms that the support letter Dr. Kreipke included in his U01 applications is not the letter submitted or approved by Actelion and that the original letter was never revised or reissued by Actelion (see Exhibit 38).

Conclusions: By his own admission, Dr. Kreipke constructed the letter of support purportedly from Actelion. There are significant inconsistencies in the explanations offered by Dr. Kreipke for why he constructed the letter of support and submitted it in two NIH grant proposals as an authentic letter of support from Mark Iglarz at Actelion, Inc. Furthermore, the Associate Director of the Actelion Senior Legal Counsel states that the support letter Dr. Kreipke included in his U01 applications is not the letter submitted or approved by Actelion and that the original letter was never revised or reissued by Actelion (see Exhibit 38).

By a preponderance of the evidence, the Investigation Committee finds that the Actelion letter of support was intentionally and knowingly misrepresented in two (2) NIH grant proposals by the respondent, Dr. Christian Kreipke and constitutes falsification as described in the WSU Policy and Procedure Regarding Research Misconduct 2010-01 and 42 CFR Part 93.103.

Allegation 6:

The respondent fabricated and/or falsified scientific data that were submitted in NIH grant proposals: 1 R01 NS064590-01 (Figs. 8), 1 R01 NS065824-01 (Figs. 1, 2, and 4) and published in at least: *Neurol Res.*, 33 (2), March 2011, pp. 176-186 (Fig. 6); *Microvasc Res.* 2006 May;71(3):197-204 (Fig. 4); and *Neurol Res.* 2007 Jun;29(4):348-55 (Fig. 2).

Following completion of the initial draft of this report, additional material from the complainant was received in the form of an email and a PowerPoint presentation that he submitted as recently discovered additional examples of scientific misconduct (see Exhibits 39 and 40). The new material involves data that were published in scientific papers, submitted in NIH grant proposals and in Department of Veterans Affairs (VA) grant proposals. Because our investigation is limited to matters pertaining to NIH funding, we were unable to thoroughly evaluate any of the material purportedly from the VA grant proposals. The committee did, however, obtain copies of the NIH grant proposals and publications in question (See Exhibits 27 and 41-46) and examined the materials purported to be instances of scientific misconduct.

Allegation 6-1

The same image was used to represent three different protocols in two NIH grant proposals and a published paper.

A. *Presence of the image in grant proposals and publications.*

Slide 1 in the complainant's PowerPoint presentation shows three figures (see Exhibit 40, p.1). One figure is purportedly from a VA grant proposal in which the respondent is P.I. and will not be considered. The second is from a paper published in March of 2011, in which the respondent is an author (Exhibit 41, *Neurol Res*, 33(2):176-184, 2011, Fig. 6) and the other is from an NIH grant proposal submitted March 7, 2008 in which Dr. Paula Dore-Duffy is P.I. and the respondent is listed as key personnel (Exhibit 42, 1R01NS064590-01, Fig 8). Figure 6B in the paper purportedly shows "ETrB (B) protein expression by western analysis" from capillaries isolated from TBI animals at various times post-impact. Figure 8E in the grant proposal purportedly shows "Western analysis of VEGFR2 protein" following exercise preconditioning.

Slide 2 in the complainant's PowerPoint presentation shows two figures (see Exhibit 40, p. 2). One figure is purportedly from a VA grant proposal in which the respondent is the P.I. and will not be considered. The second is from an NIH grant proposal submitted October 1, 2008 in which the respondent is P.I. (Exhibit 27, 1R01NS065824-01, Fig. 1). In Figure 1 of the respondent's NIH grant proposal, an image purportedly of a western analysis showing the effects of mild exercise at various times prior to TBI on VEGF expression is presented (see Exhibit 27, Figure 1, VEGF, me + TBI).

In addition, the same western blot is present in the respondent's 2008 NIH proposal, 5R01NS064976-01A1, Fig. 2 and in his 2009 5R01NS064976-01A2, Fig. 2 where it purportedly shows the "Effect of TBI on ETrA and B expression" (see Exhibit 1, Fig. 2 and Exhibit 2, Fig. 2).

