February 27, 2018.

Honorable Henry Kerner
Special Counsel
U.S. Office of Special Counsel
1730 M Street, NW, Suite 300
Washington, DC 20036

RE: OSC File No. DI-16-1945/DI-17-1294.

Dear Special Counsel Kerner,

I am writing this letter in response to an investigation mandated by the OSC to the OMI into allegations by myself and other whistleblowers. I will be commenting on the alleged violations of Human Research Practices [Allegation 1] perpetrated by Dr. [redacted] Chief of GI, facilitated by Drs. [redacted] VA CO, and [redacted] VA ACOS of Research, and covered-up by the entire administrative leadership here at the VA San Diego Healthcare System.

Allegation 1: **summarized and interpreted by the OMI were:**

1. The Chief of GI was performing unapproved human liver research, without informed consent, that places patients at serious risk.
2. The Chief of GI is not properly advising patients of their options, thereby delaying proper care.

My extensive comments below will prove that Allegation 1 is correct and the human research as practiced in this instance "…**are a substantial danger to Veterans and public health at the Veterans Affairs San Diego Healthcare System (VASDHS)."**

I will not be commenting on Allegations 2 and 3, additional malpractice outside the scope of this IRB research project, nor other violations of VA administrative practice as those allegations are outside my area of knowledge and will be covered in detail by the letters from other whistleblowers.

Role of Whistleblowers

It needs to be stated at the beginning of this discussion that every single investigation carried out by any federal agency is ultimately initiated by a whistle blower of some kind. Without the courage and ethical stamina of these individuals, the system would not be subjected to any investigations nor would it be improved through said investigations. Without these investigations, the abuse of the system and the victimization will continue unchecked.

These whistleblowers without exception know that they will suffer both personal and professional repercussions. The system that they are defending will actively and directly seek their destruction. They know that there is nothing self-serving nor anything to be gained by their actions other than the satisfaction of knowing that they are no longer part of the abuse, by standing by and letting it continue unchecked.

These individuals are in general, more concerned with the protection of individual human rights than they are careful of the success of the institution or the happiness of the leadership of said institution. They distain lying, cover-ups and unethical behavior. Indeed, many of them can get overtly angry when they encounter abuse where there is victimization. In what they see as the pursuit of their personal and professional obligations, whistleblowing, serves their conscience. These individuals are rare and while they may be

brave, their courage is not unlimited. Many of them have suffered tremendous repercussions in the pursuit of what they believe is right.

Reprisals

Every whistle blower in this case has suffered persecution. I have had my research space at the affiliate institution (UCSD) removed, suffered harassing phone calls from Dr. [redacted] the Chair of Medicine at UCSD, and a staff physician at the VA, and had my research grants expelled from the Veterans Medical Research Foundation (VMRF) due to local and subjective, unique policy enforcement of the 208. This resulted in extreme research delays and major losses of funding which continues to plague me personally and professionally. The chronic harassment from the VA Research leadership has affected not only my professional resources, but has also affected my health and family, which have suffered tremendously.

Of note after Ms. [redacted] Director of the VMRF, under the direction of Dr. [redacted] ACOS of Research expelled all our funded research from the VA, Dr. [redacted] informed me in the hallway after meeting with myself and Dr. [redacted] about our expulsion, that he "didn't really understand the 208, but that he would need to read up on it to explain it to the IRB committee". So, by his own admission at the time that he forced our expulsion from the VMRF he had "no real understanding of what the 208 entailed". But, the 208 is the policy he cited to kick us out, cost us our funding, and create hardship that is still being felt today.

Dr. [redacted] another whistleblower in this case, has had unique and subjective audits of his VA performance after two decades of outstanding evaluations, been professionally shunned and secretly investigated at the affiliate institution by Dr. [redacted] the Chair of the UCSD Department of Medicine and a staff physician at the VA, and has been forced to tolerate constant harassment and denial of his patients to standards of care by the Chief of his division at the VA, Dr. [redacted]

Another whistle blower in this case, Ms. [redacted] a female disabled Veteran administrative staff after being forced to testify to what she knew about patient standard of care, HIPAA, and other VA compliance violations, was forced by Dr. [redacted] Director, to resign after over a decade of outstanding evaluations and service.

Of course, there are federal laws against whistle blower violations but unless those laws are respected and enforced, which in this case they have not been, they are essentially useless.

Ours unfortunately is not a new scenario for the VA System. A Hearing before the Subcommittee on **Oversight and Investigation of the Committee on Veterans' Affairs, U.S. House of Representatives,** One Hundred Fourteenth Congress, First Session, " **Addressing Continued Whistleblower Retaliation within the VA", back in April 13, 2015, Serial No.114-13** has Chairman Mike Coffman(Colorado) remarking on the necessity of whistleblowers, "…The truth of the matter is that Congress needs whistleblowers within Federal agencies to help identify problems on the ground in order to remain properly informed for the development of effective legislation. For example, the national wait time scandal that this committee revealed at a hearing just over a year ago, which resulted in the Secretary of the Department resigning, simply would not have occurred without responsible VA employees stepping forward to fix problems. In the years since that scandal originally came to light, a new Secretary has come to the Department and he has stated that one of his primary missions is to end whistleblower retaliation within VA." He goes on to comment that this retaliation remains a problem…. retaliation is still a popular means used by certain unethical VA employees to prevent positive change and maintain the status quo within the Department."

According to the Honorable Chairman from Colorado, the legislation should, "…. discourage supervisors and other managerial employees from attempting to retaliate against whistleblowers by imposing more strenuous penalties for engaging in retaliation, including suspension, termination, and loss of bonuses." He further stated that, "…It is very simple. If you retaliate against or stifle employees who are trying to improve

VA, for our Nation's veterans, you should not be working for VA and you certainly should not receive a bonus for your despicable actions." I would consider forcing Ms. [redacted] resignation under the threat of a dishonorable termination sufficient injury to be called "stifling". I would also argue that the retaliations against me and all the other whistleblowers also meet these criteria.

By **April of 2016** cases of whistleblower retaliation against VA employees had risen to 35% of OSC's caseload according to Sen. Ron Johnson, (R-Wis), Chairman of the Homeland Security and Governmental Affairs Committee. He stated that, "These numbers are a clear indication of the sad state of affairs that whistleblowers are forced to endure in order to do the right thing." The hearing "Addressing **Continued Whistleblower Retaliation within the VA**", further commented that," …The Congress also passed legislation that makes it easier for the Secretary to fire poor performing and bad acting senior executive service employees. And who, in some cases, perpetuate and encourage retaliatory behavior." This should be facilitated by the new laws as the perpetrators of the whistleblower retaliations are those that were involved in and/or culpable of the original violations as is obvious by their consequent cover-up and attempts at retaliation.

Summary

If as we all assert, the federal systems are dependent upon whistleblowers for their improvement, but the system is also allowed to destroy whistleblowers**, it follows that unless there are real and effective protections exercised for whistleblowers, the system will ultimately directly through their destruction, and indirectly through the deterrence of historical observations, remove this influence of conscience from its midst.**

OMI

A large part of the problem surrounding the investigation of the violations that I identified to the Office of the Special Counsel (OSC) was the weakness and incompetence of the OMI process. Medical allegations that involve the VA are mandated to be performed by the Office of the Medical Investigator, (OMI). The OMI is itself part of the VA system. The OMI is directed by the Under Secretary of Health, also a part of the VA system. Of note, the position of Under Secretary of State, the third ranking position in the Department of State was vacated when David Shulkin was promoted to VA Secretary. This will be the third vacancy in a period of one year at the last accounting. Therefore, the OMI is at present without direct oversight.

There cannot be an unbiased investigation when the investigators are part of the system under investigation. Indeed, in the past 5 years, of all claims of whistle blowers from the VA have brought to the OMI, there have **only ever been "partially substantiation" by OMI investigations**. Allegations have never been "substantiated", but they have been "completely unsubstantiated" at the same time the **OSC has found most of their investigations "unreasonable.**

Is it that the OMI lacks the ability to "substantiate" or even "fully substantiate" a claim? While they are able to find some "fully unsubstantiated" claims? **This one-sided ability is either proof of gross incompetence or outrageous bias.** The OMI failures in the current instance were not due to incompetency or gross negligence on the part of the OMI, **but were intentional attempts to cover-up any violations or unfavorable information to the VA leadership, that their investigation uncovered**.

My telephone interview with the OMI group commissioned to investigate the allegation of human research violations covered ~ 45 minutes where they clearly and in no uncertain terms informed me that they could not investigate any of the claims unless I supplied them with the human IRB protocol that was being violated and any supporting evidence.

This is the document that has been reviewed and approved for all the human research procedures of a study. It would not normally be available to anyone other than the members of the IRB and the respective researchers. Most whistleblowers would not be able to access the document unless they were part of the

study team and as we should all be aware by now the members of any team are under extreme pressure not to speak out against the team.

This is clearly a false statement of the OMI. As they can access and audit any VA documents that they need to during the process of an investigation. The only interpretation of this that is possible is that this statement is designed to call into question their ability to investigate allegations of misconduct involving human research at the VA and to intimidate me as a whistleblower. **It places all the investigative responsibilities upon me, the whistleblower. It is more than a little ominous.**

The OMI did supply the rationale for their exclusion and denigration of my opinions. It just did not make any sense. The OMI stated in their original report, "Although the [redacted] had research experience with alcoholic patients, she does not have any medical training or credentials, is not a practicing clinician, and therefore, is not a clinical expert. Further she is not trained to perform transjugular biopsies and has not received education to determine when liver biopsies are indicated." Since my research includes this group of patients I do know quite a bit about them including the current SOC. The current allegation is not a medical one but rather an issue of research practices.

It is surprising that Dr. [redacted] Interim Medical Inspector of the OMI and the Director of the investigation into this allegation, failed to see that with all her experience. Perhaps here is a lack of training and/or experience in her practice regarding human research? Since her main job in her current position is not as a clinician but rather an investigator for the VA system, which carries the responsibility of investigating research notably human research practices, perhaps this is a serious deficiency?

The Belmont Report, a document that guides the process and approval of all federally funded human research was generated by a federally commissioned group of **scientists**, physicians, ethicists, and philosophers. My role and stated position on all the VA committees that I have ever served on is that of **scientist**, and as stated by the OMI I do have research experience with the patient population in question. Therefore, I am a scientist with research experience with ALD patients and very familiar with IRB deliberations, guidelines, and requirements.

Indeed, the Interim Director of the Office of Research Integrity for the US Department of Health & Human Services, Dr. [redacted] is a PhD. The Director, [redacted] (absent), the Deputy Director, [redacted], the Acting Division Director [redacted], are all PhDs. Dr. [redacted], the Director on temporary assignment to at USUHS, has her doctorate in microbiology, did her postdoctoral training studying the pathology of HIV and neurophysiology. She was part of the Biomedical Sciences program at Colorado State University where she performed NIH funded **basic research for nearly twenty years**. Her job as Director of Research Integrity & Compliance Review Office is that of IRB, IBC, IACUC, and GxP oversight.

Although I do not at present have Dr. [redacted] experience level, I do share some similar training. I too have many years of NIH funded basic research experience, and am a member of the [redacted] here at UCSD. Indeed, I am a graduate of said program. I have served on the [redacted], on the [redacted], and on the [redacted]. I have a decade of human research experience as well, so I am very familiar with the guidelines, policies, and laws protecting human subjects.

Director [redacted], apparently faces the same issues in her position that seem to be plaguing all the other federal offices faced with "watchdogging" federally supported research practices. When she took over in 2015, she launched, "…a top-to-bottom review of the office, which has been criticized for moving too slowly and meting out sanctions that lack teeth."

