UNITED STATES DISTRICT COURT
DISTRICT OF MINNESOTA

IN RE NATIONAL HOCKEY LEAGUE
PLAYERS’ CONCUSSION INJURY
LITIGATION

MDL No. 14-2551

AFFIDAVIT OF ANN C. MCKEE, M.D.

Ann C. McKee, M.D., being duly sworn, deposes and states that:

1. I am a Professor of Neurology and Pathology at Boston University School of Medicine (BUSM), Associate Director of the Boston University Alzheimer’s Disease Center (BU ADC) and Director of the Neuropathology Core of the BU ADC. In addition, I am the Director of the CTE Center for the BU ADC and the Director of the CTE Center’s Brain Bank (VA-BU-CLF brain bank), a collaborative project involving the United States Department of Veteran’s Affairs (VA), the University, and the Concussion Legacy Foundation (CLF), formerly the Sports Legacy Institute (SLI).

2. I am a board-certified neurologist and neuropathologist and the principal investigator on several ongoing and completed research projects investigating the progressive neurodegenerative disease, Chronic Traumatic Encephalopathy (CTE). My curriculum vitae is appended as Exhibit A.

BU ADC, CTE Center and VA-BU-CLF Brain Bank
3. Boston University’s Alzheimer’s Disease Center was established in 1996 as one of 29 centers funded by the National Institutes of Health to advance research on Alzheimer’s disease and related conditions. The BU ADC, through its CTE Center, also supports high-impact, innovative research on CTE and other long-term consequences of repetitive brain trauma in athletes and military personnel.

4. The CTE Center was founded in 2008 under a collaboration with the non-profit Sports Legacy Institute (currently, Concussion Legacy Foundation). This formal collaboration ended in 2014, and the CTE Center is now an independent Boston University academic research center whose mission is to conduct state-of-the-art research on CTE, including its neuropathology and pathogenesis, clinical presentation, genetics and other risk factors, biomarkers, methods of detection during life, and methods of prevention and treatment.

5. As part of the CTE Center, the Brain Bank was created in 2008 at the Edith Nourse Rogers Memorial Veterans Hospital in Bedford, Massachusetts (“VA Hospital”) in collaboration with the VA. The purpose of the VA-BU-CLF Brain Bank is to collect and study post-mortem human brain and spinal cord tissue to better understand the effects of trauma on the human nervous system. Donated tissue is stored in the VA-BU-CLF Brain Bank for use in studies conducted at the CTE Center as well as for studies conducted by or in collaboration with other research laboratories around the world.

6. Research discoveries made by the CTE Center are published in a variety of peer-reviewed publications and have been widely cited by scientific leaders throughout the world. Many organizations, including the National Football League and the National Football League Players Association, have voiced support for CTE Center research and have encouraged athletes to participate when possible.
Background on Chronic Traumatic Encephalopathy Research

7. Chronic Traumatic Encephalopathy (CTE) was first reported in 1928 by Harrison Martland, a New Jersey pathologist. Martland described the clinical aspects of a progressive neurological deterioration that occurred after repetitive brain trauma in boxers. He referred to this condition as “punch drunk,” but other terms were introduced over the decades that followed, including “traumatic progressive encephalopathy” and “dementia pugilistica.” By the 1940s, the term “chronic traumatic encephalopathy” was used, recognizing that the condition could arise from brain trauma of a variety of sources in both men and women. CTE has been clinically associated with symptoms of irritability, impulsivity, aggression, depression, short term memory loss and heightened suicidality. These associated symptoms typically appear 8-10 years following reported accounts of repetitive mild traumatic brain injury.

8. Currently, we understand that CTE is a neurodegeneration characterized by the abnormal accumulation of hyperphosphorylated tau protein (p-tau) within the brain. Tau proteins are proteins that stabilize microtubules. They are abundant in neurons of the central nervous system. When tau becomes hyperphosphorylated, it forms neurofibrillary tangles (NFT), causing it to aggregate, or group, in an insoluble form. This insoluble accumulation interferes with normal neuronal function and can lead to cell death. In early stages of the disease, NFTs appear to be clustered in distinct locations of the brain and, as CTE becomes more advanced, widespread brain regions become affected. This allows progressive staging of pathology and correlation of pathology findings with reported clinical symptoms. Like many other neurodegenerative conditions, CTE, at present, can only be definitively diagnosed by post-mortem examination of brain tissue, although significant efforts are
underway to improve clinicians’ ability to use available diagnostic tools to evaluate for the presence of early to late stage CTE during life.

