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WS of: Professor Martin McCaffrey
Filed on behalf of: Second Respondent
Witness Statement No: 5
Date: 01 March 2023
Filed: 02 March 2023

IN THE HIGH COURT OF JUSTICE ***Case no. 13905631***
COURT OF PROTECTION

IN THE MATTER OF THE MENTAL CAPACITY ACT 2005

ON THE APPLICATION OF

AND IN THE MATTER OF

AN NHS INTEGRATED CARE BOARD (ICB)

Applicant

-AND-

RN (by his Accredited Legal Representative)

First Respondent

TN (RN's mother)

Second Respondent

[anonymised] WITNESS STATEMENT OF PROFESSOR MARTIN McCAFFREY

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I, PROFESSOR McCAFFREY *of* the University of North Carolina, Chapel Hill, North Carolina, United States WILL SAY as follows:

Introduction:

1. I am a physician licensed to practice medicine in the State of North Carolina. I am board certified in the specialty of neonatology.

2. I attended the University of Connecticut as an undergraduate student and graduated with a B.S. degree in Biology in 1982. I completed my medical degree at Albany Medical College and graduated in 1986. I entered pediatric residency training at the Naval Medical Center in San Diego ("NMCTN") in 1989. I was assigned as a general pediatrician to Naval Hospital Guam. After completing a three-year tour of duty in Guam, I entered neonatal fellowship training in 1992 at the University of North Carolina at Chapel Hill. I completed my neonatal training in 1995 and was assigned as a neonatologist to NMCTN. This final tour of duty lasted eleven years.

3. During this period, I served as the Director of Neonatal Intensive Care for NMCTN and the Consultant to the Navy Surgeon General for Neonatal Affairs. After retiring from the Navy in 2006, I was appointed as an Associate Professor in the Division of Neonatal Perinatal Medicine at the University of North Carolina at Chapel Hill.

4. I became the Director of the Perinatal Quality Collaborative of North Carolina and was promoted to Professor in the Department of Pediatrics in the Division of Neonatal-Perinatal Medicine in 2011.

5. I have considerable experience (in a field of very limited experience) in the treatment of trisomy disorders. I am published on the topic of trisomy conditions; and currently one of the co-investigators for a proposal to evaluate the *Care of Children with Trisomy 13 and 18* to be supported by the United States NIH (National Institutes of Health) sponsored

Neonatal Research Network. Currently I serve as the Medical Advisor to the Trisomy Alliance and the Support Organization For Trisomy.

6. Additionally, I am a medical consultant for Be Not Afraid (BNA). BNA is a case management organization stationed in the US whose mission is to support families worldwide with a challenging prenatal diagnosis getting to the live birth they desire and beyond. Families dealing with prenatal diagnoses like Trisomy 13 face incredible resistance from the medical community worldwide in getting the pregnancy and pediatric care they desire for their children. In this role over 11 years and in my role as a clinical neonatologist for 27 years, I have assisted in the care of 35 infants and children with trisomy 13.

7. Attached hereto as Exhibit 1 is a true and correct copy of my curriculum vitae.

8. This statement contains my observations and assessment, based on my education, experience, training, and review of the medical literature, and which I hold to a reasonable degree of medical certainty. In this declaration, I do not speak on behalf of my employer or any institution or organization with which I am affiliated.

9. Unless indicated otherwise, all facts and matters set out in this statement are within my own knowledge and are true. Where I refer to a fact and matter which is not within my own knowledge, it is true to the best of my information and belief.

Background: Trisomy 21, 18 and 13:

10. I make my observations on several issues critical to the case of RN.

11. I have fully reviewed the statements in this case. I acknowledge that they accurately represent current recommendations from major medical organizations regarding general guidelines related to Covid vaccination.

12. I understand that UK Medical Authorities would generally recommend Covid vaccination for RN or for those individuals who suffer from a Trisomy disorder due to their classification as vulnerable individuals.