My claim was that the IRB approval and the standards of human research were being violated. By their own admission, the OMI decided that I was incompetent and irrelevant to their investigations so they disregarded all the documents and testimony that I provided to them, and treated me to a denigrating seven minute 'meet and greet' when they were onsite.

I did email the OMI as demanded, all the current IRB document as well as the history and documents supporting my allegations that same day. When the OMI did their site visit, they had no questions for me about any of the IRB document contents or anything else pertinent to the issue that I had supplied them with during our seven-minute conversation.

According to the public files contained in OSC's resources on its webpage, between 11/8/7 and 1/26/18 there have been 6 cases against VAs investigated across the country. This is out of a total of 10 federal investigative cases so far during the current reporting period, or ~60% of the total cases brought to the attention of the OSC by whistleblowers for all federal institutions! **60% of all federal complaints involve the VA, is unmistakable evidence that the VA has some serious problems that are currently on the rise, making the successful completion of their Mission Statement completely impossible to achieve.**

Of these 10 total OSC cases, 5 were medical issues and were investigated by the OMI. **Out of those 5 OMI investigations, the OSC found that 4 of those investigations were "unreasonable."** **This means that 4 out of 5, or 80% of the latest investigations conducted by the OMI were found to be unreasonably performed according to the Office of the Special Counsel.**

This says to me that the OMI has a confidence rating of 20%, which would mean that the OMI has failed at performing their duties. There should be consequences for this.

This failure to force the OMI to perform a "reasonable" investigation that leads to punitive consequences for those perpetrating the violations and those covering them up, also has a huge impact on the continuing reprisals to whistleblowers as well as denigrating and obfuscating the allegations which will not result in any inhibition of the abuse that is occurring with the VA system.

The OMI has a long history of poor performance. In response to recommendations by the OSC, VA Acting Secretary Sloan Gibson announced that the Department's Office of Medical Inspector (OMI) would be restructured to the previous Presidential Administration. He stated, "… Given recent revelations by the Office of Special Counsel, it is clear that we need to restructure the Office of Medical Inspector to create a strong internal audit function which will ensure issues of care quality and patient safety remain at the forefront."

The previous Director of the OSC also noted serious problems in the OMI. Carolyn Lerner, previous head of the OSC stated, "Even when problems are substantiated, the VA, and particularly the VA's Office of the Medical Inspector (OMI), has consistently used a "harmless error" defense, where the department acknowledges problems but claims patient care is unaffected…. This approach has prevented the VA from acknowledging the severity of systemic problems and from taking the necessary steps to provide quality care to veterans." Obviously, the former head of OSC did not feel comfortable drawing further conclusions from her statement, but conclusions are clearly there for the taking. One clear interpretation is that the VA and the OMI do not properly acknowledge the truth or severity of any claims. It further implies that at least in some instances there is collusion towards that end. In the current case that is exactly what has been allowed to happen and it appears to me that this is becoming a common practice.

Without the complete from the top-down, punitive measures and improvement of both the VA and the OMI investigative process, whistleblowers will not be respected, the retaliation will continue as will the VA systemic abuse and violations as they are all failures in leadership both within the OMI investigative teams and within local VAs that are fatal to the institution.

Summary

It has been my experience, and the data posted on the OSC website confirms this, that **either the OMI is completely incompetent, or completely unwilling to perform their investigative duties in an effective, professional, and unbiased manner.**

Culture of the VA

The culture of an institution dictates its environment, and the environment leads to the standards that are practiced by the majority of its members. These practices directly impact the quality of the product that is delivered. The culture of any group of people is portrayed, demanded, and enforced by its leaders through their own words and deeds, the words and deeds of their direct subordinates and the laws and policies that have previously been established and **that leadership chooses to enforce for that institution**. If the leadership of an institution is unlawful and disregards policies or preferentially or subjectively enforces them, even at times covering up violations of said policy, then the members and therefore the institution will be unlawful. If that leadership is allowed to continue in power there is no institutional change possible.

The past and present culture of the VA system is deplorable. When one joins the VA in any capacity there is the prevailing attitude that the VA system serves a second class/inferior patient and is therefore a second-class institution. This has been commented on by many. Senator Tom Coburn's Oversight Report **2014**, "Friendly **Fire: Death, Delay, and Dismay at the VA**", states, "…After months, and sometimes years, of being away from family and friends, service men and women should have the peace of mind to know that they are returning to a nation ready to support them. Unfortunately for far too many Veterans it is the trip that begins the longest periods of suffering. This is at the hand of the federal department created to serve them. After being gone for some of their most productive work years, some Veterans look to the Department of Veterans Affairs (VA) for basic needs like healthcare, housing, and education assistance. In healthcare, the VA has failed those it should have served."

In 2014 less than 50% of the US Veterans choose to enroll in the VA system. Not even every enrollee chooses to receive care within the VA system. This is because the ones who can afford other medical care options generally prefer it, as they are well aware of the bad reputation that the VA Healthcare system has or upon attempting to access, the VA system had very bad experiences. Of the Veterans who choose the VA for their healthcare, the majority have no other financial options. Therefore, a significant percentage of the patients at many VAs have some level of indigence.

The indigent plight of these Veterans is due to circumstances beyond their control, in many cases by medical conditions brought about by their military service and therefore is exactly what affords them of the VA privileges, and entitles them to our gratitude and respect.

That is not what they receive. The prevailing attitude is that any care, even substandard care at the VA is better than the zero care that they can afford outside of the VA. This culture is well described by Michael J. Mann, MD., renowned surgeon, and former VA doctor states in this book, "**Mission Betrayed**", "…But what if waiting times at the VA were still just the tip of an ugly, disturbing iceberg of poor care, neglect, and abuse? As shocking as many of the 2014 revelations have been, they pale in comparison to the true, appalling depth of abuse to which our veterans are routinely subjected at the VA. Just about any thoughtful medical academician who has worked at the VA could tell you that the VA wait list scandal of 2014 was nothing more than a reflection of the way everything is handled in the monolithic institution. And when an entire, badly broken healthcare system boils down to the generation and worship of a few dramatically misleading statistics, the disheartening result is not only a danger zone for our unsung heroes, but the violation of one of our nation's most important promises to a deserving, underserved population."

A White House Report: "**Issues Impacting Access To Timely Care At VA Medical facilities, " June 27, 2014**, p.3 states, "…A corrosive culture has led to personnel problems across the Department [of veteran Affairs] that are seriously impacting morale…a corrosive culture of distrust between some VA employees and management, a history of retaliation toward employees raising issues, and a lack of accountability…There is a culture across much of the Department that encourages discontent and backlash against employees. Whistleblower complaints suggest poor management, and reflect a palpable level of frustration at the local, regional, and National levels. As an example, approximately one-fourth of all whistleblower cases [OSC] is currently reviewing across the federal government come from the Department of Veteran affairs."

The Oversight Report, "Friendly Fire, Death, Delay, and Dismay at the VA" has found that, "…Thousands of Veterans have been subjected to Veterans Administration services that were inappropriate and insufficient or provided too late or not at all."

This is the current climate at the VA San Diego Healthcare System where the Chief of GI has been heard to say that **standards of care should not be applied to all patients. That the care given to severely ill patients should be limited,** in a direct violation of SOC. On other occasions he has stated that **Veterans are crazy, Obese veterans who are having problems losing weight should be put into concentration camps, and that he doesn't give a f*$k what happens to the [VA] patients and staff as long as the work gets done**. He is the Chief of GI at the VA. This is similar to the comment of Dr. [redacted] VA Director to Ms. [redacted] [redacted] upon the occasion of her forced resignation, and retaliation as a whistleblower. Dr. [redacted] told Ms. [redacted] that he "**did not care about the OSC**" in regard to her pursuit of a rescue from the retaliation. What this leadership says does not just lead to a toxic workplace environment, it establishes and a culture of intimidation, reprisals and encourages violations and cover-ups.

Dr. [redacted] is the same individual that put forth the human research study that included pregnant females as part of the group receiving a "standard of care" procedure that would involve exposing a fetus to X-rays. This was well tolerated by the entire VA research leadership. I was the only individual out of the membership of three review committees [Research safety, IRB, and the RD&C] that had any problem with this intention. The membership of these three committees would have been the only people reviewing this protocol for approval. After I explained the issue to the Safety Committee, and indirectly through an expert/additional consulting review for the IRB which I forced upon VA leadership, there was no descent to my point of view. Had I not forced the issue, it is probable that this group would have been included in the research. To this day, no one in VA leadership wants to discuss this violation or acknowledge it in any way.

The VA Acting Secretary Sloan Gibson while announcing that the OMI would be restructured, commented to the previous Presidential Administration, "… "too frequently, the VA has failed to use information from whistleblowers to identify and address systemic concerns that impact patient care." The letter also noted that VA whistleblowers "struggle to overcome a culture of non-responsiveness."

In agreement with what is an institution wide problem, Steve Cohen an opinion contributor for "**The Hill"**, and an attorney at Pollock Cohen LLP in New York and a former member of the board of directors of the United States Naval Institute, on **2/20/2018** in an article, "The **real VA scandal: No will to help veterans**", stated, "…The scandal that engulfed the Department of Veterans Affairs these past few weeks was sordid and sad. More disturbingly, it has only gotten worse, illuminating the deep-seated problems that still plague the VA. Our Veterans deserve better, starting with a full house-cleaning…. And therein, perhaps lies the root of the VA's problems: a culture where a senior staff person thinks that it is acceptable to forge documents in order to please the boss. Worse, there were no consequences for an act that was not just unethical, but illegal…The VA's culture, investigators discovered was rife with false record-keeping…the suicide rate among veterans...it is estimated that 20 veterans kill themselves every day. In 2014, the suicide rate for veterans was 22% higher than adults who had not served in the military, and 2.5 times higher among female veterans when compared to US non-veteran adult women….Significantly a study done by the National Academies of Science, Engineering and Medicine for the VA found that half of US veterans who served in Afghanistan are not getting the care that they need….they[veterans] are tired of the partisan bickering that has diverted our attention from the real problems and the will to address them…they [VA] are trigger-loaded to say "no"… be more responsive…We need to change the VA culture so that the default is to say "yes" and figure out how to help veterans... The real scandal isn't…It is the ongoing immorality of not adequately helping those who have given so much to serve the country."

Summary

The only way to change this culture of abuse, immorality, and retaliation is to **provide unbiased oversight by complete overhauls of the VA leadership and the leadership, and practices of the OMI and to institute severe punitive actions against both leaderships for violations, whistleblower retaliation, or cover-ups of violations.**

Transjugular Liver Biopsies in Patients with Decompensated Alcoholic Hepatitis

While the OMI and their medical experts (all with conflicts of interests as they benefited from the samples taken in some way) have explained the technical aspects of the procedure itself very well, but they have failed to explain it at all in the context of these patients and that is really the only issue at stake.

The patients included in this group have decompensated alcohol related liver disease (ALD). This includes a deterioration in liver function, with cirrhosis coagulopathy, ascites, and hepatic encephalopathy. That means that in addition to the disease of alcohol addiction, they have limited liver function and a propensity to bleed uncontrollably. The short-term mortality of these patients can be as high as 10-20% at one month without the additional risks of any procedures that could challenge any of their physical limitations.

That means that these patients each have as high as 20% chance of being dead in one month, without undergoing any medical procedures. Any medical procedure that is performed on them that increases any one or more of these challenges, such as bleeding as a transjugular biopsy would, proportionally makes it more likely (**higher than a 20% chance**) that they will die in one month.

Is it truly reasonable or ethical to ask any one of them to decrease their already limited life expectancy for any reason, including research for which they will derive no benefit?

For the purposes of using this procedure for research or indeed even standard of care it is important to note two things, the tendency of ALD patients to bleed, their coagulopathy, and their impaired cognitive ability due to their hepatic encephalopathy.