9. In March 2013, the National Institutes of Health (NIH), supported by the Foundation for NIH’s Sports Health Research Program with funding from the National Football League, launched an effort to define the neuropathological characteristics of CTE. One of the initial projects was to convene two consensus meetings of expert neuropathologists to define, as a group, the neuropathological criteria for the diagnosis of CTE, and to distinguish it from pathologies of other neurodegenerative diseases associated with tau protein aggregation (known as “tauopathies”), including Alzheimer’s Disease. This panel of expert neuropathologists met in 2015 and 2016. Using digitized images of 11 cases of CTE from the BU CTE Center brain bank, they found that the p-tau pathology of CTE is unique and can be easily distinguished from other tauopathies.

10. According to the NIH consensus panel, the defining lesion of CTE or its pathognomonic lesion, consists of an accumulation of abnormal tau in neurons and astroglia distributed around small blood vessels at the depths of sulci in the cortex of the brain in an irregular pattern. Supportive features of CTE were also identified and defined. 1 The panel noted that, thus far, CTE has only been found in individuals who were exposed to brain trauma, typically multiple episodes. The consensus panel’s determinations validated the preliminary diagnostic criteria reported by McKee et al (2013) and confirmed the criteria

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1 Supportive features include abnormal p-tau immunoreactive pretangles and NFTs preferentially affecting superficial layers, pretangles, NFTs or extracellular tangles primarily in CA2 and CA4 of the hippocampus, NFTs in subcortical nuclei, including the mamillary bodies and other hypothalamic nuclei, amygdala, nucleus accumbens, thalamus, midbrain tegmentum, isodendritic core, p-tau immunoreactive thorned astrocytes at the glial limitans in the subpial and periventricular regions, p-tau immunoreactive large grain-like and dot-like structures, and TDP-43 immunoreactive neuronal cytoplasmic inclusions and dot-like structures in the hippocampus, anterior medial temporal cortex and amygdala.
always used by the CTE Center for the diagnosis of CTE when evaluating its donor brain tissue.

11. A second NIH consensus panel met in 2016 and evaluated the digital slides of 29 cases of CTE from the BU CTE Center. The second panel confirmed the original panel’s findings, and further characterized the staging of pathological severity.

12. In addition to the consensus panel’s determinations, the CTE Center has been actively conducting research on the clinical presentation and symptoms of CTE, the risks associated with playing contact sports, the risks of beginning to play sports at a young age, genetic modifiers of the disease, co-morbidities, and its pathological progression. The BU CTE Center has been remarkably productive (more than 60 peer-reviewed manuscripts since 2008). Nonetheless, there are numerous questions still left to be answered. The uninterrupted progression of ongoing work by the CTE Center and the VA-BU-CLF Brain Bank is critical to finding these answers particularly because these answers impact public health for athletes as well as military veterans.

Research Participant Recruitment, Brain Donation and Confidentiality

13. As Director of the CTE Center and Director of the VA-BU-CLF Brain Bank, I manage the brain donation program. I am also currently the principal investigator on a U01 project funded by NINDS and the National Institute of Biomedical Imaging and Bioengineering (NIBIB), entitled “Understanding Neurologic Injury and Traumatic Encephalopathy” (UNITE). UNITE examines the neuropathology and clinical presentation of brain donors who, based on prior athletic or military exposure, are designated as at risk for the development of CTE.
14. I oversee the process of subject recruitment and brain donation. For a majority of brain donors, the subjects’ next of kin or legally authorized representative (LAR) contact the Brain Bank and agree to donate. While living, some study subjects agree to donate their brain and spinal cord after death. But the next of kin or LAR is still asked to consent to the donation at death, and is assured that the donor’s name will not be disclosed, and that no personally identifiable information will be used or disclosed. This statement is also included on the CTE Center website. In addition, consent forms executed by living participants in UNITE, and required by the University’s Institutional Review Board (which evaluates human subject and other research pursuant to federal regulatory requirements), promise confidentiality and prohibit the sharing of a participant’s identifiable information with third parties.

