IN THE UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF OHIO
EASTERN DIVISION

DERIC REES AND CEONDA REES, INDIVIDUALLY AND AS NEXT FRIEND AND GUARDIAN OF BABY T.W.B. ON BEHALF OF THEMSELVES AND ALL OTHERS SIMILARLY SITUATED.
Plaintiff,

VS. **CASE NO. 3:18-cv-0511**

MCKESSON CORPORATION;
CARDINAL HEALTH, INC.;
AMERISOURCEBERGEN CORPORATION;
PURDUE PHARMA L.P.;
PURDUE PHARMA, INC.;
THE PURDUE FREDERICK COMPANY, INC.;
TEVA PHARMACEUTICAL INDUSTRIES, LTD.;
TEVA PHARMACEUTICALS USA, INC.;
CEPHALON, INC.;
JOHNSON & JOHNSON;
JANSSEN PHARMACEUTICALS, INC.;
ORTHO-MCNEIL-JANSSEN PHARMACEUTICALS, INC. n/k/a JANSSEN PHARMACEUTICALS, INC.;
JANSSEN PHARMACEUTICA INC. n/k/a JANSSEN PHARMACEUTICALS, INC.;
ENDO HEALTH SOLUTIONS INC.;
ENDO PHARMACEUTICALS, INC.;
ALLERGAN PLC f/k/a ACTAVIS PLC;
WATSON PHARMACEUTICALS, INC. n/k/a ACTAVIS, INC.;
WATSON LABORATORIES, INC.;
ACTAVIS LLC; and
ACTAVIS PHARMA, INC. f/k/a WATSON PHARMA, INC.,

Defendants.
_____/

MEMORANDUM IN SUPPORT INCLUDING DEDICATED NEONATAL

ABSTINENCE SYNDROME LITIGATION TRACK CLASS

NOW COME Plaintiffs and Putative Class Representatives Deric Rees and Ceonda Rees as the next friend of Baby T.W.B., individually and on behalf of all other similarly situated who suffer Neonatal Abstinence Syndrome, hereby presenting this memorandum supporting the Plaintiffs' proposed Case Management Order. In support thereof, Plaintiffs state as follows:

I. INTRODUCTION AND JURISDICTION

Infants born with Neonatal Abstinence Syndrome present this Honorable Court with a unique opportunity to assure delivery of life-changing medical intervention and a chance at a productive adult life. Members of this putative class by definition suffer from neurotoxic drug exposures, bear no contributory fault whatsoever, and share common issues of fact and law revolving around the fault of the Defendants.

Tens of thousands of infants born in the US each year develop NAS, and the number has increased nearly 5-fold between 2000 and 2012 and continues to grow. The period of hospitalization for NAS averages 16 days and hospital costs for a typical newborn with NAS are $159,000-$238,000 greater than those of healthy newborns. Recent evidence shows that long-term cognitive development is impaired in these children and will require comprehensive therapy from physicians and nurses, speech and language therapists, physical and occupational therapists, early enrichment programs, special education programs, and later assistance with job or vocational training. The long-term care and therapy required for NAS infants cannot be underestimated.

As of today, undersigned counsel will have filed federal class actions in West Virginia, Illinois, California, and Missouri[1] seeking equitable relief and money damages aimed at securing

[1] Civil Action Nos.: West Virginia (2:18-cv-00385), Illinois (3:18-cv-00511), California (pending), Missouri (4:18-cv-00352).

dedicated funding to help alleviate the suffering visited upon this wholly innocent class by the Defendants. The instant Rees matter is a class action filed in the Federal Court for the Southern District of Illinois and was recently transferred to the MDL without objection, and the transfer of the West Virginia and Missouri class actions are currently pending.

Due to what can only be categorized as an epidemic of addicted newborns , we propose the establishment of a separate Infant NAS Litigation Track which consolidates all four class actions for class discovery and that the West Virginia and Illinois cases move forward before this Court for determination of Class Certification and Partial Summary Judgment on the Issue of Liability. In the event of success on the issue of Class Certification, the cases will be transferred to their original districts for trials on the merits. Underlying this strategy is the hope that as the issues of fact and law are developed an agreement can be reached creating a nationwide settlement class.