B. *Primary data:*

Laboratory notebooks and computer files: Examination of the sequestered laboratory notebooks for experimental protocols corresponding to the data described for this image and attempts to locate the data from which the figures were constructed were unsuccessful.

Evidence of misconduct.

- A. Was the same image used in two different NIH grants and a published paper to illustrate the results of three different experiments?

Analysis of the image in Figure 1 of Exhibit 27 (1R01NS065824-01) and the images in Exhibit 41 (*Neurol. Res*, 33(2):176-184, 2011, Fig. 6), Exhibit 1 (1R01NS064976-01A1, Fig. 2), Exhibit 2 (1R01NS064976-01A2, Fig. 2) and Exhibit 42, (1R01NS064590-01, Fig. 8) revealed that all five of the purported western blots are identical.

The conclusion of the committee is that the same image was used in at least five separate instances to represent three different proteins in three different experimental protocols.

- B. Does the preponderance of the evidence suggest that the data were falsified by the intentional, knowing or reckless act of the respondent?

The first two instances in which the western blot was used were in two separate NIH grant proposals submitted within two months of each other, in which Dr. Kreipke is the P.I. The first proposal, 1R01NS065824-01 (Exhibit 27, Fig. 1), was received by WSU SPA on October 1, 2008 and the second grant proposal, 1R01NS064976-01A1 (Exhibit 1, Fig. 2), was received by WSU SPA on November 17, 2008. The same figure also appeared seven months later in Dr. Dore-Duffy's NIH grant proposal 1R01NS064590-01 (Exhibit 42, Fig 8), in which Dr. Kreipke is listed as key personnel. The members of the Investigation Committee find it highly unlikely that the same western image could have been unintentionally used to represent three different proteins, in three different experiments, in three different grant proposals within such a short period of time. The committee was unable to ascertain what the figure actually represented in any of the grant proposals and similarly, in the 2011 paper (see Exhibit 41, *Neurol. Res.*, 33(2):176-184, 2011, Fig. 6).

Conclusions: By a preponderance of the evidence, the Investigation Committee finds that the images and data in question were intentionally and knowingly misrepresented in NIH grant proposals and a published paper by the respondent, Dr. Christian Kreipke and constitute falsification as described in the WSU Policy and Procedure Regarding Research Misconduct 2010-01 and 42 CFR Part 93.103.

Slide 3 in the complainant's PowerPoint presentation shows two figures (see Exhibit 40, p. 3). Here, the complainant compares a figure, purportedly from the respondent's VA grant proposal, to a similar figure presented in an NIH grant proposal submitted March 7, 2008 in which Dr. Paula Dore-Duffy is P.I. and the respondent is listed as key personnel (Exhibit 42, 1R01NS064590-01, Fig 11). Because proper evaluation of these images would require access to the VA grant proposal, the committee was unable to evaluate the material presented in slide 3.

Slide 4 in the complainant's PowerPoint presentation compares figures purportedly from two VA grant proposals, and an NIH grant proposal to a figure from a paper published in 2007 in which the respondent is an author (see Exhibit 43, *Neurol Res.*, 29:375-381, 2007, Fig. 2). Members of the committee searched for the image in question in the respondent's NIH grant proposals but were unable to locate it. Because the other instances of the image are purportedly in VA grant proposals, the committee was unable to evaluate the material presented in Slide 4 (Exhibit 40, p. 4).

Allegation 6-2

The same image was manipulated and used to represent two different experimental results in an NIH grant proposal and a published paper.

A. *Presence of the image in grant proposals and publications.*

Slide 5 in the complainant's PowerPoint presentation (see Exhibit 40, p. 5) compares a figure from an NIH grant proposal submitted October 1, 2008 in which the respondent is P.I. (Exhibit 27, 1R01NS065824-01, Fig 2C) to a figure purportedly from a paper published in 2007 (see Exhibit 43, *Neurol. Res.*, 29:375-381, 2007). During our investigation of this material, however, we discovered that the image in the grant proposal is not present in the 2007 paper (Exhibit 43) but is instead present in a paper published in 2006 in which the respondent is first author and Dr. Jose Rafols is corresponding author (see Exhibit 44, *Microvascular Res.*, 71:197-204, 2006, Fig. 4B).