Abnormal Blood Clotting and Bleeding of ALD Patients

During this procedure patients with ALD have a much greater chance of bleeding that can go unnoticed, be difficult to stop, and may result in their death than non-ALD patients. Therefore, since this procedure is life-threatening to ALD patients given their coagulopathy, if it is not imminently necessary to save life, its performance should not be contemplated on ALD patients.

If a research study provided some benefit (**which the research study under discussion does not**) to ALD patients, i.e. A novel life-saving medication was being tested using them as subjects, then the correct way to incorporate these subjects into a study would be, as is well known and documented, to "**minimize risks to the subjects**". In this instance INRs, or prothrombin times together with other bleeding and clotting parameters could be measured prior to the inclusion of a subject, allowing specific exclusion criteria for subjects with coagulopathy and risk of bleeding to be removed from participating in the study due to their increased risk.

Decreasing the risk by excluding subjects with higher tendencies to bleed and providing a benefit to the subjects that are included such as a treatment, would rescue the benefit/risk ratio and allow the IRB to approve this kind of study in good conscience.

There was nothing remotely resembling these parameters or benefits built into the study in question. It is the responsibility of the PI, in this case Dr. [redacted] Chief of GI to **minimize the risks and maximize the benefits to his research subjects** and explain this to the IRB. It is up to the IRB to **obtain all the information necessary for an informed review and then disapprove any application built on unethical, dishonest, inaccurate, unsound, or biased information.** The IRB is also duty bound to disapprove an application that has a poor risk/benefit ratio and severely discipline the PI who proposes it.

Cognitive Impairment of ALD Patients

The other problem that these patients bring to any medical procedure is that they are cognitively impaired. The disease prevents them from having the intellectual ability to understand the risks of, or the benefits from, undergoing any medical procedure for themselves. Therefore, for this study and all other life threatening, non-life saving procedures, a surrogate needs to be appointed to make those decisions for them. Typically, this is a family member who is already legally responsible for their care.

This was another standard mandated by the OHRP, that I demanded to be included in the initial IRB against the documented wishes of Dr. [redacted] It remained a condition of the current approved IRB as well.

The OMI found that one patient apparently did have this privilege granted. However, it was not made part of the patient's records. Therefore, it did not happen. Everything that happens must be documented in the patient's records. Anyway, according to the OMI investigation, none of the other patients received this level of care. Therefore, every single patient, except that one and it remains in question as undocumented, failed to receive this level of care demanded by the IRB approval.

That makes 27 violations of the IRB approval on this issue alone that the OMI found during their investigation but did not consider to be "substantial". If 28 violations of the mandates and standards of the Office of Human research protections are not substantial then nothing regarding human research will be, as these are mandates protecting the basic human rights of autonomy.

Autonomy is one of the basic principles provided by the ethical foundation for research decreed in the **Belmont Report**. This report is a guide for all IRB deliberations. "It was generated by a federally commissioned group of scientists, physicians, ethicists, and philosophers, and published in 1979. The three primary ethical principles cited in the Belmont report are: **autonomy, beneficence, and Justice**.

Autonomy refers to the right of an individual to determine what activities they will or will not participate in. Implicitly, full autonomy requires that an individual be able to understand what they are being asked to do, make a reasoned judgment about the effect participation will have on them, and make a choice to participate free from coercive influence. The cornerstone of protecting autonomy is the informed consent process, whereby an investigator provides a potential research participant with full disclosure about the nature of the study, the risks, benefits and alternatives, and an extended opportunity to ask questions before deciding whether or not to participate. Populations presumed to have diminished autonomy, by impaired cognition (for example, children, cognitively-impaired elderly, or mentally ill subjects) or of circumstance (for example prisoners or **seriously ill people**) are vulnerable populations. In some of these cases (children and prisoners) special safeguards to protect their autonomy are required by regulation.

Cognitively impaired subjects are a "special/vulnerable population" that requires extra protection. They require a trained individual, in this case a medical specialist that is not part of the research study, but approved by the IRB to do so, to evaluate the level of cognition that each subject has and make recommendations as to the consent process and the parameters of the subject's participation in the study.

This was not performed to the required standards for any of these 28 subjects. This is not only 28 violations of the currently approved IRB but a violation of the human rights of 28 Veterans.

Dr. [redacted] a virtual stranger to each of them, has made a life or death decision on their behalves, for which he has received funding and co-authorship in publications. This would not be acceptable or humane practice for even a convicted murderer on death row. How is it acceptable for 28 of our American heroes?

Please see additional notes on the cognitive impairment of a specific subset of these patients below (Care, and Consent Violations Sections).

History of current Investigation

I would not want anyone to get the wrong idea about my own views on human research, so while I do not need to for the purposes of this letter, I will clarify them anyway.

I am a scientist. It is all that I have ever wanted to be. I do biomedical research that means I look for cures for diseases. Most of if not all of what I investigate is relevant to humans and so obviously I do use human samples.

I have been involved in excess standard of care sample studies, archival sample studies, and even prospectively acquired sample studies. With these studies over a decade of research, I have never been tempted to take shortcuts or to fail to protect the identity, autonomy, dignity, rights, and appreciate the sacrifice of my human subjects. To violate any of these principles compromises my integrity, the science, the funding, and the motivation/cause behind the work. I do not believe that intentionally violating an IRB or manipulating the system to benefit one person is the right thing to do.

I feel strongly about these principles, so when I see someone violating them it makes me angry. When the same individual tries to damage me because I spoke out about their behavior it makes me angrier still. I have been angry about these issues for a very long time now. Despite that, I and the other whistleblowers have behaved within the norms of this institution, and followed the procedures in our disclosures even while suffering multiple reprisals.

The allegations against the current human research study began in February of 2013, when Dr. [redacted] Chief of GI initiated a human research study utilizing Veteran subjects. He proposed to use pregnant females as part of his group of subjects. He **designated** all the subjects in the study **as standard of care** [males and females, pregnant and not-pregnant] to the IRB.

The other inclusion criteria, or ability for the people to be part of the study was that they needed to have a diagnosis of alcoholic hepatitis. There would be no direct benefit to the subjects in the study. The risk involved in a healthy person undergoing a transjugular liver biopsy, the procedure in this study, is minimal. However, I have described the added risk and its causes for a patient with ALD, due to an increased coagulopathy, above. There were no healthy subjects proposed or approved until recently, after it was discovered that they had been used in the study without explicit IRB approval during the OMI investigation.

Therefore, by policies established by the Office of Human Research Protection (OHRP), this research that puts the human subject at lethal risk without benefit [harmful risk/benefit ratio] could never be approved by any IRB. Therefore, the only way that the PI, Dr. [redacted] could get it approved was as standard of care, he would be able to do his research which would allow him to obtain a contract for the studies worth $150,000.

Pregnant subjects were intentionally included by Dr. [redacted] in his original group of subjects for this study which he labeled standard of care. Here is the elephant in the room. Dr. [redacted] problem in using these subjects is that no one on or off the IRB should agree that a human fetus can be exposed to X-rays for any purposes except to save the life of the mother or child. **It is never a "standard of care".** It is always a "special circumstance "that needs to be carefully clinically evaluated.

The potential damage to a fetus from radiation has been well established. The fundamental effects of ionizing radiation on the developing fetus are intrauterine growth retardation and defects in the central nervous system (microcephaly, mental retardation) [CMAJ 2008 Dec 2; 179(12):1293-1296].

Since a child born from a patient with alcoholic hepatitis, is likely to already be compromised by having fetal alcohol syndrome, a good clinician would treat this mother and fetus with extreme caution. It is a very high-risk pregnancy. An X-ray would never be the standard for care of this patient.

Since the pregnant subjects were included in the group and no distinction was made towards their treatment, the entire group must be judged standard of care or research by these same criteria.

Because the one part of the group is not standard of care by this argument, then none of the group can be considered standard of care the way that it was presented to the IRB. If we suppose that this group is included for research purposes, as was my argument, then there are extremely stringent rules for using pregnant subjects in research. There is no circumstance where it is acceptable to put the life of the fetus at risk for research purposes even with parental consent.

The laws and policies that govern research on pregnant women, human fetuses, and neonates are very familiar and important to all of us who perform human research studies. They are clearly outlined and can be found easily.

A reliable source is the **NIH website, 45 CFR 46, Subpart B.** Part of it that is relative to this issue states,

"…. this section, this subpart applies to all research involving pregnant women, human fetuses, neonates of uncertain viability, or nonviable neonates conducted or supported by the Department of Health and Human Services (DHHS). This includes all research conducted in DHHS facilities by any person and all research conducted in any facility by DHHS employees….

(f) Pregnancy encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery….

§46.203 Duties of IRBs in connection with research involving pregnant women, fetuses, and neonates. …. In addition to other responsibilities assigned to IRBs under this part, each IRB shall review research covered by this subpart and approve only research which satisfies the conditions of all applicable sections of this subpart and the other subparts ….

§46.204 Research involving pregnant women or fetuses…. Pregnant women or fetuses may be involved in research if all of the following conditions are met:

(a) Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;

(b) The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;

(c) Any risk is the least possible for achieving the objectives of the research;

(d) If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions e) If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions of subpart A of this part, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.

(f) Each individual providing consent under paragraph (d) or (e) of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;…."

Therefore, clearly not this is not standard of care nor viable as a research option in this scenario. Of note, I was the only individual to have a problem with the inclusion of pregnant subjects and the exposure to X-rays of a fetus. Perhaps this is because I was the only one that was familiar enough with the procedure to be able to see the consequences. Perhaps it was because I was the only one to read the protocol carefully. Perhaps it was due to my previous interactions with Dr. [redacted] It could not be because I was the only woman looking at the protocol, because although I did not ask him, Dr. [redacted] informed me that the other reviewer on the IRB looking at this protocol was also a woman. There is a fairly strong environment of chauvinism here at the San Diego VA Healthcare System.

After jumping through many hoops for Dr. [redacted] and Dr. [redacted] I did get this issue investigated back in 2013. I took it to both the ACOS of Research, Dr. [redacted] and the CO, Dr. [redacted]

Dr. [redacted] did investigate it at that time. His **assumption** at the beginning as he told me was that it was not intentional on Dr. [redacted] part to include pregnant subjects. After questioning, Dr. [redacted] in writing Dr. [redacted] made it very clear to Dr. [redacted] and myself that the inclusion <u>of pregnant subjects into the protocol by was intentional.</u>

<u>At that time the first protocol, including pregnant subjects was rejected outright by the IRB as unethical research.</u>

At that time, Dr. [redacted] stated to me that he would remove all the liver biopsies from the protocol because the IRB had decided that none of them were standard of care, as I had argued all along. Unless the liver biopsies were a condition of the contract and then only archival samples would be allowed into the final protocol.

This was the decision that I was convinced of by Dr. [redacted] the CO. That was his statement/decision to me at the conclusion of the investigation of this IRB proposal. I asked what kind of discipline was going to be given to Dr. [redacted] for this research and human rights violation. Dr. [redacted] replied that it was his opinion that Dr. [redacted] has "learned his lesson". <u>I was led to understand that there would be no consequences to Dr. [redacted] for this serious research violation, the intentional proposition to expose fetuses to X-rays</u>.

When this is related to anyone of conscience, it harkens back to the historical violations of humans perpetrated by researchers prior to the OHRP guides, The Nuremberg Code, The Belmont report, The World Medical association declaration of Helsinki, and Federal Regulations 45CFR 46, and 21 CFR 50.

These guidelines were all generated so that atrocities such as those that occurred during the Nazi experiments on Jewish prisoners during World War II (which are considered war crimes), The Tuskegee syphilis study, the case of Ellen Roche, among too many others, do not continue to occur in the process of human research.