13. What these declarations fail to consider, as do the randomized clinical trials which are the foundation of the approval for the use of the current Covid vaccines, is the unique molecular features of individuals with an extra chromosome.

14. The generic term for this is aneuploidy and describes an individual with more or less than 46 chromosomes. Typically, humans have 46 chromosomes. When one extra chromosome is present, we call the condition trisomy. RN possesses an unusual partial extra 13 chromosome in all the cells of his body. This is properly considered a partial trisomy 13 condition with the extra chromosome material present in every cell of his body based on testing performed. This is distinguished from mosaic trisomy conditions in which there are some cells with a normal number of chromosomes present.

15. Individuals with trisomies, the most common being trisomy 21 (Down syndrome), followed by trisomy 18 (Edward syndrome) and then trisomy 13 (Patau syndrome), are characterized by variable medical conditions. Organ system impacts can include the heart, the lungs, the kidneys, the endocrine system, the gastrointestinal tract, and the brain. While there are common features in terms of developmental delays and shorter stature, abnormalities in organ systems can be quite variable.

16. *Trisomy* 13 is one of the rarest manifestations of a trisomy disorder. Some of the most severe impacts on organ development, and indeed on developmental potential, are seen in trisomy 13. All individuals have severe cognitive and motor impairment. In individuals with trisomy 13 there are abnormalities in cardiac development, leading to significant heart disease, in 80-90% of cases. Other common features include cleft lip with or without palate, polydactyly, brain anomalies including holoprosencephaly, microphthalmos, and omphalocele.

17. A key question for researchers over the years is what exactly mediates the development of these anomalies? It has been presumed that an extra chromosome and an increase in the production of genetic material leads to these aberrations. This is a very simplistic view which basic researchers now believe may be partly true but is not fully explanatory.

18. Laboratory work has been conducted to determine whether the features of common trisomies in humans, trisomy 21, trisomy 18 and trisomy 13, result from the impact of added gene expression due to an extra chromosome, or a disruption in the balance of chromosome activity and genetic processes due to the additional chromosome. Several gene expression studies of different human tissues have been conducted. Overall, these studies highlight (1) the upregulation of some genes in the trisomic chromosome and (2) dysregulation of the genome as a whole. In essence the abnormal clinical conditions we see in individuals with trisomies are a complex combination of both factors.[1]

19. This complex interplay clearly has consequences on organ development as seen in the multiple medical conditions characterizing individuals with trisomy 13. The pathways are intricate and still not definitively understood by molecular researchers but the path of genetic material proceeds from the chromosome and its individual genes in the cell nucleus to transcription of mRNA, to movement of mRNA out of the nucleus to the cytoplasm. Here mRNA is translated by ribosomes to proteins. Proteins are then dispatched to other cell locations or transported through cell membranes for release into the circulation to travel to distant sites where they perform key regulatory or enzymatic duties.

20. Recognizing this basic processing of genetic material in the cell is critical to understanding why an mRNA vaccine, which will employ cell genetic processes as part of its therapeutic mechanism, deserves special consideration in patients whose genetic processes are perturbed.

21. Each of these processing steps is irreducibly complex and as advanced as we are in understanding these processes, compared to even a decade or two ago, there is much we do not know. There are a host of molecules which regulate every step of these processes.

22. Research in the past 15 years has brought to light how aneuploidy, an abnormal number of chromosomes, by altering the products and reactants in given cell processes due to altered gene copy numbers on the chromosomal scale, can profoundly affect cellular behavior and physiology. This occurs not only during fetal development but is characteristic for critical cellular processes throughout the lifetime of an individual. The last two decades have seen rapid advances in the understanding of the causes and consequences of aneuploidy at the molecular and cellular levels. It is clear aneuploidy imposes general stress on cells that stems from an imbalanced genome and, consequently, also an imbalanced overall protein production profile or proteome. [2]