B. *Primary data:*

Laboratory notebooks and computer files: Examination of the sequestered laboratory notebooks for experimental protocols corresponding to the data described for this image and attempts to locate the data from which the figures were constructed were unsuccessful.

Evidence of misconduct.

A. Was the same image used in an NIH grant proposal and a published paper to illustrate the results of two different experiments?

The complainant alleges that the black and white image in the 2006 publication and the color image in the 2008 grant proposal are identical but that one is rotated 180° with respect to the other. The committee isolated the images from the grant proposal and the paper and compared the inverted images (see Exhibit 45). The conclusion of the committee is that the two images are in fact the same image except that one has been rotated 180°. In the 2006 paper, the image in question purportedly represents *calponin immunoreactivity in endothelial cells prior to TBI* (see Exhibit 44, *Microvascular Res.*, 71:197-204, 2006, Fig. 4B), while in the respondent's NIH 2008 grant proposal, however, the same image purportedly represents *immunofluorescent labeling of lectin in the capillary bed of the smCx in animals subjected to strenuous exercise prior to TBI*, demonstrating that strenuous exercise prior to TBI decreases capillary density in the smCx (Exhibit 27, 1R01NS065824-01, Fig 2C).

The conclusion of the committee is that the same image was rotated and used to represent two different experimental protocols, treatments, and results.

B. Does the preponderance of the evidence suggest that the data were falsified and/or fabricated by the intentional, knowing or reckless act of the respondent?

The image in question was used first in Kreipke et al. (2006) (Exhibit 44, *Microvasc Res.*, 71:197-204, 2006) to represent *calponin* immunoreactivity and was used again approximately 18 months later in Dr. Kreipke's NIH grant proposal (Exhibit 27,

1R01NS065824-01, Fig 2C) to represent *lectin* immunoreactivity. The members of the Investigation Committee find it highly unlikely that the same image could have been unintentionally rotated 180° and used to represent two different experimental results within 18 months.

Conclusions: By a preponderance of the evidence, the Investigation Committee finds that the images in question were intentionally and knowingly misrepresented in the NIH grant proposal and a published paper by the respondent, Dr. Christian Kreipke and constitute falsification as described in the WSU Policy and Procedure Regarding Research Misconduct 2010-01 and 42 CFR Part 93.103.

Allegation 6-3

The same series of six images was used to represent two different experimental results in an NIH grant proposal and a published paper.

A. Presence of the image in grant proposals and publications.

Slide 6 in the complainant's PowerPoint presentation (see Exhibit 40, p. 6) compares figures from two VA grant proposals, an NIH grant proposal submitted October 1, 2008 in which the respondent is P.I. (Exhibit 27, 1R01NS065824-01, Fig 4) and a figure from a paper published in 2007 in which the respondent is last author and the corresponding author is Dr. Jose Rafols (Exhibit 46, *Neurol. Res.*, 29:348-355, 2007, Fig. 2). The committee was unable to evaluate the images purportedly from the VA grant proposals. The image in the published paper and the respondent's NIH grant proposal, however, were analyzed.

B. Primary data:

Laboratory notebooks and computer files: Examination of the sequestered laboratory notebooks for experimental protocols corresponding to the data described for this image and attempts to locate the data from which the figures were constructed were unsuccessful.

Evidence of misconduct.

- A. Was the same series of images used in an NIH grant proposal and a published paper to illustrate the results of two different experiments?

In the 2007 published paper (Exhibit 46, *Neurol. Res.*, 29:348-355, 2007, Fig 2), the image purportedly of "Fluoro-Jade (FJ) stained cross-sections through the upper layers of the sensorimotor cortex below the impact from brains of sham-operated (A), 15 minutes (B), 4 (C), 24 (D) and 48 hours (E and F) after TBI". In the respondent's 2008 NIH grant proposal, however, the same image is used to illustrate the effects of mild and strenuous exercise prior to TBI on FJ staining of smCx tissue (Exhibit 27, 1R01NS065824-01, Fig 4). Thus, the figure in the paper was used to illustrate neuronal damage, as indicated by FJ staining, at various times following TBI and the

identical figure was used in the respondent's grant proposal the following year to illustrate the effects of exercise prior to TBI on neuronal damage.