It was incorrectly stated in the OMI reports that I was ever allowed to interact with the IRB on this matter. <u>I was forbidden by Dr. [redacted] to ever speak or contact the IRB directly</u>. He claimed that it was against VA policy. However, it was my understanding that the liver biopsies would be designated not standard of care and only archival samples would be allowed into the approved IRB protocol. Clearly, this is a violation of research policies that is being facilitated by the CO, Dr. [redacted] and tolerated by the ACOS, Dr. [redacted]

In not allowing me to be part of further IRB communications or deliberations Dr. [redacted] controlled what was finally approved for the human subjects into this IRB and did not allow the subsequent IRB annual approvals and future IRB members to be impacted by this or any other prior information.

<u>That the leadership [Chief of my division, GI] of any institution would consider a pregnant woman in the throes of alcoholism as nothing more than fodder for research that would risk the health of the mother and the life of the fetus for no direct, immediate, or measureable benefit is abhorrent to me.</u>

<u>That the rest of the leadership, the CO, the ACOS, and even the Director that would facilitate, allow, and cover-up this act of inhumanity makes it a very threatening institution for all of us to work in, and be served</u>

by. **If one of us is risked in this manner, we all are. Every person who does not stand against it, and knows about it, becomes responsible.**

As this issue was going south rapidly with the VA leadership, Dr. [redacted] who had to protect his patients while Dr. [redacted] was jeopardizing their care with his 'research', took our allegations to the affiliate institution, UCSD [Dr [redacted]] where Dr. [redacted] is also a faculty in an effort to stop the violations and still solve the problems 'internally'. This was back in **June 2013** and under the conditions of the original IRB approval which were limited to "**archival samples**".

This letter states:

"Dear [redacted]: I would prefer not to have to do this but I feel that I have no choice. My situation as a faculty has been negatively impacted by [redacted] behavior **since I opposed his intention to obtain research liver biopsies disguised as SOC**. …….

As I discussed with you several weeks ago, [redacted] **has tried to convince me to accept that liver biopsies for severe alcoholic hepatitis is SOC. I refused to accept his position as it has not been the opinion of Hepatologist (Dr. [redacted] at UCSD, nor the position of the AASLD and not my personal clinical opinion**."

"His attempt to pass the liver biopsies as SOC in this cohort at the VA IRB was also strongly objected to. The reviewers were concerned about the attempt to use federally funded facilities and personnel in performing this research without any financial compensation to the VA. In effect, he tried to use resources to do/fund his research. The reviewers for the VA IRB were also concerned about the high risk to patients (without deriving any benefits), given that it was not SOC. His protocol was approved at the VA R&D (with the VA IRB as a subcommittee) for archival biopsies only. Archival meaning paraffin blocks already in existence that had been acquired and used for patient care. Obviously, since it is not SOC, these biopsies do not exist. [redacted] has a subcontract with the University of North Carolina for liver biopsies in these patients; this is a substantial COI that makes his claim that the biopsies are SOC unethical. He is now instigating the prospective accrual of 'archival' biopsies. His actions are already outside of the approved limits of his protocol. ….. [redacted] actions are wrong in many ways: …… and 3] places an unnecessary risk of morbidity and mortality under false pretenses (an unethical way to procure liver samples for research without consent or IRB approval). The AASLD guidelines do not recommend [routine] liver biopsy given the high risk/benefit ratio.

…… [redacted] **had asked many fellows to alert him about the admission of these patients for potential liver biopsies ….**"

Dr. [redacted] supervisor, Dr. [redacted] Chief of GI at UCSD, pushed the allegations up the chain to Dr. [redacted] the Chair of Medicine, who pushed it back to the VA to Dr. [redacted] Chief of the VA Medical Service but also his subordinate at UCSD as we all are.

Obviously, Dr. [redacted] would inform Dr. [redacted] the Director of the San Diego VA System. Nothing was done about this issue at that time either, **except maybe that was when the modification to include "excess standard of care" samples was included to cover what Dr. [redacted] had informed leadership that Dr. [redacted] was already doing off IRB approved protocols.**

Dr. [redacted] informed Drs. [redacted] and [redacted] again in **November and December of 2016**. When nothing was done this second time, he then took his concerns to the OSC. Every effort was made by all the whistleblowers to resolve the problems if not at the level of the VA itself then at best still internally at the level of VA/UCSD.

During the investigation, prior to and after their site visit, I fully informed OMI of the problems in the use of pregnant subjects in this study, OHRP policies, standard of care legalities, the currently approved IRB, my

experiences with VA and UCSD leadership regarding this issue, the investigation performed on this IRB by Dr. [redacted] etc. In short, I gave OMI everything that I had or knew on this matter.

OMI never questioned me about any of these issues nor did they ever make any mention of it in any of their subsequent reports. I know that they received it as for most of it, as I do have email acknowledgements but I have no idea at all whether or not they read it.

Indeed, if they did read it they chose to completely ignore it and act like it never happened. They did mention in one report that I was not a knowledgeable witness, as I had no clinical degree.

Perhaps my lack of any real insight to these problems in their opinion is what led them to completely discount all my information and only interview me for 7 minutes? Alternatively, because I was the only real insider to this problem that they chose to ignore me? I guess I should be grateful, they interviewed [redacted] for almost 2 hours and she was forced to resign her position at the VA. The retaliation against me at the VA and UCSD started after my confrontation with Dr. [redacted] and Dr. [redacted] about the use of pregnant subjects in research and continues to this day.

Summary

In my opinion, we don't require more laws or policies, we need better oversight, protection, and enforcement of the ones that we already have. How are additional laws going to help when the VA and OMI leadership are not forced to uphold the present rules, laws, and policies?

Terms of Approval of Current IRB

What was approved and is in the **current IRB** and all the previous ones except the initial is, "…**excess standard of care and archival**…" in reference to the liver biopsy samples obtained from alcoholic hepatitis patients by transjugular biopsy.

"…**The Medical Center's IRB Protocol Application, Version 1.17 (10/20/2014)10, Inclusion criteria for Alcoholic Hepatitis patients states…liver biopsy is not required for this protocol. The protocol assures that archival liver biopsy tissue from patients is only used if published guidelines are followed…specifically these guidelines show that the biopsies are done to assist clinical decision making for severe alcoholic hepatitis…. If the medical and consulting GI physicians make a clinical diagnosis of alcoholic hepatitis, without a liver biopsy, then the patient is a candidate to be enrolled in the study."**

Of note here is that **as stated by the PI, Dr.** [redacted] in his IRB approval, if the diagnosis has already been made prior to the biopsy as is the requirement then by his own admission, then the liver biopsy cannot be for SOC in these patients at this time. It must have been performed at some point prior to his research even by his own criteria. This logic is included in the current IRB and was available to the OMI during their investigation.

Pregnant subjects have been excluded but all evidence of the investigation by Dr. [redacted] has been 'forgotten' by VA and OMI leadership. I do have evidence that supports my claims that multiple people knew about the intentional use of pregnant subjects for this IRB, including Dr [redacted] who was a recipient of the SRS Minutes (see below).

An excerpt from the **SRS Meeting Minutes** at the time of the review of this initial proposal states, …"**2.2** Investigator: [redacted] Project Title**: Integrated Approaches for Identifying Molecular Targets in Alcoholic Hepatitis,** Project ID: **1167598 ,** Protocol#: **H120108,** Application Type: Initial Protocol **,** Reviewer: [redacted] **M** [redacted] Reviewer Summary/Comments: The PI proposes taking transjugular liver pressures and biopsies, blood, urine, and stool from Veteran patients with alcoholic hepatitis. Pregnant

women are included as are decompensated cirrhotic patients. This cohort has severe medical risks for this procedure. The reviewer had a number of additional concerns regarding subject safety and standard of care. These were communicated to the VADSHS IRB for follow up. The staff list is incomplete. The description of the project is missing. The hazards are incomplete. The proposal has major inaccuracies and missing information that makes it impossible to evaluate."

Because the inclusion of pregnant subjects was in the initial submission and found to be intentional in a VA investigation by the Dr. [redacted] VA CO this was a clear violation and unethical by all human research standards. What should have occurred would have been a complete investigation of the entire protocol and severe disciplinary action taken against Dr. [redacted]

The Department of Veterans Affairs VHA Handbook 1202.1;8 f (2) states that, "…studies disapproved for ethical considerations may not be carried out in VA space, or with VA resources, even if the project is funded by another agency." I asked Dr. [redacted] what would happen to Dr. [redacted] **He replied that he believed that Dr. [redacted] had learned his lesson.** Nothing was done except to facilitate his research by the CO and ACOS.

Dr, [redacted] as the ACOS and Dr. [redacted] as the Director of a facility that have an agreement to follow the standards of the Office of Human Research Protection (OHRP) do have an obligation stipulated by the OHRP to do certain things in this instance.

As stated by the OHRP, **46.123 Early termination of research support: Evaluation of applications and proposals.** (a) The department or agency head may require that department or agency support for any project be terminated or suspended in the manner prescribed in applicable program requirements, when the department or agency head finds an institution has materially failed to comply with the terms of this policy….(b) In making decisions about supporting or approving applications or proposals covered by this policy the department or agency head may take into account, in addition to all other eligibility requirements and program criteria, factors such as whether the applicant has been subject to a termination or suspension under paragraph (a) of this section and whether the applicant or the person or persons who would direct or has/have directed the scientific and technical aspects of an activity has/have, in the judgment of the department or agency head, materially failed to discharge responsibility for the protection of the rights and welfare of human subjects (whether or not the research was subject to federal regulation).

It goes further to state, "…**§46.122 Use of Federal funds.** Federal funds administered by a department or agency may not be expended for research involving human subjects unless the requirements of this policy have been satisfied.

Since, the initial version of the protocol was officially **rejected** by the IRB and investigated by the CO, because of the unethical inclusion of the pregnant subjects and their proposed exposure to X-rays, following the above policies, further submissions of this protocol for IRB approval should have been terminated. **Instead, they were facilitated.**

The current study does state that the liver transjugular biopsies from the alcoholic hepatitis patients need to be "**excess standard of care and archival**".

Definitions of Excess Standard of Care [Back to Basics]

"Excess"

Excess means an amount of something that is more than necessary. In this context it means more than is needed to make a medical diagnosis. In order to know whether an amount of liver is sufficient to make a diagnosis, the material needs to undergo the entire process of diagnosis.

In this scenario, it is obtained from the patient by a needle through the jugular, passed into the liver into the needle and collected outside the body. The collected material from a single pass into and out of the liver is

put into formalin for fixation and sent in its entirely to the Pathology service where it is embedded into paraffin, sliced, stained, and then observed for features of a given disease. In this case to 'diagnose' Alcoholic Liver Disease (ALD).

It is not unusual for the size of the liver obtained in this way to be too small for a definitive clinical diagnosis to be made because there is not enough of the markers of the disease to be observed.

In this regard if a piece of the sample is removed prior to the processing and diagnostic analysis being complete, it does jeopardize the diagnosis which is the sole argument for the process being standard of care. Therefore, taking any of the sample for research or any purpose other than clinical diagnosis/care prior to the completion of the diagnosis**, as certainly was done in this case**, is in direct conflict with standards of care. It jeopardizes the sole stated purpose of obtaining the biopsy and invalidates the standard of care process and argument.

In all the 28 patients, the clinical coordinator(s) were present when the radiologist obtained the liver biopsies and prior to formalin fixation, prior to sending it for Pathological evaluation and diagnosis, removed a portion and flash froze it for research purposes.

Of 8 patients included in this study and randomly chart reviewed by Dr. [redacted] one of their care providers, 6 of them had suboptimal amounts of biopsy material remaining when the materials arrived at Pathology. Seventy-five percent of the randomly reviewed had their SOC completely invalidated by the removal of material for research prior to complete clinical analysis.