23. While we do not know all the mechanisms, we know these imbalances in individuals with trisomy 21 have lifelong implications including significant risk for premature aging, development of early Alzheimers, increased risk for developing cancers, and a predilection for developing high blood pressure in the lungs (pulmonary hypertension) and arrythmias.[3,4,5]

24. We do not have similar data in cases of trisomy 13 as it is only over the last decade that we have realized that with medical support some of these individuals can survive for years and even decades.[6]

25. One of the notable effects of trisomy is a reduced ability to react to oxidative stress. This is a critical element of survival. Oxidative stress is a phenomenon caused by an imbalance between production and accumulation of oxygen reactive species (ROS) in cells and tissues and the ability of a biological system to detoxify these reactive products. Damaging oxidative stress occurs due to a reduction in antioxidant defense caused by defects in the defense mechanisms and/or increased reactive oxygen species (ROS) synthesis. When there is an overload of ROS, oxidized damage occurs in biological components and cell components such as proteins, lipids, mitochondria and DNA.[7]

26. Recent studies have shown that mitochondrial dysfunction caused by oxidative stress plays an important role in neuronal damage and neurodegenerative diseases, which can be directly connected to the medical condition's trisomy 13 phenotype. Additionally oxidative stress and failure to detoxify oxygen reactive species is a key component in the development of cardiac failure and myocarditis. ROS and oxidative stress have been noted as critical factors in the development of myocarditis. Oxidative stress overwhelming the capacity of anti-oxidative systems are generated in severe inflammation.[7]

27. This is the mechanism some have proposed for the development of post-Covid vaccination myocarditis. The injected mRNA in the vaccine is translated and results in the production of spike protein presented on the surface of cells. The desired effect is that this spike protein, presented by the patient's cells, will stimulate antibody production and allow development of immunity. It is documented that in some individuals, predominantly young males (variably 5-39 years of age depending on the studies reviewed), that myocardial injury, myocarditis, will develop. It is postulated that the presentation of spike provokes in a minority of vaccine recipients an inflammatory cascade including the secretion of inflammatory cytokines followed by the migration of phagocytes and cytotoxic T cells to the site. This Inflammatory cascade causes tissue damage and myocardial cell death.[8]

mRNA-based vaccine in patients with impaired genetic processing:

28. This process raises issues of concern for those who suffer from a trisomy disorder. As described, individuals with Trisomy 13 have derangements in the processing of DNA, transcription of mRNA and translation of mRNA to proteins based on their abnormal chromosomal number. Additionally, the ability of individuals with trisomy 13 to respond adequately to oxidative injury is impaired.[7]

29. The effectiveness and safety of Covid vaccines in a cohort of any trisomy patients, never mind trisomy 13, has never been studied in randomized clinical trials. The data supporting effectiveness for the Covid vaccines does not include individuals with extra chromosomes. For other vaccines and therapies this makes reasonable sense. Every patient subset cannot

be evaluated for potential efficacy and safety for every therapeutic or vaccine, but in determining the efficacy and safety of an mRNA-based vaccine in patients with impaired genetic processing and reduced ability to limit oxidative stress, caution is warranted. This is an overriding fundamental principle of medical ethics, first to do no harm.

30. While our current understanding of cell processes in trisomy 13 individuals is extremely limited, what we do know makes it clear that processing of DNA and RNA is different than the processing which occurs in humans with 46 chromosomes.

31. We also know that the ability of patients with trisomy 13 to adequately respond to oxidative stress is limited. The basis of the effectiveness of the current Covid vaccines relies on the presumption based on the results of the clinical trials, that individuals have the ability to normally process mRNA (spike protein mRNA) in this case, as well as the ability to mount an adequate response to the oxidative stress that may occur from the immune response generation of spike protein may generate. We have no reason to presume that trisomy 13 individuals challenged with the potential oxidative stress induced by a spike protein mRNA injection would share the same safety profile currently reported for Covid vaccines in 46 chromosome individuals.