II. PURPOSE OF NEONATAL ABSTINENCE SYNDROME CLASS ACTIONS

This class action aims to secure dedicated, Court-administered funding from the Defendants for medical monitoring, medical treatment, and compensatory/punitive damages for a Class of infants diagnosed at birth with Neonatal Abstinence Syndrome (NAS).

Avoiding the Mistake of the Tobacco Settlements

The importance of insuring delivery of injunctive relief to NAS babies makes critical the need for court administration of any monies awarded to pay for medical monitoring and treatment so that such funds cannot be diverted to other purposes.

While counties, cities, and states certainly deserve the reimbursements they seek from the Defendants in related cases, there exists the very real possibility that sovereign government entities may divert such reimbursements to other legitimate state interests as happened on occasion with funds allocated to states from the Tobacco Settlements.

Dedicated, court-administered funding for the NAS Class also will provide budgetary relief for governmental entities because it will place responsibility where it belongs- on Big Pharma and not on cash-strapped, politically-vulnerable state Medicaid budgets.

Equitable Relief Requiring Defendants to Fund Medical Monitoring and Treatment

It cannot be disputed that babies born with Neonatal Abstinence Syndrome come into this life experiencing extreme pain and distress, suffer altered brain development and face an increased risk of latent medical conditions caused by their ecurrent and prolonged *in utero* opioid exposures. A central feature of the NAS Class Actions is that they seek equitable relief in the form of a Court-administered replenishing, dedicated no limit fund to provide medical monitoring and medical treatment for the benefit of the Class Members who face continued medical and developmental challenges throughout life stemming from their exposure in the womb.

One area of concern that might not come to mind when considering risks these babies face is the fact that they are more susceptible to speech and language disorders. It is encouraging to note that testing and intervention are readily available. The Goldman-Fristoe Test of Articulation measures the ability of children up to age three to produce age-appropriate speech sounds. Later, the Preschool Language Scale Test can be used to measure the child's ability to receive and process words that are spoken to them and measures child's skills to express thoughts and ideas. Left untreated a child may be unable to express basic wants or needs, experience difficulties in learning to read and may be unable to interact with others. Early intervention and placement with a licensed speech therapist is proven to be effective and most children are released from speech therapy by age nine but the total cost for such testing and treatment may easily reach into the tens of thousands of dollars per child. Undiagnosed or

untreated speech disorders can ruin a child's life, but the medical risks extend to every system in the body. Earlier intervention improves the prognosis, shortens duration of treatment and reduces the burden on any medical fund that may be eventually established.

It is a medical fact that babies born addicted to opioids face an increased risk of an array of different conditions. These often include, but are not limited to, speech disorders, cognitive delays, behavioral disorders, movement and coordination problems, limited resilience and stress disorders.

These babies are born with altered brain development, which generally result from smaller numbers and impaired development of brain cells (neurons), decreased growth of nerve fibers (axons and dendrites), and substantial reductions in the connections (synapses) between brain cells in adjacent or remote regions of the brain. How the opioids cause the impaired brain development has been established through animal studies that were confirmed by brain imaging studies in human subjects.

Please find attached for the Court's further edification a brief report by Dr. Anand which explains in further detail the necessity for babies born addicted to opioids to have access to medical monitoring and treatment.

Money Damages to Fund a Start into a Productive Adult Life

Most infants diagnosed with NAS are born into financially difficult circumstances such that upon reaching the age of majority many will not have the resources for a successful start into adulthood life. Money damages placed in trust with a Guardian ad Litem can provide these children with a much-needed springboard into a productive adult life.

The NAS Class Actions filed by undersigned counsel seek class-wide readily-calculable money damages to compensate Class Members for medical expenses associated with the

immediate post-birth treatment protocol for NAS. These damages will reach into and beyond tens of thousands of dollars per infant and are easilty known via analysis of medical billing codes. While many of the medical bills are likely subject to statutorily mandated Medicaid reimbursement, such reimbursements typically only take a portion of the total medical expenses and are often resolved on a class-wide basis on favorable terms to Class Members.

Additionally, in the event of a class-wide settlement it is likely that multiplier will be applied to compensate for non-class, follow-on damages for pain, suffering and emotional distress that will more than offset any reimbursements to Medicaid such that a very substantial economic benefit be conferred to the Class.

Mingo County Coal Slurry Litigation as Model

Mingo County, West Virginia lies nestled against Virginia and Kentucky in the extreme southwestern part of West Virginia. Mingo is a place with a violent, tragic history. It is the home of Putative Class Representatives Walter and Virginia Salmons.