The conclusion of the committee is that the same image was used to illustrate two different experimental protocols, treatments and experimental results.

- B. Does the preponderance of the evidence suggest that the data were falsified and/or fabricated by the intentional, knowing or reckless act of the respondent?

The images in question were used first in Rafols et al. (Exhibit 46, *Neurol. Res.*, 29:348-355, 2007, Fig. 2) to represent *neuronal damage at various times following TBI* and were used again approximately 17 months later as preliminary data in Dr. Kreipke's NIH grant proposal, (Exhibit 27, 1R01NS065824-01, Fig 4) to represent *the effects of exercise on neuronal damage following TBI* showing that "forced strenuous activity led to exacerbation of neuronal injury and, thus, supports our hypothesis that strenuous activity prior to TBI leads to poorer outcome." The respondent further states "If our hypothesis is correct (which is supported by preliminary data), we would be able to make suggestions as to how to develop safer training paradigms for both military and athletes which would include either daily mild exercise or, in the case of more rigorous sports or military training, a day of rest before "hitting the field". This would ultimately provide a no-cost alternative to help protect against the deleterious effects of head trauma."

Conclusions: By a preponderance of the evidence, the Investigation Committee finds that the images in question were intentionally and knowingly misrepresented in the NIH grant proposal and a published paper by the respondent, Dr. Christian Kreipke and constitute falsification as described in the WSU Policy and Procedure Regarding Research Misconduct 2010-01 and 42 CFR Part 93.103.

Response to Allegation 6: Dr. Kreipke's response to Allegation 6 (Exhibit 47) stated "It was noted previously that some figures were mistakenly inserted into the grant in question, likely due to the chaotic situation that we were facing with the abrupt change of PI, the unfortunate termination of my previous mentor during the time that this grant was submitted and to the similarity of the findings to other findings in our laboratory." The western blot discussed in Allegation 6-1 was used to represent three different proteins, in three different experiments in three different grant proposals within approximately 10 months. The Investigation Committee does not find Dr. Kreipke's explanation credible.

Respondent's witness list.

The respondent also provided a list of six witnesses to be called in his defense. The committee interviewed all of the witnesses listed on Dr. Kreipke's list with the exception of Dr. Rafols.

- 1. Professor Jose Rafols, Ph.D.** In his written statement, the respondent stated that Dr. Rafols would "...testify that all data and all experiments conducted in our laboratory are reviewed in lab meetings by ALL lab personnel. Dr. Rafols will also testify that all

experiments are conducted by multiple personnel in the laboratory so as to avoid a single member of the laboratory from having sole determining power of an experiment's outcome (e.g., due to the time intensity of behavioral investigations, in many cases up to 10 different people collect data for one experiment). He will testify that he participates directly in many of our histological experiments as well as in the interpretation of all data. He will testify that he directed the laboratory until Dr. Christian Kreipke assumed the role of PI in October of 2009". The committee repeatedly requested that Dr. Rafols meet with the committee but he never confirmed his attendance at any of the five dates and times offered to him. He did request that all of the committee's questions be submitted to him in written form so that he could answer all questions posed to him in writing. The committee, in consultation with WSU's Office of General Counsel, declined his request because the WSU Policy clearly requires interviews with witnesses.