There are as OMI stated various opinions about the relevancy of liver biopsies in clinical care. However, the current standards do not include this cohort of patients nor do they agree with the 'standards' that Dr. [redacted] describes and the OMI and VA IRB have accepted.

In a Review Article ('**Use of Liver Imaging and Biopsy in Clinical Practice'**; **N Engl J Med 2017; 377:756-68.**), Drs. Elliot Taper and Anna S-F Lock (former **President, American Association for the Study of Liver Diseases**) stated that "…. both diagnostic accuracy and disease staging depend on specimen size. Small biopsy samples may be nondiagnostic or may not reveal cirrhosis. Analyzing images of more than 27,000 "virtual" biopsy samples of variable length, Poynard and colleagues found that **accuracy was maximized by assessing specimens that were at least 3 cm in length**.". In addition, the authors commented that …" biopsies are associated with complications, including pain (in 30 to 50% of patients), serious bleeding (0.6%), injury to other organs (0.08%), and in rare cases, **death (up to 0.1%)**." Further, the authors mentioned that "… the average direct cost of a percutaneous liver biopsy is $1,558 (in 2016 U.S. dollars), which rises substantially for biopsies performed by the transjugular route." Relevant to this discussion, Drs. Taper and Lock recommend that "Strategies **that reserve biopsy for indeterminate results reduce the number of biopsies needed to accurately risk-stratify patients by more than 70**%, as compared with biopsy-first approaches".

If an additional pass through the liver is executed **because of this research 'need'** and it is not explicitly stated in the consent process, as it is not in this study, then this is an increase in the risk that these patients are suffering. This is clearly suggested by multiple of the biopsies described below. That it is not noted in the chart how many passes were performed by the Radiologist in attendance is a gross dereliction of medical chart standards.

Finally, **the authors do not include Alcoholic Hepatitis among those liver diseases for which liver biopsy is important in the clinical** (non-research) **setting** (" Biopsy remains important for the diagnosis of some liver diseases — notably, autoimmune hepatitis, small-duct primary sclerosing cholangitis, and antimitochondrial antibody–negative primary biliary cholangitis — and for treatment decisions in some cases of chronic HBV infection.")

These experts call into question the use of liver biopsies over other diagnostic alternatives. They also describe the size requirements for all biopsies. These experts also acknowledge the potential lethality of this procedure albeit in relatively stable patients which ALD patients are not. They, as discussed are at much greater risk during this procedure.

The biopsy sizes available in the medical charts were;

Patient #1 [redacted] SUBOPTIMAL

Patient #2 [redacted] **SUBOPTIMAL**

Patient #3 [redacted]. Optimal

Patient #4 [redacted] Undetermined

Patient #5 [redacted] **SUBOPTIMAL**

Patient #6 [redacted] SUBOPTIMAL

Patient #7 [redacted] SUBOPTIMAL

Patient #8 [redacted] **SUBOPTIMAL**

Only one of the patients reviewed of the eight could be considered optimal for a diagnosis after Dr. [redacted] took a piece from each of them for research. It is entirely possible that the piece that he had removed is exactly what led to the other 7 being suboptimal and therefore of very limited value in making a diagnosis.

Thus, using Drs. [redacted] and [redacted] recommendation of at least 3.0 cm as an optimal size of the liver biopsy for diagnosis accuracy, 6 out of 8 liver biopsies transferred to Pathology (after Dr. [redacted] removed a piece of the liver biopsy) has a suboptimal length; one had an undetermined length; and only 1 out of 8 was optimal. This is both a violation of the policies governing human research protections and medical malpractice.

Therefore, there are 28 more serious IRB violations in obtaining a piece of each biopsy, as performed in this case prior to the diagnosis being completed.

There are an additional 28 potential violations of multiple passes probably being performed during the biopsy procedure. These potential violations <u>were never investigated by the OMI but they should have been obvious and easy to investigate for an experienced clinician</u>.

As only, a Pathologist can decide a diagnosis after full processing and microscopic analysis of such a sample. Excess material from these kinds of procedures is always already embedded in paraffin due to the standards of the procedures for clinical practice. However, in this case, the research material was taken pre-clinically, as it **was preferred to be fresh frozen material for the purposes of this research study.**

<u>As described here by definition, this is the prospective acquisition of human material</u>. It is impossible for anyone familiar with human research principles to see this procurement in any other way once the details are known. **Prospective acquisition of human liver samples is explicitly an off-protocol event and a violation to the approval of this IRB**. The OMI had every opportunity to explore and evaluate the details of this procurement. They simply chose not to.

This procurement as performed does not mean the goals of "**excess**" so it is 28 more very serious violations of the approved human IRB protocol.

Summary

In summary, by removing a piece prior to the completion of diagnosis for care for his own research purposes, Dr. [redacted] has potentially invalidated a majority of the biopsy material's use for making a diagnosis, thus violating its SOC potential and committing medical malpractice.

"Standard"

There are criteria of standard of care to this IRB approval that must be satisfied as well. A legal definition of standard of care is, **"… based on the customary practices of a given medical community and an average physician or specialist within that community**…..." **In legal terms, the level at which the average, prudent provider in each community would practice. It is how similarly qualified practitioners would have managed the patient's care under the same or similar circumstances."**. While it seems like the definition of standard of care should be that care which is best for the patient, we need a more legal and defined definition for an IRB evaluation. Certainly, this is an additional problem with this IRB. They lack a standard/accepted definition of Standard of care with which to do their reviews. Therefore, they have no benchmark with which to decide whether what the PI says is standard of care in their institution is or not. This is clearly a fatal flaw in their process, as then they must accept a biased opinion, that of the PI, and base their review on it.

Virtually every IRB review has some level of claim of standard of care. The advice of the OMI that suggests the IRB to call on independent consultants in each clinical specialty to supply this expertise for each review as needed is untenable.

The legal definition used in malpractice law of standard of care is sufficient and you do not need to be a clinician or a specialist to interpret it. Indeed, if it is human rights that we are trying to protect, and there are already legal benchmarks available why wouldn't IRBs use them?

So, was it standard of care to perform transjugular biopsies on patients with alcoholic hepatitis at the VA San Diego Healthcare System at the time of this research protocol submission? How many of the specialists or practitioners performed it at the VA San Diego healthcare System on ALD patients?

No. it was not and Dr. [redacted] was well aware that it was not. **None of these procedures had been performed at the VASDHCS on ALD patients prior** to Dr. [redacted] demanding them after May 2013.

Indeed, prior to submitting the human research protocol in May 2013, Dr. [redacted] approached Dr. [redacted] and Dr. [redacted] in his division and told them that he wanted to start performing transjugular biopsies on patients with ALD. Dr. [redacted] informed him that since they were not performing transjugular biopsies on patients with ALD due to the risks involved and the extremely low diagnostic/treatment benefit, it would be research and would need an approved IRB prior to any being performed. Dr. [redacted] replied that they should just try 10. Apparently, that is the minimum number he needed to fulfill the $150,000 contract.

Therefore, legally, if **standard of care**, the procedure needs to be **standard** that is <u>having been performed regularly in that institution on those patients</u>.

So, has it been done many times on ALD patients here at the VA? Ever Before?

No. Never.

No, alcoholic hepatitis patients had ever had transjugular biopsies in the VA San Diego Healthcare facility by any of the physicians prior to Dr. [redacted] deciding to procure them for his research purposes. Indeed, Dr.

[redacted] had never performed this procedure on these patients prior to wanting to start the process for his research.

So not **standard**.

"Care"

In addition, if standard of **care**, the procedure would need to be performed for patient **care**. That would mean that it would need to be performed **prior** to said care, **be necessary** for said care, and **have an impact** on said **care in all instances where this procedure is executed**.

The details of care for the 28 patients in question were readily available for the OMI to investigate. Apparently finding out the total number of patients impacted was as deep as the OMI wanted to investigate. As these patients are under the care of the entire GI Division at the San Diego Healthcare System and they do receive care in Dr. [redacted] Liver Clinics, he randomly accessed 8 of the 28 patients for compliance to standard of care and clinical standards.

This is something that both the OMI and Dr. [redacted] the VA CO should have done. Dr. [redacted] has an obligation as CO to audit all human protocols with consents annually. Which he had documented as doing for this study. It is inconceivable that any audit failed to find these serious issues of if one believes that this procedure was "standard of care" then they are malpractice the way that they were performed.

However, if they are designated "research" then they are in violation of human research practices and the IRB approval. Either way they are extremely serious patient violations and should have come to light much sooner.

This is EXACTLY what I was stating was happening in my complaints. This is exactly what I warned Dr. [redacted] would happen if he and Dr. [redacted] facilitated this human protocol for Dr. [redacted] It is an obvious pattern of behavior that anyone can see unless they are in denial due to Dr. [redacted] academic position and connections.

The data below was accessed by Dr. [redacted] the Hepatologist providing care to these patients. He shared it with me for this report. There is no PHI contained below and Dr. [redacted] has shared no PHI with me. Dr. [redacted] did share this patient data with the OMI April 4, 2017. They elected to ignore these data during their investigation of our allegations.

Another important note in the SOC for these patients is that in most if not all the care is urgent. The standards of for the care to be initiated in a timely manner because the clinical needs of these patients are dire. If a biopsy was a SOC requirement it would need to be performed by all parties (Hepatologists, Radiologists, and Pathologists) expediting the procedure. There is no evidence or history of this being the case for any of these patients. Indeed, the opposite seems to be true. That in all the cases examined, the biopsy is unable to impact care because it is only available after care has been initiated.

Eight patients randomly selected to audit, that underwent Transjugular Liver biopsy and were part of the Clinical Study included the following:

- Patient # 1.

On [redacted], a UCSD/VASDHS GI Fellow and a UCSD GI Attending diagnosed this patient with ALD and initiated what were in their opinions, standard of care (SOC) treatment regimens. This SOC did not include the recommendation or performance of a liver biopsy (thus, in their experience, **the SOC did not require a liver biopsy for patients with this disease.)**

However, Dr. [redacted] became the GI Attending and he indicated a need for a liver biopsy.

The Informed Consent Form (ICF) was signed on [redacted] without any cognitive assessment by an experienced, and unbiased expert even though the Medical Resident noted on [redacted] that the patient has had "increasing confusion". This is a definitive assessment of cognitive impairment documented in the medical chart records and available to any audit.

Thus, the informed consent without a cognitive assessment is in violation of either the research protocol or is medical malpractice, for the liver biopsy (whether determined to be a clinical or research procedure) but is also a clearly documented IRB violation of the stool and blood research consented samples as all the consents require an unbiased expert assessment and a designated representative legally entitled to consent for the patient if there is cognitive impairment.

In this case the cognitive impairment has been established, so without a legally appointed representative to consent for the patient, the consent is null and void and all samples must be excluded from any research practices as they have not been consented appropriately for such, and all funding agencies and journals notified etc.

The patient started treatment on [redacted] but the liver biopsy report was not available until [redacted] (thus, **the liver biopsy could not have any impact on the treatment/care**).

Since temporally it was not possible for the biopsy to impact care, then it was not taken for the purposes of medical care. There is only one possible need for this biopsy, the research sample procurement that Dr. [redacted] was conducting.

Therefore, another IRB violation, and an instance of medical malpractice, as Dr. [redacted] himself has argued (and Dr. [redacted] and the OMI have supported his claims) that the biopsies are SOC.

When there are violations of SOC, they are medical malpractice. If the clinical claim is that a life-threatening procedure is needed for clinical care, (as in this case by Dr. [redacted] but then cannot have been used and therefore needed, for clinical care and this was obvious at the time, then it is medical malpractice.