32. That being the case, the question becomes is it worth vaccinating a trisomy 13 individual with the hope that the vaccine will prevent disease? Medical intervention, or non-intervention, is always a risk vs benefit calculation.

33. First it should be acknowledged that while some have portrayed myocarditis as rare in vaccinated individuals, recent data suggests it is more common than initially appreciated. Yasuhara et al report alarming rates of 1/12,000 for adolescent males.[9] Israeli data reports a rate of 10/100,000 in 16-24 year olds.[10] A third study reports a rate of 1/30,000 in males 5-39 years after the initial vaccine course.[11]

34. Second, some report that myocarditis is a self-limited event that resolves over weeks. In a review published this month that is not always the case, in fact in this study evaluating 854 adolescent patients, 15.6% of patients were left with left ventricle systolic dysfunction and

a reduced ejection fraction. Most were classified as mild dysfunction, 14.3%, but 1.3% had severe LV systolic dysfunction. These patients are at risk to develop long term cardiac failure and are at risk for sudden death.[9]

35. In June 2021, the US FDA and the CDC held urgent meetings and concluded the mRNA vaccines may cause heart damage or myocarditis in young persons.

36. In 2022 Finland and Sweden limited some Covid vaccines in young males due to the risk of myopericarditis.

37. The only data regarding trisomy patients and myocarditis after Covid vaccine is a relatively small sample size of 1673 vaccinated Down syndrome patients with 3 developing myocarditis (17/10,000) While a small sample, and definitive conclusions regarding adverse effect rates in the Down syndrome population should not necessarily be drawn here, it does portend that there may be more risks certainly to trisomy 21 patients than those with a normal number of chromosomes. There is no data related to trisomy 13 individuals.[12]

38. The risk vs benefit calculation must be applied. What is the risk to RN for the contraction of severe Covid? There is no reliable data reporting the risk for hospitalization or ICU admission for Covid based on age. World data for infection fatality rate, however, has been published based on age. For individuals 20-29 years of age the infection fatality rate is 2/100,000.[13]

39. RN's risk for death from Covid disease is harder to quantify. The fatality rate for 20–29-year-olds is 2/100,000 for Covid, but it is reasonable to ask if RN's risk is different given his trisomy 13?

Comments on Other Expert Testimony

40. We do not have any significant population data for morbidity and mortality from Covid for any trisomy individuals, never mind individuals with trisomy 13. Dr. D cites an article reporting an increased risk for hospitalization from Covid for individuals with learning

disabilities in the UK.[14] It is difficult to apply the data generated from this study to particular patient populations.

41. The overarching problem in this study is the definition of a Covid hospitalization or death. Is it death or hospitalization with or from Covid? This is the challenge the world has faced.

42. We know well we were testing for Covid using a PCR technology not created for general population screening for virus, certainly in asymptomatic individuals.[15] The limitations and variability in running PCR tests on such a massive scale have been described.[16] Further, populations we decided reasonably as possibly at risk were likely tested far more intensively than other groups of patients.

43. In addition, the subgroups that make up a "learning disabled" population, like Down syndrome patients, often have significant underlying medical conditions which, Covid aside, make them more likely to require hospitalization.

44. Last, categorically stating the "learning disabled" are at higher risk is medically naïve. Individuals are learning disabled for a multitude of reasons and this conclusion more likely describes a group that was more exhaustively tested for Covid than those without such disabilities.

45. Dr. D uses a critical reference to support the following key statements made by him.[17]

46. From Dr. D, "although some cardiac issues have been raised that are attributable to the vaccine, cardiac issues (typically this means myocarditis) are worse following natural infection than cardiac issues associated with vaccination even with sequential (i.e booster) dosing."

47. From Dr. D, "Young males may be more at risk from particular vaccine regimes from a myocarditis perspective, but there are alternative explanations for those findings, and also alternative vaccine strategies that are not encumbered by such concern."

