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- 11. Parliament of Australia, Biotoxin-related illnesses report 10/17/18.
- 12. Submission to the inquiry into biotoxin-related illnesses in Australia 6/28/18.
- 13. Consensus Statement, Surviving Mold; IMR 2018; 4: 1-47.
- 14. <u>A Gene Primer for Health Care Providers 1/18.</u> Shoemaker and Ryan, eBook.
- 15. Inflammation induced chronic fatiguing illnesses. IMR 2017; 3: 1-27.
- 16. HERTSMI-2 and ERMI. Shoemaker and Lark 2016.
- 17. HERTSMI-2 and elevated MSQPCR reduces VIP benefit. Shoemaker and Lark 2017.
- 18. RNA-Seq on CIRS patients treated with VIP. Ryan and Shoemaker MRA 2016; 4: 1-10.
- 19. Surviving Mold, Medical Consensus 2015.
- 20. NeuroQuant Volumetric Key.
- 21. NQ. VIP corrects gray matter nuclear atrophy in CIRS. IMR 2017; 3: 1-14.
- NQ. Use of Shoemaker Protocol to correct volumetric abnormalities in NeuroQuant. Lead author, S McMahon, MD. Journal of Neuroscience and Clinical Research 2016; 1: 1-4.
- 23. NQ. Defining NQ abnormalities in CIRS. NTT 2014; 45: 18-26.
- 24. Ciguatera Transcriptomics in CIRS, Ryan et al. BMC Medical Genomics 2015; 8: 15-27.
- 25. CDC, Health Hazard Evaluation HETA 2005-0135-3116.
- 26. Policyholders of America Research Report 7/27/10. Shoemaker and McMahon.
- 27. Lyme complement split products C3a and C4a. Int Arch Allergy Immunol 2008; 146: 255-261.
- 28. Lyme/Babesia. Atovaquone plus CSM. Advances in Therapy 2006; 23: 1-11.
- 29. Cyanobacteria and CIRS. Cyanobacteria Harmful Algal Blooms. Hudnell, ed. 2008.
- 30. Pfiesteria diagnosis, MMJ 1997; 46: 521-523 Shoemaker.
- 31. Pfiesteria treatment, MMJ 1998; 47: 64-66. Shoemaker
- 32. Pfiesteria, EHP Grand Rounds PEAS 2001; 109: 539-545. Shoemaker.

- 33. Pfiesteria, EHP 2001; 109: (supplement 5) 791-796. Res/Rec. Shoemaker.
- 34. Pfiesteria, cognition Lancet 1998; 252: 532-539. Maryland Pfiesteria Team.
- 35. CIRS-WDB 2003 (Johanning) case control Shoemaker.
- 36. CIRS-WDB 2004 Prospective Re-exposure Trial. NTT Shoemaker and House.
- 37. CIRS-WDB 2006 NTT Double blind, placebo-controlled prospective trial.
- 38. CIRS-WDB 2006 Homeland Security, FEMA; Report to St. Bernard Parish, New Orleans Louisiana. Symptoms and VCS from Katrina 2/22/06.
- 39. CIRS-WDB MR Spectroscopy corrected by VIP in CIRS 2007 IACFS/ME meetings.
- 40. CIRS-WDB IACFS/ME Bulletin 2009. Pediatric CIRS case/control.
- 41. CIRS-WDB Health. 2013; 5: 396-401. VIP corrects proteomic abnormalities in CIRS.
- 42. ACOEM 2011 Rebuttal. Shoemaker.
- 43. Lincoln Military Housing. First Norfolk clinic master. 6/29/12.
- 44. Lincoln Military Housing. Second Norfolk clinic master. 8/20/12.

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Thank you for the opportunity to discuss the current state of the science regarding adverse human health effects acquired following exposure to the interior environment of water-damaged buildings (WDB).

I have attached my CV in support of my education, training and experience.

Reviewing the 2008 GAO, it is still true that the public may not be sufficiently advised of indoor molds creating a potential health risk. More importantly, however, we now know that of the three groups of indoor-dwelling microbes, bacteria, actinomycetes and filamentous fungi, the dangers posed by molds are a distant third on the list.

It remains true that exposure to WDB is a daily occurrence in the United States. It is true that multiple components of filamentous fungi may cause inflammatory responses that in turn cause disease. We now know that the disease-causation aspects are intimately tied to differential gene activation/suppression. As we all know deep down, whatever goes on in health and disease is going on in DNA.

It remains true that fragments, simply biologically-produced chemicals, are not alive but can cause adverse health effects. Claims of benefit from sterilizing indoor environments without removal of fragments is not supported by any academic work.