What this is **not** is SOC. What it **is, is Dr. [redacted] using the GI Division and this group of ALD patients as his own pool of research subjects through manipulation, dishonesty, and coercion, and without proper IRB oversight.**

- Patient # 2.

The Informed Consent Form (ICF) was signed on [redacted] without any cognitive assessment by an experienced and unbiased expert even though the UCSD/VASDHS GI Fellow noted in the medical chart on [redacted] that the patient was "tearful during the conversation".

In addition, the patient was taking Lorazepam, that is an exclusionary medication to provide any type of Informed Consent. Thus, the informed consent without a cognitive assessment is in violation of the protocol and all the samples derived from this patient, liver, stool, and blood can never be used for research and punitive actions need to be taken as described above.

The patient was started on SOC treatment on [redacted] but the liver biopsy report was not available until [redacted] (thus, **the liver biopsy did not have any impact on the treatment/care**).

Therefore, if as Dr. [redacted] Dr. [redacted] and the OMI claim that these liver biopsies were for standard of care, why do they not impact care? Why are they only ordered by Dr. [redacted] after SOC has already been started by other caregivers?

- Patient # 3.

On [redacted], a UCSD/VASDHS GI Fellow and a UCSD/VASDHS GI Attending diagnosed the patient but did not recommended a liver biopsy (thus, in their experience, **the SOC did not require a liver biopsy for patients with this disease.)**

However, as soon as Dr. [redacted] became aware of this patient that was not under his direct care at the time, he indicated a need for a liver biopsy.

The Informed Consent Form (ICF) was signed on [redacted] without any cognitive assessment by an experienced, and unbiased expert even though the Medical Resident noted in the medical chart on [redacted] that the patient has had "hallucination yesterday for which he was given one dose of IV Ativan [Lorazepam]."

Thus, the informed consent without a cognitive assessment and with a cognition impairing drug being present is in violation of the protocol.

Without a properly executed informed consent the stool, and blood samples cannot be used for research and appropriate measures need to be taken as discussed above.

- Patient # 4.

On [redacted], a UCSD/VASDHS GI Fellow and a UCSD/VASDHS GI Attending performed a diagnosis without recommending or ordering a liver biopsy (thus, in their experience, **the SOC did not require a liver biopsy for patients with this disease.**)

However, as soon as Dr. [redacted] became aware of this patient [redacted]), he indicated a need for a liver biopsy.

The Informed Consent Form (ICF) was signed on [redacted] without any cognitive assessment by an experienced, and unbiased expert. Thus, the informed consent without a cognitive assessment is in violation of the protocol and negates the stool and blood samples to be used for research purposes as described above.

- Patient # 5.

On [redacted], a UCSD/VASDHS GI Fellow and a UCSD/VASDHS GI Attending diagnosed the patient but did not recommended a liver biopsy (thus, in their experience, **the SOC did not require a liver biopsy for patients with this disease)**.

However, as soon as Dr. [redacted] became aware of this patient ([redacted]), he indicated a need for a liver biopsy.

The Informed Consent Form (ICF) was signed on [redacted] without any cognitive assessment by an experienced, and unbiased expert. Thus, the ICF without a cognitive assessment is in violation of the protocol.

Thus, the informed consent without a cognitive assessment is in violation of the protocol and negates the stool and blood samples to be used for research purposes as described above.

- Patient # 6.

On [redacted], a UCSD/VASDHS GI Fellow and a UCSD/VASDHS GI Attending diagnosed the patient but did not recommended a liver biopsy (thus, in their experience, **the SOC did not require a liver biopsy for patients with this disease**). Treatment had started on [redacted] by the Medicine team without requesting a liver biopsy.

However, as soon as Dr. [redacted] became aware of this patient ([redacted]), he indicated a need for a liver biopsy.

The Informed Consent Form (ICF) was signed on [redacted] without any cognitive assessment by an experienced, and unbiased expert even though the patient was taking Lorazepam. Thus, the ICF without a cognitive assessment is in violation of the protocol.

Here is another patient with violations of SOC and research consent violations. Therefore, medical malpractice and violations of IRB and human research protections.

- Patient # 7.

On [redacted], a UCSD/VASDHS GI Fellow and a **UCSD Hepatologist & Liver Transplant Attending** made the diagnosis without recommending a liver biopsy (thus, in their experience, **the SOC did not require a liver biopsy for patients with this disease**).

However, as soon as Dr. [redacted] became aware of this patient ([redacted]), he indicated a need for a liver biopsy.

The Informed Consent Form (ICF) was signed on [redacted] without any cognitive assessment by an experienced, and unbiased expert. even though a Medicine Resident states on 10/13/2016 "… overnight the patient received oxycodone for pain". This patient with very poor liver function and liver cirrhosis so is clinically predicted to metabolize the oxycodone very slowly. Thus, the informed consent without a cognitive assessment is in violation of the protocol.

Another clear example of violations of IRB and human research protections with expressly stated punitive enforcements. It also strongly suggests another example of medical malpractice because SOC would have been initiated by the clinicians that made the diagnosis at that time. This would have been 24 hours before the consent was signed and well before the biopsy was fully processed and available.

- Patient # 8.

On [redacted], a UCSD/VASDHS GI Fellow and a UCSD/VASDHS GI Attending performed a diagnosis but did not recommended a liver biopsy (thus, in their experience, **the SOC did not require a liver biopsy for patients with this disease**).

However, as soon as Dr. [redacted] became aware of this patient ([redacted]), he indicated a need for a liver biopsy.

The Informed Consent Form (ICF) was signed on [redacted] without any cognitive assessment by an experienced and unbiased expert. Thus, the ICF without a cognitive assessment is in violation of the protocol.

Therefore, these samples are also subject to all the punitive enforcements described above.

The **VHA Handbook 1004.01** states:

[12.d] "When the determination of lack of decision-making capacity is based on a diagnosis of mental illness, **a psychiatrist or licensed psychologist must be consulted in order to ensure that the underlying cause of the lack of decision-making capacity is adequately addressed**. However, even in this instance, the practitioner who will be performing the treatment or procedure remains responsible for the final determination of decision-making capacity with respect to informed consent for that treatment or procedure."

13 (3) "Patients must not, as part of the routine practice of obtaining informed consent, be asked to sign consent forms "on the gurney" **or after they have been sedated** …

The responsibilities of the Facility Director [Dr. [redacted] and Service Chief [Dr. [redacted] are clear in these instances.

If a violation that is clearly outlined in the VA Handbook, such as this consent process is brought to their attention, as it has been in this instance, they are required to take immediate and punitive action. Neither of them even initiated any kind of investigation into these allegations.

The violations of consent whether for research or standard of care require to be informed and understood. In the case of patients with ALD there is the presence of cognitive impairment that caused the IRB to mandate an unbiased expert evaluation of and a legally appointed representative to consent if necessary.

Consent Violations

All 8 of the above cases were in violation of this IRB statute. Further, in the one case that the OMI claims was appropriate and a representative consented for a cognitively impaired patient, there is no documentation in the medical chart. The legal status of the representative was not documented. This lack of documentation is another fatal flaw in both the processes of the IRB and the OMI investigation.

Another condition of consent that is required by all human research protection standards, and medical practices, and outlined clearly in the VA Handbook, cited above, is the requirement that all patients consenting **not be "…sedated…".** Five of the 8 randomly checked patients were under the influence of serious medical sedation when they were consented by Dr. [redacted] These are five violations of the VA handbook, 5 instances of medical malpractice, and 5 violations of the IRB and principles of human research protection.

Care Violations

It should be clear to anyone auditing these charts, clinician or not, that if one data point, A (a biopsy procedure in this case) has the expressed need to **impact** another data point, B (the medical care that a patient receives/SOC), then it, data point A, MUST come before the impacted data point, B.

If as in these cases data point B (SOC) comes before A (the biopsy), then A (the biopsy) can have no effect on B, (the care) as it has already happened.

It was very clearly documented in 3 of the cases that SOC (B) did come before the biopsy was available (A). In all three of these cases there can be no doubt that the biopsies were ordered because Dr. [redacted] wanted them for his research purposes and the biopsy results had no impact at all on SOC. Therefore, these 3 biopsies were not obtained for SOC, even though Dr. [redacted] has maintained this to be the case to the IRB and OMI investigation.

These are both human research/IRB violations and medical malpractice.

The other 5 cases from the 8 randomly selected examples of patients from Dr. [redacted] study, were also highly suggestive of **'the cart before the horse'** logic used by Dr. [redacted] in his medical and research practices.

In these cases, the diagnosis always has been made at least 24 hours and sometimes days before Dr. [redacted] becomes aware of the patient. Therefore, the biopsy cannot be used to make a diagnosis. But that is its cited role in SOC. It is SOC to immediately implement care upon a diagnosis. So, if SOC is being followed by these other practitioners and we have no reason to believe that it wasn't, SOC would be initiated in these cases well before the biopsy information became available.

It would not take a lot of additional information to prove research violations and medical malpractice in these additional 5 cases and all 28 cases were available to the OMI during their investigation, they simply chose not to review them.

Of note, the accepted IRB approved process of obtaining patients for research studies is either to treat them directly in the clinic (as your own patients), or to get referrals from the clinicians who are treating them in their clinics. Unless you have an IRB approval for prospective accrual of specific samples, the researcher cannot have any impact on SOC with any form of sample acquisition.

In this case the acquisition of a piece of the liver biopsy prior to the culmination of processing would have negatively impacted SOC if as Dr. [redacted] claimed the SOC was dependent upon the biopsy.

Indeed, even in the case of an IRB approval to obtain prospective samples, the sample acquisition can never negatively impact SOC nor can it fail to satisfy the research risk/benefit ratio standards.

It may well be difficult to predict how a specific individual is going to abuse the system. But once you have the prediction and pattern outlined for you as Dr. [redacted] and [redacted] did and you fail to perform the mandated audits in a satisfactory manner, then you share a big part of the responsibility of that abuse.

It may be difficult for the OMI to watchdog an institution as large as the VA but once a whistleblower alerts them at great professional and personal risk to themselves to a violation, and supplies them with all the information required to fully investigate it and they do not, then they also share the blame for these violations.

These were not hard violations to see coming, nor were they hard violations to find and substantiate.

The only way not to find them in an audit, or substantiate them in an investigation is to not want to. The cover-up that has happened here has taken more effort and done more damage than would have been done if Dr. [redacted] and Dr. [redacted] would have stopped this protocol at the level of the initial IRB.

There was additional damage to all the individuals involved including Dr. [redacted] and the VA leadership at each subsequent level of facilitation and cover-up by the VA and then by the OMI.

If this had been halted at any point, preferably at the beginning by Drs. [redacted] and [redacted] there would have been fewer violations of all kinds and while the actions of Dr. [redacted] would have been inhibited, his guilt would have also been minimized so even the punitive damages due to him would have been avoided.

Of note, there were 7 different attending physicians [MDs that are board certified to practice Internal medicine as well as the Specialty of GI] and 7 different Fellows [MDs certified in to practice Internal Medicine and rotating through GI to become eligible to take the test to become board certified to practice the Specialty of GI] involved in the diagnosis and care of these patients.

All of them had professional positions at both the VA and UCSD, the affiliate institution. None of them ordered or even recommended a transjugular liver biopsy on these patients. All of them were readily available to talk to the VA IRB during the approval and modification process or to the OMI during their investigations. None of them were questioned. The only individuals that were questioned were those with conflicted interests.

Further, these examples demonstrate what is done with this kind of patient at the VA. In practice the only clinician that ordered this kind of procedure on these kinds of patients was Dr. [redacted] and that was only at a time when he had a use for the biopsy material derived from the procedure.

Summary

So, the acquisition of these liver samples was not excess, because pieces were removed prior to completion of diagnostic analysis jeopardizing standard of care.