15. Next of kin and LARs frequently express their concern, and anxiety, about the confidentiality of the information that might be uncovered as part of the CTE Center’s research. Family members often tell us that they do not want the deceased donor’s identity being uncovered, either directly or through deduction. This is particularly true with regard to personal information disclosed as part of a clinical interview(s) with the donor prior to death or with his/her family after death. Family members and donors understand that such information, if disclosed, will allow for third party identification by deduction. This information includes, but is not limited to, an individual’s status as a professional athlete, the number of years he/she played, the position he/she played as part of sports, major medical events, the experiences he/she had earlier in life and other biographical data specific to a particular donor. (Other families and donors allow us to publicly announce our research results, but we do not make such public statements without express authorization to do so.)
16. My colleagues in the CTE Center and I have taken great care to preserve participant and donor confidentiality. My research depends on the trust that the donors, and their families, place in us. It is an incredible privilege to be entrusted with another individual’s brain, and to be given an accurate glimpse of their life and the personal moments, some of which were quite difficult, that were a part of it. Our promise of absolute privacy and confidentiality is critical to preserving this trust. If potential donors and their families fear that they will become embroiled in litigation or that their reputations, or those of their deceased loved ones, might be harmed if their identities become known as part of litigation, we could not successfully continue the VA-BU-CLF Brain Bank or the Brain Registry. As a result, much of my work, including all our work on CTE and finding answers to the critical questions surrounding athlete and veteran safety, would be threatened.

Brain Specimen Preparation and Deidentification

17. Gathering the primary research materials responsive to the NHL Subpoena, and conducting the necessary deidentification process, for just the research I oversee alone, poses not only an insurmountable burden, but also is impractical. Compliance becomes virtually impossible when we consider all of the CTE-related research conducted by faculty and scientists affiliated with the CTE Center. A third party could not reduce this burden or conduct any of the necessary steps on our behalf, because the consents we currently have in place strictly limit access of private, confidential information to Boston University researchers. While consents do allow for third party researchers to be provided with access to samples for the advancement of research, education, science or therapy, this consent is limited to the provision of samples on a deidentified basis only. In addition, the materials are housed at the VA Hospital under an agreement with Boston University. The VA Hospital
is a HIPPA-covered health care facility and third party access, even if restricted to the research space, raises significant additional confidentiality concerns unrelated to the Brain Bank itself.

18. While confidentiality is one important reason that third party offers to “share this burden” are untenable, the other is that the volume of information, the fragility of many of the items at issue and their importance to ongoing and future research cannot be overstated. Moreover, I take my role as steward of the research materials under my control seriously, along with my promises to preserve anonymity, and, accordingly, would have to participate and review every piece of information that left my laboratory to ensure that it complies with the protections we have put into place to preserve the trust of our donors.

19. To better understand what is being asked of the CTE Center, the VA-BU-CLF brain bank protocol is appended as Exhibit B. The brain bank contains approximately 400 brains from donors. The protocol calls for the production of approximately ~172,000 gross photographs of each brain and spinal cord. Each of the individual photographs contain, within the image, a marker designating the autopsy number of the donor. The autopsy number is considered a patient identifier, and under no circumstances are we allowed to give out the autopsy number of a subject. HIPAA regulations state that we must eliminate the autopsy number and replace it with a de-identified “pincode” that cannot be traced back to any specific patient before we give out any materials. To eliminate the autopsy number from each individual photograph would require approximately 10 minutes per photograph; assuming a “de-identification” rate of six photographs per hour, this process would take more than 28,600 hours, or, assuming a 40-hour work week, in excess of 13 years. In addition, the protocol produces approximately ~120,000 photomicrographs of stained slides of the brain and spinal cord of donors, which also contain identifiers. The preceding time line assumes a
third party has the technical expertise necessary to perform these tasks; if not, even more
time will be needed to complete the de-identification process. The process of merely locating
nearly 400,000 photographs and digital photographs, gathering them into secure boxes or
copying them onto CDs to give to a third party would require an estimated additional 4 hours
per brain donor.