2. **Anthony Kropinski (laboratory technician).** In his written statement, the respondent stated that Mr. Kropinski would "testify to the fact that the accuser, Christian Reynolds, has made multiple threats (including graphic death threats and malicious harm) against the laboratory and Dr. Kreipke. He will testify to the fact that the accuser, did not follow lab protocol, did not properly document data, had access to all data, and attempted to manipulate data on several occasions" (see Exhibit 14, p. 3). The committee asked Mr. Kropinski about the threats and his responses are located in Exhibit 48 on pages 51-59. Mr. Kropinski also discussed Mr. Reynolds' adherence to laboratory protocols and his handling of data (see Exhibit 48, pp. 71-73). Mr. Kropinski's statements regarding Mr. Reynold's manipulation of data are addressed in Exhibit 48, pp. 74-75.
3. **Justin Graves (laboratory technician).** In his written statement, the respondent stated that Mr. Graves would testify that "Dr. Dorothy Nelson stated in his presence that she is acting as the "prosecutor" in my misconduct case. He will testify that in his presence Dr. Nelson stated that she would not sequester Dr. Rafols' computer (despite its having data on it of relevance to the inquiry) because she did, "not want to disrupt a tenured member of the faculty". He will testify also that the accuser threatened, within his hearing, the laboratory and Dr. Kreipke personally. He will also testify to the fact that Christian Reynolds often did not follow required protocols when conducting experiments" (see Exhibit 14, p. 3). The committee asked Mr. Graves about Dr. Nelson's purported statement that she was acting as a prosecutor. His response is located on page 19 of Exhibit 48. Mr. Graves response when asked about Dr. Nelson's refusal to sequester Dr. Rafols' computer may be found on pages 19 and 20 of Exhibit 48. Mr. Graves' testimony regarding Mr. Reynolds' purported threats to Dr. Kreipke and to the laboratory is on pages 21-24 of Exhibit 48.
4. **Brandon Cantazaro (potential MD/PhD student).** In his written statement, the respondent stated that Mr. Cantazaro would testify "that Christian Reynolds and an individual (Michael Fronczak) who was fired from my laboratory in November 2010, were seen in my office on February 6, 2011 (two days before the scientific misconduct charges were filed) working on my computer" (see Exhibit 14, p. 3). The committee asked Mr. Cantazaro if he had seen Mr. Reynolds in Dr. Kreipke's office working on his computer. Mr. Cantazaro's response is on pages 99-100 of Exhibit 48.

5. **Dr. Linda Hazlett, Ph.D. (chair of department):** In his written statement, the respondent stated that Dr. Hazlett “will testify to the fact that she tried to seek explanations about my case, as she was told she could, from Dorothy Nelson, but was either ignored or subsequently was told not to have any involvement. She will further testify that she tried to locate some of the grants in question but could not, which supports the contention that that they are not mine nor anyone's in the department”. The committee asked Dr. Hazlett about her interactions with Dr. Nelson and Dr. Hazlett’s response is on pages 2-7 of Exhibit 49. Dr. Hazlett was also asked about her inability to locate the grant proposals in question and her response is on pages 14-18 of Exhibit 49.

6. **Dr. Glenn Kaatz, MD (Director of Research, VA):** In his written statement, the respondent stated “Dr. Kaatz will testify that he conducted a thorough investigation which included testimony from some of the witnesses listed above, and including Christian Reynolds, and concluded that there was no evidence of scientific misconduct. His report has been forwarded through VA channels to Washington. Further, he will testify that he talked to Dr. Nelson to inform her of the results of the VA investigation and of the testimony by witnesses who informed him of the graphic threats made by Christian Reynolds against me. He was informed that the Office of Vice President for Research had no interest in the VA investigation and would proceed with their own investigation”. The committee interviewed Dr. Kaatz and he addressed the issues raised by Dr. Kreipke throughout his testimony (see Exhibit 50).

Concluding remarks

Corrections to the scientific record.

The Investigation Committee was formed to investigate a complaint lodged by Mr. Christian Reynolds, a former graduate student in Dr. Kreipke’s laboratory in which he claimed that Dr. Kreipke had misrepresented figures and data published in a special edition of the journal *Neurological Research*. During the course of our investigation, several additional instances of misrepresentation were discovered involving at least five published manuscripts, 14 NIH grant proposals and numerous public presentations that extended our investigation beyond the special edition of *Neurological Research* for which Dr. Kreipke and Dr. Rafols served as editors (see Exhibit 13, p. 143).