It was not standard in that it had never been performed on this specific group of ALD patients here at the VA.

Nor was it clear that it was for their medical care because in all the cases that were reviewed, medical diagnosis and care had been rendered **PRIOR** to the biopsy being procured.

This is not only 28 examples of violations of human research protection, but also examples of jeopardizing the health of veterans for little if any research benefit. That the IRB approved such a frail document in terms of human protection and the CO let it stand for years is a hard example of what is wrong with the VA and OMI leadership.

Archival Samples

In the current approved protocol, the liver samples need to be **both** "excess standard of care **and** archival." Those are the terms of the past and present iterations of all the IRB approvals on this project.

OMI incorrectly stated that it was a previous version of the protocol that referred to archival samples. However, even in that case OMI would have a problem with their justification as the PI has always procured the samples in the same manner. THEREFORE, even if OMI had been correct, the PI would have been in violation of his IRB protocol during all approvals. Obviously, the OMI is fine with ignoring past as well as present violations.

The definition of archival is also very clear from all the human research training that all researchers are responsible to know. Archival means **already obtained** for either clinical or previous research purposes ("**on the shelf**") prior to any initiation of research on this protocol.

Were there samples "on the shelf" [they would have been paraffin embedded and maybe not suitable for this research, which should have been another clue to the IRB and the OMI to investigate the protocol a little more] prior to this study being approved and initiated?

No. There were not any available, "on the shelf" in the Pathology Department or anywhere else in the VA.

No IRB should approve a research project with archival samples stipulated where there are no archival samples available from other prior research or clinical purposes. Since it was not standard of care (SOC) at this institution, and no IRB would approve a study with this poor a risk/benefit ratio for research, there were no samples available as archival. Therefore, at the initiation of the study there were no liver biopsies from transjugular procedures of Alcoholic Hepatitis patients available for Dr. [redacted] studies.

Therefore, these samples were not archival.

This is something that both the OMI and the IRB as well as anyone else could investigate if they were sufficiently motivated to do so. The OMI chose to dissimulate on this issue, incorrectly claiming a previous but approved iteration of the IRB protocol had the archival samples on it.

Indeed, Dr. [redacted] was aware of the lack of available archival and properly fresh/frozen fixed samples for his research because he tried to get these samples procured by Dr. [redacted] and [redacted] back in May 2013 without an IRB approval (reference discussion above).

Dr. [redacted] was also complicit in this deception of the IRB, as I told him at the time of the investigation of the initial IRB protocol, that there would be no archival samples for these reasons. He replied that Dr. [redacted] just needed the "possibility" of obtaining samples to keep the contract (the $150,000). This was **not a "possibility" it was motivation** for Dr. [redacted] to violate the approval terms of his IRB that was provided by Dr. [redacted] under the guidance of Dr. [redacted]

Dr [redacted] confirmed this account in an email that was provided to the OMI investigators but was also ignored. He stated, "I confirm that in May 2013, Dr. [redacted] asked Dr. [redacted] and me (at the time

a Staff Physician Hepatologist) [in the presence of Dr. [redacted], a Co-Investigator on the current and previous IRB] to approve the performance of liver biopsies as Standard of Care for patients with Alcoholic Hepatitis for a research study that Dr. [redacted] wanted to start at the VASDHS. Because this was not the SOC at the VASDHS, at the [redacted] Association for the Study of Liver Diseases, or at the University of California, San Diego (where we were Professors). Dr. [redacted] and I denied Dr. [redacted] request.

Dr. [redacted] persisted and said something like ' Let's try with 10" Dr. [redacted] and I asked him to place a research protocol with the VASDHS IRB and ended the meeting. I also would like to confirm that Dr. [redacted] harassed me with great animosity and sent me to have a Psychiatric evaluation of which he obtained the report. I was very depressed and didn't refuse to undergo this illegal Psychiatric evaluation. In addition of this violation, Dr. [redacted] also violated my HIPPA rights as a federal employee by accessing the Psychiatric report."

Dr. [redacted] is yet another whistleblower that that suffered retaliation by VA leadership.

Other Standard of care 'experts' Consulted

My opinions informed or not, concerning the issues of standard of care, the use of pregnant subjects in research, and common decency were ignored by the OMI on the basis that as a non-clinician, only a PhD who has extensive research experience with this cohort, I could not really have anything of relevance to say on this matter. Apparently, it is standard OMI practice to discredit and denigrate whistleblowers as much and as quickly as possible.

The medical opinions of Dr [redacted] a board-certified gastroenterologist and a Fellow of the American Association of the Study of Liver Diseases, and Dr [redacted] an internationally practicing hepatologist, on staff at the VA, concerning the standard of care issue were also ignored by the IRB, the CO, ACOS of Research, the VA Director, and OMI.

Interestingly, the three of us do have a couple of things in common. We respect patients but we especially respect the patient population here at the VA, and we share a common sense of ethics and adherence to policies that protect human rights. We also have the fact that we do not benefit from the acquisition of these samples or this research in any way on our side in our argument to be heard. Nor are we collaborators with Dr. [redacted] Therefore, we have no conflict of interest in this issue.

Instead, collaborators/co-authors of Dr. [redacted] and Dr. [redacted] himself were asked to comment on the issue of this procedure. These were general comments and not specifically suited to the investigation.

While Dr. [redacted], the hepatologist at the affiliate institution in charge of the liver transplant program, did correctly state that the procedure itself is the optimal one for ALD patients, he failed to be completely honest. It carries a lethal risk for this cohort but is the only option that could be acceptable in a clinically emergent or urgent scenario exclusively for care/lifesaving purposes.

He also failed to mention that UCSD is not part of the liver portion of the IRB study and that this procedure is not performed on this group of patients as standard of care or for research purposes at UCSD. The OMI also failed to stress that Dr. [redacted] is an active collaborator of Dr. [redacted] who has published using these samples and will need to retract portions of said publications if an IRB violation is discovered.

The OMI also failed to clearly state that the IRB elicited this advice after the IRB approval, not before as would be correct IRB procure. Perhaps the OMI distorted Dr. [redacted]'s accounts, sharing only the parts that suited their purposes. If so, that was a discredit to Dr. [redacted]. Regardless of how it happened, Dr. [redacted]'s account is incomplete, not entirely relevant, and so grossly misleading.

It should be clear that Dr. [redacted] is not an unbiased resource and never should have been consulted by the IRB as to the appropriateness of any part of his protocol. Even if the IRB had consulted him prior to approval

and not after as they did, would it have been the correct action. That the IRB got his stipulations to standard of care for these patients after his IRB was already approved reeks of an attempt albeit a weak one of a cover-up.

In this regard, it is interesting to note that the **Chief of GI has commented in open forum to much agrimony and dissent, that he does not believe that severely ill patients should receive standard of care as they are going to die anyway.** These are the self-expressed standards of care of the individual that the **OMI**, the **ACOS of Research**, the **CO**, and the IRB relied on for an evaluation of standard of care.

The IRB failed to ask about any conflicts that either 'expert' might have such as the benefits that they had already derived from the study in giving their opinions. The IRB also failed to make any of these standard of care enquiries BEFORE approval of the IRB. They only started actions as part of the OMI investigation and recommendations.

It should be obvious to everyone that common sense would dictate that the IRB request numbers performed or already available samples from any procedures that are requested as either excess standard of care or archival on a protocol from the PI that is proposing the protocol.

In all instances, the PI will know availability, as he/she would have already checked to know what kind of protocol he/she needs to propose; an archival, an excess standard of care, or a prospective accrual. In this case, Dr. [redacted] was aware that there were no archival samples available. He also knew that the procedure was not standard of care. That is clearly shown by his attempt to get Dr. [redacted] and Dr. [redacted] to acquire the necessary samples for him without an approved IRB.

After ascertaining that he could not get archival samples, that the samples were not standard of care, and he could not get the samples procured without an IRB approval, as he could not convince Drs. [redacted] and [redacted] to perform human research without IRB oversight, Dr. [redacted] then set out to get an IRB approved in any form. He fully intended to prospectively procure the samples in violation of the IRB as from the beginning his staff was always taking a piece before diagnostic analysis was complete and fresh/freezing it for research purposes.

After more than two decades doing human research, it should be considered that Dr. [redacted] is very knowledgeable of the principles of human research protection. The evidence strongly suggests that he simply chooses to violate these principles when it is expeditious for his research purposes.

The OMI had its own role in this problem as well. The OMI's point, "The **IRB did not initially utilize qualified clinical consultants to determine if transjugular biopsies were standard of care. However, the IRB did later consult with other providers with expertise in caring for patients with liver disease; these providers offered information that transjugular biopsies are the standard of care for patients with, or suspected to have, alcoholic hepatitis."** This is another OMI statement that is misleading at best and complicit at worst.

General Description of Study and Role of PI

There are two studies covered by this single IRB. That is where the procedural and review problems come from.

One study is centered at UCSD, the affiliate institution, and is a study of the microbiome of ALD subjects. It is a study of what microbes are residing in these patients. It requires a control or normal patient group, stool samples passively obtained, and a blood draw exclusively for research purposes. The alcoholic hepatitis patients were approved by the IRB to be part of this study and to be research consented for these minimally invasive procedures. The PI of these studies is Dr. [redacted], who is a Co-Investigator on the VA IRB. Even though all the work on the stool and blood was performed at UCSD, there was no UCSD IRB and initially no VA MTA either.

Unfortunately, in all the machinations by the IRB PI, Dr. [redacted] the approval of the control group was neglected so that resulted in these patients being used without an approved IRB protocol. A lot of this confusion could have been avoided if Dr [redacted] had been allowed by Dr. [redacted] to shepherd his own VA IRB on his own project. But then perhaps Dr. [redacted] would have lost the enforcement of co-authorship, and Dr. [redacted] would have earned a greater academic independence?

The main study and the one providing the funding, was to obtain liver samples from individuals with alcoholic hepatitis to supply them to a bio-repository in North Carolina, supported by an NIH grant. This data repository would be used to look for potential biomarkers [including genetic genotyping] of the disease. What should be obvious from this description is that any benefit to participants is not assured, not obvious, and in the undetermined future.

The sole role of Dr. [redacted] is to obtain the liver samples and deliver them to the bio-repository. For that he is the PI on a contract administered by the VMRF, from which Dr. [redacted] as ACOS gets matching funds from the federal government. In this regard, as Dr. [redacted] has used the standard of care criteria in obtaining these research samples, so that the VA also has to pay for their procurement.

A regular percutaneous biopsy can be up to $2000 per patient. A transjugular biopsy can be double that. Therefore, these studies would cost Dr. [redacted] the money he received for them ($150,000) if he had come through with the designated ten. Since he got the VA to pay the bill for his research samples, he was able to accrue 28!

28 liver biopsies that have gone to North Carolina for their research endeavors cost the VA ~$56,000-$112,000. Since there is quite a bit of convincing evidence that they are not standard of care, this is getting the VA to pay for research samples that were already NIH funded. I am not clear whether it is the NIH or the VA that is being defrauded or both. Certainly, the **VA MUST be reimbursed by Dr. [redacted] for this research expenditure,** and the NIH needs to be informed of this fraud and the IRB violations.

In supplying these 28 biopsies to the parent institution in North Carolina, Dr. [redacted] benefits by being a co-author on all resulting publications. It is expected that his 'donation' of 28 instead of 10 samples will get him a very good place in the authorship line.

What is left uninvestigated here and unresolved is that by NIH funding guidelines these allegations need to be shared and fully investigated by the local IRB, and R&D which was not done. Also, any violations need to be reported to all funding administering agencies (University at North Carolina, VMRF, NIH, and VA Central Office as an IRB violation) as well as any journals in which the materials/data from this IRB has been used. A violation of this magnitude and all this mandated reporting will have serious funding and publication consequences for everyone involved.