20. Under the protocol, we also have 264,000 glass microscopy slides and 40,000
large landscape glass slides containing sections from the brain donors. I estimate that
locating and packaging these glass slides for transport would require a minimum of 4000
hours. Because these glass slides hold human tissue, the transfer to a third party would also
require authorization. Most donors have consented to the transfer of donated tissue samples
to third parties only if the sample is de-identified. As a rule, brain banks do not give out their
primary data, that is, the actual glass slides that were produced by the brain bank laboratory,
as that would risk losing their primary data forever. Primary data must remain under the
jurisdiction of the original research lab. Transfer of other tissue samples to other laboratories
is done if it is for the advancement of research, education, science or therapy and if the
researcher requesting the samples is a NIH-funded investigator with approved research
credentials. Moreover, as the attached protocol shows, the preparation of the glass slides
represents significant time and resources. The slides are fragile and carry significant risk of
breakage with packaging and transport. If lost or damaged, the slides cannot be replaced and
critical source material from individual donors could be lost forever.

21. The process of de-identifying and removing the primary research materials
from the VA facility would be highly disruptive to both my laboratory and to the VA facility
itself. In practical terms it would shut down my research. It would require untold people-
power, which I do not have access to, and around the clock effort, likely made by scientists
and research colleagues whose time would be much better spent towards advancing important research questions and discovery. And the concerns I have described do not even factor in the time it would take to de-identify the clinical reports conducted by and under the direction of my colleague Dr. Robert Stern, who discusses that topic in detail in his affidavit.

22. Most critically, the removal of the research materials requested by the NHL Subpoena prevents their usage in ongoing and future research endeavors. This includes not only my research, but also the research of my colleagues and my collaborators around the world that rely on the work we do as part of larger collaborative studies. The ripple effect of inaccessibility of such data, even if time limited, is unfathomable.

23. Following all this effort toward de-identification, we would ultimately be left with slides, photographs and largely redacted reports that contain little to no information linking the neuropathological findings to biographical information of an individual. For example, I would expect one could not even discern from redacted reports whether data are associated with professional hockey players, professional football players or with an individual that never played a sport in his/her life given the high profile nature of any donor’s professional status. Scientifically, I have difficulty understanding what new information either party to the NHL Players’ Litigation would glean from such materials.

*Heightened Importance of Preserving Integrity of Sensitive Research*

24. Scientific debate and discussion are critical to research advancement. Hypotheses get challenged, methodologies critiqued and, through this, outputs get improved and built on. The aim of all of our CTE-related research is to publish our findings. Publication is an essential prerequisite to professional advancement, future funding opportunities and the reputational success of any scientist. More importantly, publication
allows for sharing information with the public at large and with peers all over the world who can use it to advance their own research program or, as the case may be, to challenge its underlying interpretations. Methodologies are shared to allow third-party replication. The CTE Center occasionally approves the sharing of brain tissue with other researchers, on a deidentified basis, conditioned on its utilization to further scientific research.

25. Prior to submission of an article reporting on original research, however, scientists often crowdsource their ideas and analyses in private correspondence—through laboratory meetings, hallway discussions, the exchange of results and drafts and, at times, through active debate. The NHL Subpoena’s invasive demand for all CTE-related pre-publication discussions, including with peer reviewers retained by journals, threatens the foundation on which science thrives. BU’s lawyers have told me that the NHL, in its legal brief, has narrowed that request only to “published publications,” but that does not really minimize the scope of this invasive request. If individuals worry that any scientific discussion, question or edit made to a draft article could be picked apart at a later date by a litigant to serve its own needs, open and frank discussion becomes vulnerable. Science cannot thrive under the cloud of such uncertainty. It will diminish the quality, pace and breadth of our work and will negatively impact the entire field of study.

26. For CTE-related research, as for any scientific question that directly impacts large, multi-billion dollar industries, the stakes of preventing this “chilling” effect are even higher. It could discourage new talent from entering the field or experts from asking questions and providing unvarnished scientific answers. The science would inevitably slow, due to the disruptive effect of the litigation and the reduction in those willing to risk being dragged into it. This could discourage the influx of new talent, new sponsors and new donors. This would be detrimental to society at large, as additional knowledge of the science
of CTE can only benefit the individuals, institutions and industries impacted by its devastating effects.