Dr. Kreipke worked for Dr. Jose Rafols as a Research Assistant (Postdoc) from November 22, 2004 until November 14, 2008. He was appointed Assistant Professor (Research) on November 15, 2008 and then to a tenure-track Assistant Professor in the Department of Anatomy and Cell Biology on November 30, 2009. The earliest instances of misrepresented data identified during our investigation were in a paper published in 2006 and the others occurred when Dr. Kreipke was a Postdoc in Dr. Rafols’ lab and when he was an Assistant Professor (Research).

In his written response to the revised allegations 1-3 Dr. Kreipke states that the incorrect figures were inadvertently used because of their similarity to the correct ones and that the correct figures

had been located and submitted to the journal editor who accepted them as a “minor mistake that was corrected” (see Exhibit 14, p. 1). During his interview, Dr. Kreipke identified the editors to whom the corrections were submitted as Dr. Jose Rafols, his postdoc mentor and collaborator, and the managing editor, Ben Roitberg (see Exhibit 13, p. 19). Dr. Kreipke provided the replacement figures that were submitted to the editors in his written response to the revised allegations (see Exhibit 14, pp. 8-10). The Investigation Committee requested that the RIO obtain copies of the original replacement figures and supporting data. On August 22, 2011, the RIO requested that Dr. Kreipke provide the committee with the original files from which the replacement figures were obtained including tiff files, data files with figures, including the file names, creation dates, and where the replacement files are stored electronically and/or in laboratory notebooks. The RIO informed Dr. Kreipke that representatives from the Research Compliance office would collect these data from his laboratory/office.

On August 29, 2011 Dr. Kreipke emailed one (1) of the replacement tiff files entitled “Clazo 24 h 10X smCx2 n1.tif” (see Exhibit 51). Dr. Kreipke was subsequently reminded that the Research Committee had requested all of the primary data for the material submitted as replacement data in his response to the allegations and to the journal editors. Dr. Kreipke responded on September 7, 2011, that the material would be available for pickup the following day, September 8, 2011.

On September 8, 2011, Dorinda Monson, Associate Director, RCR and John McBride, Associate Director, Research-IT retrieved a copy of the tiff file that Dr. Kreipke emailed on August 29, 2011 (Exhibit 51). When Ms. Monson asked Dr. Kreipke if he had any other documents or files that he wanted to give to the Investigation Committee he replied that he did not. Thus, of the data Dr. Kreipke submitted as replacement figures to correct the errors in his publications (see Exhibit 14, pp. 8-10) to date, the Investigation Committee has only received a single tiff file from Dr. Kreipke (Exhibit 51) and a statement that “The correct notebook which references when the animals were generated to ultimately generate this figure is the one pertaining to Clazo and Mino treatments (page 1).” with no supporting information indicating its authenticity.

The committee was unable to locate the replacement file, Clazo 24 h 10X smCx2 n1.tif, among the files sequestered from Dr. Kreipke’s computer. We were, however, able to locate a file entitled “BQ123 24 h 10X smCx2 n1.tif” with the creation date of October 30, 2008 among the sequestered files containing an image that is identical to the image in the Clazo 24 h 10X smCx2 n1.tif file that Dr. Kreipke submitted as a replacement (see Exhibit 52).

This suggests that the respondent changed the title of the “BQ123 24 h 10X smCx2 n1.tif” file, which apparently shows the effect of BQ123 treatment on FJ staining of neurons, to Clazo 24 h 10X smCx2 n1.tif and then submitted the file to the journal and to the Investigation Committee claiming the image shows the effects of clazosentan on FJ staining of neurons.

Actions recommended for published papers containing fabricated and/or falsified material.

The earliest instance of misconduct discovered by the Investigation Committee occurred in 2006 and the most recent instance involving purported corrections to published papers occurred in September, 2011. The Investigation Committee therefore considers it highly unlikely that any data provided by Dr. Kreipke to correct the fabricated and/or falsified data identified in this

report can be independently verified and validated. The Investigation Committee therefore recommends that the following papers be retracted:

Kreipke CW, Rafols JA, Reynolds CA, Schafer S, Marinica A, Bedford C, Fronczak M, Kuhn D, Armstead WM (2011). Clazosentan, a novel endothelin A antagonist, improves cerebral blood flow and behavior after traumatic brain injury. *Neurol Res.* **33**(2):208-13.