Inhalation remains the most common route of exposure, with ingestion a theoretical possibility. The world's literature has at least 100 studies showing presence of mycotoxins in urine, a putative marker of exposure to WDB, in healthy people. The focus on ingested mycotoxins as the source of adverse human health effects is not supported by current literature; there is little support for ingestion to be a source of the differential gene activation that is the marker for chronic inflammatory response syndrome (CIRS).

It is true that adverse health effects arise from immune-mediated mechanisms; indeed, this is the main source of illness. We must add to previously described mechanisms the recent discoveries by transcriptomist James Ryan, PhD that suppression of ribosomal and nuclear encoded mitochondrial genes remains the basic feature of chronic fatiguing illnesses from biological sources, including but not limited to WDB.

It remains true that immune mechanisms associated with specific health symptoms can be difficult to tease out but now with more sophisticated proteomics and transcriptomics, these difficulties are falling by the way side.

The call for research to determine adverse health effects for low-dose, long-term exposure has been repeated multiple times. The list of 37 symptoms seen in at least 30% of patients in a series of 10,000 in one clinical practice in Pocomoke, Maryland show that this truly is a multi-symptom, multisystem illness (see handout for roster of symptom clusters). Work with HLA DR since first published in 2003 has confirmed that certain genetic make-ups will have an increased relative risk of illness based on immune response genes found on chromosome 6.

As far as remediation goes, once again the science has advanced rapidly. We now know that removal of particulates smaller than 0.3 microns, together with removal of endotoxin, actinomycetes and possibly mVOCs, with readily available, inexpensive commercial devices not only shows improvement in proteomic measures but also now shows improvement in dysregulated transcriptomics measures.

We support the discussion of establishing a cause of the relationship between exposure in illness that includes (i) epidemiologic association; (ii) experimental exposure in humans and animals (NB: SAIIE shows prospective acquisition of illness with re-exposure in approximately 95% of patients in three days). We agree with the GAO that the one study addressed by Ms. Kramer today that "inhaled toxins were an improbable source of negative health affects (i) ignores science; (ii) ignores logic and (iii) ignores the language in the study that is cited.

Now that transcriptomics research has confirmed that the inflammatory basis of exposure to endotoxins, actinomycetes and filamentous fungi has shown both acute illness symptoms and long-term illness symptoms, we can leave behind the ideas of naysayers that claim there is no illness acquired following exposure to the interior environment of WDB.

We agree that there has been little progress in Federal guidance looking at illness caused by exposure of the interior environment of WDB with a notable example of the CDC/NIOSH study (attached) that attacked the conclusions that my work has presented. Specifically, in a case/control study looking at a water-damaged high school in the New Orleans area (Fortier High School) the NIOSH investigators not only confirmed the multisystem, multi-symptom illness that

we have published previously but also confirmed the Visual Contrast Sensitivity deficits in cases that our group had published previously. Curiously, there was failure of the investigators to then provide treatment of affected individuals.

Regarding nervous system effects, multiple studies cited by the GAO supported the existence of such abnormalities. Now that we have an FDA-cleared test, called NeuroQuant, we can not only show evidence of a fingerprint of a brain injury acquired following exposure to WDB but also show correction of gray matter nuclear atrophy with use of a published, peer-reviewed protocol. The application of these findings to illnesses characterized by neurologic and cognitive impairment are ongoing.

While I remain concerned that the work of our group was ignored by the 2008 GAO (including a randomized, clinical trial from 2006), I have submitted a list of documents that reasonably support my contention that the advances of "mold research" creates a solid framework to put an end to the fabricated source of controversy regarding this illness.

From symptoms, VCS, proteomic biomarkers and transcriptomics we have retrospective studies, case/control studies, prospective studies and placebo-controlled trials in several of the CIRS sources from cyanobacteria to dinoflagellates and WDB. Our roster of trained health care providers expands every week. Their focus is on data used to guide clinical practice and confirmation of the process of science as applied to WDB. As we expand our 2000-patient NeuroQuant dataset, we are seeing new applications to correction of enlarged lateral ventricles and grey matter nuclear atrophy. Finally, the incredible advances in application of RNA Seq has let us correct dysregulation of ribosomal and nuclear encoded mitochondrial gene suppression as seen in CIRS and essentially all chronic fatiguing illnesses we have studied to date.

In part due to the example of CIRS-WDB, we have used vasoactive intestinal polypeptide to correct proteomic abnormalities, transcriptomic abnormalities and grey matter nuclear atrophy. The ongoing application of CIRS-WDB to other inflammatory illnesses is underway.

Sincerely,

Ritchie C. Shoemaker, M.D.