48. A careful reading of the reference provided by Dr. D reveals a key finding he fails to mention. The article clearly states that there is a markedly increased risk for myocarditis after vaccination in men less than 40. When all ages are looked at this is not the case, but RN is 24 and in the myocarditis high risk group now being recognized by experts around the world.

49. RN absolutely is in the group of patients at highest risk for developing myocarditis after a Covid vaccine and despite the statement by Dr. D, the article offers no alternative explanations for the development of myocarditis in younger men receiving these vaccines.

50. The article Dr. D uses as a reference definitively states that the findings of increased risk for myocarditis in younger men has been reproduced in multiple other studies.[18,19]

51. In fact the reference Dr., D uses to justify his position that RN should be vaccinated clearly states, "The risk of vaccine-associated myocarditis is consistently higher in younger men (<40 years of age), particularly after a second dose of mRNA-1273, where the number of additional events during 28 days was estimated to be 97 per million people exposed. An important consideration for this group is that the risk of myocarditis after a second dose of mRNA-1273 was higher than the risk after infection."

52. The article goes on to state, "These findings may justify some reconsideration of the selection of vaccine type, the timing of vaccine doses, and the net benefit of booster doses in young people, particularly in young men."

Application of Medial Analysis to RN:

53. I have had the opportunity of examining the Medical Records of RN; and his mother has been available to discuss any particular issues.

54. RN is a young male who based on his age and sex is at higher risk for myocarditis following Covid vaccination.

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55. Based on knowledge of derangements in cellular processes in trisomy 13, and the established means by which Covid vaccines trigger an immune response, he is likely at an even higher risk for myocarditis and other adverse events related to Covid vaccination.

56. Based on the data we have, the risk for RN for myocarditis would be approximately 10/100,000 to 1/12,000.[9,10.] His risk for death from Covid is 2/100,000.[13]

57. His risk for a severe adverse event in this case, with vaccination, based on the data we have, is 5- times higher than his risk for death from Covid.

58. It would require denying current knowledge about trisomy 13, its impact on genetic processing and diminished ability to react to oxidative stress, and the data we have on vaccine related myocarditis and risk for death from Covid for RN, to not presume that RN's risk for an adverse reaction, especially myocarditis, would be elevated above the predicted 1/12,000 to 10/100,000 incidence of myocarditis for his sex and age, which is only further complicated by the inherent vulnerabilities associated with trisomy.

Conclusion:

59. In my opinion there is significant risk to exposing RN to the current Covid vaccines.

60. The risk is significant due to his age, sex and his chromosomal constitution.

61. The benefit of vaccination is far less than the risk we are able to calculate.

62. In my professional opinion, it would not be in RN's 'best interests' medically to be given the Covid vaccinations.

63. The care of those with trisomy is a highly individualized process. The personal care of any individual is subject to considerable variability and the particular needs of any individual.

Those with trisomy 13 (and partial trisomy 13) were traditionally deemed to be "lethal" or have at best a very limited lifespan, often under a year. Medical advances have made great strides in recent years and many individuals with trisomy go on to have complex but fulfilling lives.

64. RN has entered his third decade. This would be due in large part to the devotion and commitment of RN's mother to overseeing his health and working tirelessly to develop, in partnership with the medical community, intricate, personalized care regimens.

65. In my professional medical opinion, it would be erroneous to disrupt RN's highly successful, individualized, and successful caring collaboration without clear identification of an individualized benefit for him to vaccination.

66. The benefit of the drastic and potentially dangerous step of mandating RN be vaccinated is simply not established in this case.

I believe that the facts stated in this witness statement are true. I understand that proceedings for contempt of court may be brought against anyone who makes, or causes to be made, a false statement in a document verified by a statement of truth without an honest belief in its truth.

SIGNED: *Martin J McCaffrey*

Professor McCaffrey

DATED: *01 March 2023*

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