Dore-Duffy P, Wang S, Mehedi A, Katyshev V, Cleary K, Tapper A, Reynolds C, Ding Y, Zhan P, Rafols J, Kreipke CW. (2011). Pericyte-mediated vasoconstriction underlies TBI-induced hypoperfusion. *Neurol Res.* **33**(2):176-86.

Kreipke CW, Schafer PC, Rossi NF, Rafols JA (2011). Differential effects of endothelin receptor A and B antagonism on cerebral hypoperfusion following traumatic brain injury. *Neurol Res.* **32**(2):209-14.

Rafols JA, Morgan R, Kallakuri S, Kreipke CW (2007). Extent of nerve cell injury in Marmarou's model compared to other brain trauma models. *Neurol Res.* **29**(4):348-55.

Kreipke CW, Morgan NC, Petrov T, Rafols JA (2006). Calponin and caldesmon cellular domains in reacting microvessels following traumatic brain injury. *Microvasc Res.* **71**(3):197-204.

Analysis of additional letters of support.

The Investigation Committee also requested confirmation of the authenticity of nine support letters submitted by Dr. Kreipke in his grant proposals (see Exhibits 53-61). The RIO wrote to each of the purported authors asking for confirmation of the content and signature of each of the letters (see Exhibit 62). Each of the purported authors responded except Dr. Smith, who according his secretary, was traveling and inaccessible.

The others all reported that the letters were authentic with the exception of Susan Margulies, Professor of Bioengineering, School of Engineering and Applied Science, Department of Engineering, University of Pennsylvania who in her response (see Exhibit 63) states:

- “1. I have checked my electronic records, and find no record of being asked to submit any letter for the revised (early Nov 2010) grant submission.
 2. The signature on the attached letter is not mine.
 3. I was asked to write a letter of support in August 2011, and have attached it. You will notice the wording is identical. Note that the signature is not.
 4. I have no similar letter on my computer with an October 27, 2010 date.
- I cannot verify the signature or accuracy of the letter you sent me.”

The support letter in Dr. Kreipke's U01 application purportedly from Dr. Margulies (Exhibit 31, p. 87) is addressed to Dr. William Armstead, Ph.D., Research Professor, Department of Anesthesiology and Critical Care, University of Pennsylvania. In a follow-up phone call on October 27, 2011, the WSU RIO spoke with Dr. Margulies who stated that in August of 2011 she was sent the text for a letter of support from Dr. William Armstead and that the text matched the text in the letter in Dr. Kreipke's 2010 U01 proposal. She also explained that she copied the text from Dr. Armstead into her letterhead and applied her electronic signature.

There is no letterhead on the October 27, 2010 support letter purportedly from Dr. Margulies in Dr. Kreipke's U01 application (see Exhibit 31, p. 87) and Dr. Margulies clearly states that the signature is not hers and that she has no record of having written that letter. The fact that Dr. Margulies received a request for a support letter from Dr. Armstead containing text that is identical to the letter submitted with Dr. Kreipke's U01 application raises concern about the authenticity and validity of this support letter. Both of the individuals mentioned in this particular letter, however, are at the University of Pennsylvania. Thus, further investigation into this issue would be beyond the purview of the WSU Investigation Committee and no further inquiries were made.

Response to Dr. Kreipke's comments on the Draft Investigation Report

The committee received Dr. Kreipke's comments on the Draft Investigation Report on November 29, 2011 (See Exhibit 69). The response is in three parts.