27. All major scientific journals subject their articles to a robust, largely effective, review by scientific experts in the field in question prior to publication. This process is confidential to ensure that scientific reviewers can speak freely with a unifying goal of improving the scientific output. Similar to my preceding comments regarding the chilling effects of producing private scientific communications, production of peer reviewer comments on pre-publication manuscripts could also undercut the integrity of the research enterprise. Without question, this will negatively impact the quality of the work produced, the willingness of scientists (who volunteer for this role) to serve as peer reviewers and the trust the public has in an enterprise that we all rely on to advance medical knowledge.

Response to NHL Position

28. I have read Dr. Rudy Castellani’s affidavit, submitted with the NHL’s Memorandum of Law in Support of its Motion to Compel Production. In paragraph 12, Dr. Castellani states that “most publications depict microscopic pathology deemed “representative . . . in support of the case and the hypothesis,” and that he would like access to copies of gross pathology photographs, all brain slides, and clinical data so he can “verify the accuracy of the reports, evaluate for other pathological processes that may be significant, and conduct a full, independent neuropathological analysis of the cases.” This is not the way science works or should work. First, as I hope the foregoing paragraphs have demonstrated, I am required to submit representative images by the journals given the enormous volume of data we generate in support of our conclusions. Almost all manuscripts, in any field, do so. Second, if I provide the thousands of slides and images I maintain to every researcher who
doesn’t understand or, for whatever reason, doesn’t believe in my scientific conclusions or has a belief that he/she could ‘do the science better’, there would be no ability for my lab to actually conduct studies that progress science. Instead, my papers go through a rigorous scientific review by scientific experts in the field prior to their publication. I respond to any questions they may have and, as necessary, provide supplemental data and materials to verify to these experts every conclusion reached. It is apparent that Dr. Castellani, who is well-known in the field for his belief that there is no link between concussions and CTE, wants to undermine my peer-reviewed, accepted research conclusions.

29. Notwithstanding my frustration with the implications, I would not object to providing Dr. Castellani with the material he describes in paragraph 13 of his affidavit with respect to the late Lawrence Zeidel. My research colleague examined Mr. Zeidel’s brain and made a pathological diagnosis of CTE. I am confident that any neuropathologist who reviews the data with a neutral view will reach the same conclusion. I understand and acknowledge that Mr. Zeidel’s Estate is a participant in this lawsuit, and for that reason, his case takes on added significance. His Estate has authorized the CTE Center to disclose certain information which has already been provided to the NHL’s lawyers. However, for the reasons I have described in this affidavit, I strenuously object to providing the NHL, Dr. Castellani, or any researcher, information on any other research subject whose family has not consented to the intrusive disclosure sought by the NHL. And, for the reasons I have described in this affidavit, I urge the Court to consider the devastating impact that the open-ended legal discovery the NHL seeks will have on the future of my research.

Conclusion

30. The work of the CTE Center and of my scientific collaborators around the
world has produced significant new information about the effects of repetitive concussive and subconcussive impact on an individual’s long term health. As discussed in the preceding paragraphs, two separate NINDS sponsored consensus panels of expert neuropathologists concluded that CTE is a distinct disease with defined pathological criteria for diagnosis. They reached this conclusion after reviewing pathology slides from 40 cases of CTE from the BU CTE center. The existence of CTE is not a question for debate. The consensus findings, and those in the published literature, have been of tremendous importance to not only professional athletes, but also to child athletes and members of the military and to those tasked with their care. There remains, however, much research and discovery to be made to further advance the CTE discussion. I fear the impact of an intrusive and over-reaching subpoena, possibly aimed at undermining this entire field of discovery, on the integrity of these future research efforts on this critical topic and, in turn, on any area of research that might impact well-resourced and well-organized litigants. I, along with members of my laboratory, respectfully ask this Court to prevent this very real risk from being realized.

Further affiant sayeth not.

Subscribed and sworn under the penalties of perjury.

Ann McKee, M.D.

Date: February 3, 2017