This is the impetus behind the cover-up that the VA leadership is perpetuating. It benefits VA and OMI leadership and to some extent the leadership at the affiliate institution to have these allegations be unsubstantiated.

In this regard the OMI has mandated changes to the IRB to 'fix' these violations. Fortunately, these mandates are against the policies of the OHRP. "**Federal regulations and guidelines do not allow for review and post hoc approval of studies that have already been conducted involving human participants, human biological materials, or identifiable data that can be connected to any living individual. The VA and all other research institutions have a legal obligation to follow the U.S. Office of Human Research Protections (OHRP), and it is obligated to comply with the ethical principles of The Belmont Report and the federal regulations for the protection of human participants**." It is a violation of the principles of human research to attempt to seek approval for human research that has already been performed without said approvals.

While there are various acceptable procedures to deal with violations, none of them include modifications to an approved IRB to consider preexisting samples obtained without IRB approval. They do include

complete descriptions of all non-approved research being provided to the IRB, an automatic cessation of all human research until which time that IRB approvals can be investigated for compliance fully, "**destruction of all samples that were illegitimately obtained, punitive damages to the responsible parties, and acknowledgement that none of the data from the unapproved research can ever be utilized or published."** **All individuals, institutions, publications, and funding agencies, involved or impacted by these violations must be notified**

It is a concern that the OMI is so ignorant of the basic rules, regulations, and laws that are the tenants of human research and IRB processes. In acknowledging but obfuscating this violation of human research and recommending a post hoc approval/modification to 'fix' it, the OMI is not only facilitating the violation but they are now also in violation themselves by suggesting a process that is in violation of rules, policies, and laws.

If one could get approval after research was performed on human subjects what would be the point of ever seeking it prior approval? Approving human research that has already been performed without approval is essentially condoning human research that has been done without an IRB approval and that is expressly against all policies of the OHRP.

What guidelines from the OHRP stipulate is serious punitive actions and restrictions to be imposed on those individuals who do perform research without IRB approval. In many cases, these punitive measures and restrictions may be assessed on the IRB in question that failed to protect their human subjects participating in research projects under their supervision.

Consent process

An informed consent process for either clinical procedures or research includes some common features. For both since the consent is required when there is intervention/interaction with a living individual that may carry risks for that individual the consent or their agreement to have a procedure must be clear and understandable to that individual.

It may be obvious but, we will state it here anyway, all consents for procedures must occur before the procedure in question. If the procedure is for medical care or it has been independently determined that it is standard of care then the procedure must take every opportunity to impact said care. This means a diagnosis followed by care, changes in care or novel implementations of care should result from the procedure.

When you know that specimens from patients, taken for any purpose are going to be used for research **purposes and if you are able to consent the patients, then you must consent them** [OHRP]. This is the ultimate golden rule of human research consent.

By violating the consent process, Dr. [redacted] removed freedom of choice form these patients. However, he did much worse; he put their lives in danger for this research. He also lied to them and coerced them to get their consent. These patients were told by Dr. [redacted] that they required these procedures to receive medical care. It was implied that without these procedures they would not get quality medical care.

This is another violation of the principles of human research. Research participation can never be compelled, manipulated, or forced in any way. It must always be voluntary.

Dr. [redacted] however, has enough experience to know that patients who are gravely ill and even those that are not, are very reluctant to give any kind of consent to a procedure that has risks of serious complications and that has no direct and immediate gain to them. He is aware that these patients, with ALD are very reluctant to undergo even minimally invasive procedures for real clinical interventions. Therefore, the possibility of getting an informed research consent from them is extremely small. Hence, his machinations to get his procurement labeled standard of care.

Even if the procedure is assumed albeit incorrectly, to be standard of care, the consent process as standard of care was violated by Dr. [redacted] In this regard it is not just an IRB violation but medical malpractice and a violation of human rights.

That is another IRB violation. Human research subjects cannot be compelled to participate at any level.

The consent process for research, as the subjects' gains might not be as strong or clear carry additional requirements. Research consent according to the OHRP, the federal office that control human research policies, must in addition to, "…meeting all requirements of human subject regulations must include a description of specimens/data and process used for collecting them. Risks, including risks to privacy and confidentiality, and methods to protect risks. Description of the purpose of the collection and the conditions for sharing, and the types of research to be conducted. Statements of the right to withdraw, what will happen when the specimens are no longer useful or the repository loses support, or is transferred to others…whether the results will be returned, commercial use, if any, for sharing profits. Plans for re-contact, if any, details about where and how long the specimens will be stored, genetic uses and information on the consequences of DNA typing…. conditions of sharing with other researchers…what will happen to specimens when no longer useful, when repository loses support, or is transferred to others…"

None of the research consent criteria was satisfied because Dr. [redacted] lied about the procedure being standard of care. Indeed, because of all the secrecy and manipulations by Dr. [redacted] there are consent violations for not only the liver sample study portion of the IRB but <u>also for the minimally invasive, stool and blood sample study portion of the IRB.</u>

Because the liver samples were consented as standard of care and not research consented there is not accompanying HIPAA waiver from the IRB that can be associated to these samples so they are not covered at all by the IRB as they are 'not research samples'. There were omissions in the HIPAA waiver and consent for the blood and stool samples going to the UCSD study as well making that part of the study also in violation of the IRB.

An "**August 31, 2016 VHA DIRECTIVE 1605.01 8 (b)** For research purposes, where the only remuneration received by VHA or its business associate is a reasonable cost-based fee to cover the cost to prepare and transmit the protected health information for such purposes…" stipulates that VA researches not profit from PHI. There are similar directives on human materials. These issues were also ignored by the OMI during their investigation.

Genotyping

The study driven by the VA liver biopsies is to discover biomarkers of ALD. Since it is not an inclusion criterion that the group of patients have any other conditions such as viral infections, etc. it is obvious that the search for biomarkers will entail the use of genetic sequencing or genotyping of the human material.

It is a violation of the OHRP of consent **not to directly inform the donors of specimens that said specimens are going to undergo genotyping.** Donors must be specifically consented for this type of analysis or it cannot be performed. Therefore, since it was not consented as such, no genotyping can be performed on the liver samples procured under this IRB as standard of care. Since the purpose of this biorepository is to identify markers of ALD, that purpose is not possible to pursue with these samples. It is a violation of the patients' rights to do so. This cannot be corrected after the fact by a modification to consents that have already intentionally been executed in this manner.

<u>Instead what needs to be done is to admit the institutional failure, call back all the samples and the data that they have generated and destroy it as it was obtained without a proper consent. Again, all funding and publishing entities need to be notified explicitly of these violations.</u>

The VA itself has some additional limitations on Material Transfer Agreements and the limitations of using veteran's samples for genotyping that must be assured and in place before any research is initiated. This is another issue that was not investigated by the OMI.

Of note, any of these subjects/patients that are Native American tribal members need to be specifically informed about what kind of research is being done on their DNA. **April 21, 2010** the Havasupai Indians had a banishment order against Arizona University for improper research done on consented samples. The won the return of their samples, halting all future research with them along with financial damages against the University and Dr. Markow, then at University of Arizona, now at UCSD.

Tribal rights are in addition to federal rights. The Native American population is significant in San Diego so it is significantly possible that some of these patients are Native American. These issues were also not investigated by the OMI.

Other issues found by the OMI during investigation into our allegations

There were other violations of the human research IRB approved protocol that were uncovered during the OMI's investigation of our allegations. OMI's argument is that as these violations were not alleged at the initiation of their investigation so while they are violations that were uncovered, they shouldn't count.

This seems like the worse kind of immaturity, and really should be beneath any federal institution. The Office of medical Inspector, in charge of protecting the clinical and research practices for Veterans should not result to such idiotic arguments if it wants to retain any semblance of respect at all.

The OMI further states in their report, that "… **Current training for study coordinators is inadequate as evidenced by the study coordinator obtaining consent before she was approved by the IRB to be part of the protocol, the presence of poorly maintained and incomplete research records, and miscommunication between the Chief, GI, and the study coordinator."** This statement is another substantiation of allegations of conducting human research without proper consents. For the consent to be valid, a minimum condition is that the individual [study coordinator] administering the consent needs to be approved by the IRB.

If said individual is not IRB approved at the time that the consents are administered, then all those consents are not IRB approved and so all are invalid and the result is that human research is being conducted without an approved consent. Research materials obtained without an approved consent must be destroyed. All involved individuals and institutions including funding institutions must be informed of these violations and these samples can never be used for research/publication purposes.

It is a shame that while the OMI did find these violations the only recommendation was that the "…**Chief, GI should provide more direct oversight of this study to ensure that research staff is adequately trained, that research records are appropriately maintained, that he has a clear understanding of where specimens are being shipped, and that protocol amendments adding new staff to the study are approved before any research procedures occur**."

The **Chief, GI** has been doing human research at the VA for over 35 years at facilities in Minneapolis, San Francisco, and San Diego. He does not lack in training or knowledge. What he lacks is an adherence to policy and law, and what he has is an excess of ambition that over reaches his abilities and an insensitivity to the patients that he is paid to serve, that is astounding.

His interactions with this particular study coordinator could not possibly be any closer, and he is according to the approved IRB the only individual involved in the shipping of liver samples to North Carolina.

Another violation that the OMI documented was that**," … The Health Insurance Portability and Accountability Act (HIPAA) authorization and informed consent document did not inform the control**

subjects that personally identifiable information (PII) would be sent to the co-investigator's lab at the academic affiliate.

Also, the IRB Protocol Application did not specify how the Primary Investigator planned to use information obtained from the "dietary questionnaire" or whether the PII from this document would be transferred for use in the co-investigator's lab." So, the OMI's finding that the control subjects were not included in the IRB approval, is followed by another finding that the consent process is fatally flawed by the study coordinator administering the consent where not being on an IRB protocol, and finally the OMI finds that the contents or lack thereof of the consents are a violation of HIPAA rules, and regulations.

To remedy this violation, the OMI stipulates, "**The IRB must also require an amendment to the informed consent document and HIPAA authorization to reflect that control subject specimens containing protected health information (PHI) will be disclosed to the academic affiliate. The IRB must address any instances of PHI and PII being disclosed to the academic affiliate without the subjects' consent or HIPAA authorization"**.

Again, according to HIPAA standards and federal regulations," … **do not allow for review and post hoc approval of studies that have already been conducting involving…identifiable data that can be connected to any living individual**." Therefore, the recommendation by the OMI is against federal mandates and will not solve or repair the violation. This is more than enough to substantiate the allegations of," … **performing unapproved human liver research, without informed [research] consent, that places patients at serious risk…. not properly advising patients of their options…"**. I would argue that the OMI found not only evidence of the cited allegations but I would agree with the OMI that they found IRB and HIPAA violations that went beyond our stipulated allegations.

However, I disagree with the OMI that the additional findings do not matter and are of no consequence because the whistleblowers did not make specific mentions of them. That is just crazy. There is no other way to describe those sentiments.

This is an extreme failure of leadership at the VA and the OMI. VA leadership is ultimately responsible for all the medical, whistleblower, and research violations that have occurred and continue to occur. The history of the VA is to simply move these individuals around. When they create problems or at least fail to control or solve the problems, and instead cover them up, the leaders are simply moved to another VA. Many times it is a promotion!

This is what needs to stop. Responsibility needs to be taken. Actions need to be punitive to force change. Amends need to be made to all the victims, to the patients and to the whistleblowers. [redacted] needs to be reinstated. Myself and other whistleblowers deserve acknowledgement, apologies, and protections and in some cases remuneration for financial damages sustained.

Respectfully,

[redacted]

[redacted]