In Part I, Dr. Kreipke expresses concerns about the process followed by the Investigation Committee leading to the findings of misconduct in several of the allegations. A major focus of Part I is the potential for conflict of interest (COI). Dr. Kreipke expresses concern that the Investigation Committee outside member, Dr. Margot LaPointe, Vice President for Research, Henry Ford Hospital, was conflicted because she is an adjunct professor in the Department of Physiology at the WSU School of Medicine and the complainant, Mr. Christian Reynolds, joined one of the laboratories in that department as a Ph.D. student during the investigation. While it is true that Mr. Reynolds did transfer to a laboratory in the Department of Physiology, this occurred sometime during the investigation and none of the members of the Investigation Committee were aware of it. In addition, Dr. LaPointe has never attended a Physiology Department function (e.g., faculty meeting, seminar, committee membership) since her appointment in Nov. 2003. Though Dr. Zhang does work at Henry Ford Hospital, Dr. LaPointe is not involved in his research and has never been on any of his grant proposals. He was interviewed to provide specific scientific expertise on neuronal imaging, an area in which he is highly qualified. A COI form was signed by all of the members of the Investigation Committee at the beginning of the investigation (see Exhibit 70) and the RIO, Dr. Dorothy Nelson, polled the committee before each of the interviews to determine if a COI existed. No COIs were identified.

Dr. Kreipke also expresses concern that the committee ignored testimony about his integrity. While several of the witnesses made comments, both positive and negative regarding Dr. Kreipke's integrity, the Investigation Committee restricted its focus to clearly demonstrable scientific analysis of the allegations. This was the case both during deliberations and when writing the Investigation Report. Thus, the Investigation Committee chose not to address any of the personal comments regarding Dr. Kreipke or any of the others involved in the investigation.

Several references to Dr. Katz' testimony are made in Dr. Kreipke's comments. Dr. Katz conducted a separate investigation on allegations involving funding from the Department of Veterans Affairs Rehabilitation Research & Development and he was called as a witness at Dr. Kreipke's request. During his testimony Dr. Katz read parts of his report containing statements from several of the individuals he interviewed and he read parts of the report containing his conclusions. As noted by Dr. Kreipke, one of the individuals cited by Dr. Katz was Dr. Kreipke's mentor, Dr. Jose Rafols. Because the items discussed by Dr. Katz involved a separate investigation, were second hand and were not gathered by the committee and because his conclusions were based on evidence not reviewed by the Investigation Committee, the members of the Investigation Committee chose not to discuss Dr. Katz' testimony in our report, though his testimony was included along with all of the others who were willing to be interviewed. As noted in our report, we did invite Dr. Rafols to meet with the committee but he would only agree to respond in writing to written questions.

In Part II, Dr. Kreipke addresses specific issues raised by the allegations. Dr. Kreipke claims that in virtually every instance, the purported misconduct is due to errors in labeling,

bookkeeping, and organization. He also asserts that the erroneous data present in his papers and grant proposals do not alter the validity of the results or their interpretation. Throughout his interview, Dr. Kreipke stated that the instances cited in the allegations were due to errors and were not intentional and that the findings of the studies would not be significantly different had the correct data been used. The Investigation Committee addresses these claims in the Investigation Report and we do not feel that further comment is necessary.

Dr. Kreipke also requests that none of his papers be retracted because two of the manuscripts have already been corrected and the others contain the correct data. As we noted in our report, because the data supplied to us as errata also appeared to have been “misabeled” and because the data in the other papers were used in multiple documents to represent different experiments, we have no way of confirming the authenticity of the data in the original papers or the “corrected” ones.

In Part III, Dr. Kreipke reiterates his concerns in Parts I and II, regarding the Katz testimony, record keeping, labeling errors and stresses again that the conclusions of the papers and grant proposals would not have been significantly different had the correct data been used.

In addition, Dr. Kreipke expresses confusion regarding our statement in the Investigation Report that the pattern of misconduct goes back to at least 2006. This statement was based on our analysis of Kreipke CW, Morgan NC, Petrov T, Rafols JA (2006). Calponin and caldesmon cellular domains in reacting microvessels following traumatic brain injury. *Microvasc Res.* 71(3):197-204. See Allegation 6.

In summary, we disagree with Dr. Kreipke’s allegations that members of the committee were conflicted and, we stand by the analyses and conclusions described in our report.