Eric Eyre, a Charleston Gazette reporter, won a Pulitzer Prize last year for his coverage of the Opioid Crisis. His reporting brought light the fact in that Big Pharma shipped over 20 million opioid pills to this impoverished county of only 25,000 people.

Opioids are not the first neurotoxin to poison the children of Mingo County.

The children of Mingo County town called Rawl were poisoned by lead-laden coal slurry injected abandoned mines near the domestic water wells their families depended on for drinking water. As with opioids, the lead in the coal slurry damaged the child's brains. As with opioids, the developmental damage of coal slurry effected not only their childhood but their entire lives. As with opioids, the victims of coal slurry were often born into dire economic circumstances.

The West Virginia Supreme Court transferred the matter to West Virginia's Mass Litigation Panel. Once there the litigation moved on a fast track which resulted in the certification of settlement class establishing a $5 million trust to fund the equitable relief of a community-wide medical monitoring program and a money damages settlement matrix which awarded $35 million in damages for individual non-class money damages for an array of causes actions sounding in property, tort and personal injury.

In the interceding seven years, hundreds of those poisoned by coal slurry in Rawl have taken advantage of the medical monitoring program. Now that the first three rounds of medical testing have been completed, a team of epidemiologists is analyzing the data to develop testing and treatment protocols for use by the residents' treating physicians to address the novel health care challenges facing this poisoned population.

Those children of Rawl each got a head start into adult life on their eighteenth birthday when the QSF Trustee distributes their money damages. The result has been heartwarming. Brittany Sammons, like many others, used her money to secure an education, became a nurse and now is starting a family of her own. Many others used their money to buy trucks, moved to cities where jobs were available and started productive adult lives.

Money is going to be a necessity if these children born with NAS are to have a chance at a productivity. Unless provided an opportunity to start a productive adult life, many of the Class Members will become a drain on government-sponsored assistance programs for decades to come. Big Pharma's greed caused these problems. Big Pharma should pay for their greed, not the taxpayers and certainly not the children who are nothing but innocent victims. The NAS Class Actions provide a vehicle to achieve this noble goal.

III. LIMITED-LITIGATION TRACK FOR NAS CLASS ACTIONS

A limited-litigation track dedicated to the NAS Class action provides the most efficient way to surmount any barriers that may exist to a global resolution benefiting tens of thousands of blameless children who were born addicted to opioids and who face innumerable challenges caused by the actions of the Defendants.

Designations of "Test" NAS Class Actions

Undersigned counsel respectfully suggest that the Court designate the putative NAS class actions filed in Charleston, West Virginia and East St. Louis, Illinois as test cases. Test NAS class actions present a scenario in which "bellwether class actions" provide the most logical path to global resolution of the barriers to settlement.

Anticipated defenses based on varying state law jurisprudence across the country made the prospect of litigating the certification of nationwide class action filed in a single state less favorable to the plaintiffs than the prospect of filing individual federal class actions in separate states with pleadings tailored to the idiosyncrasies of each state's jurisprudence for tort liability and equitable relief. Successful test class actions, however, certainly pave the way for the negotiation and certification of a nationwide settlement class delivering the global resolution demanded by the plight of tens of thousands brain-damaged babies born addicted to opioids.

West Virginia and Illinois Class Actions as Test Cases

Undersigned counsel suggest that this Honorable Court select the federal class actions filed in West Virginia and Illinois as test cases to which the concept of "limited litigation" be applied.

Salmons v. Purdue, [2:18-cv-00385], the West Virginia case, is an obvious choice because West Virginia's catastrophic experience with the opioids and the Big Pharma's early targeting of the Mountain State have made that venue not only ground-zero for the burgeoning NAS epidemic but has also fostered an iron-will among West Virginia's health care community to address what is quickly becoming an existential threat to state already facing extreme economic and public health challenges.

Rees v. McKesson [3:18-cv-00511], the Illinois NAS class action, should be chosen as a bellwether NAS class action because this action in East St. Louis, Illinois will bring an element of diversity reflecting the fact that opioid addiction reaches across racial divides. There is an incorrect and racially-insensitive perception that the opioid crisis is a problem primarily afflicting rural, white populations. This is simply untrue. Addiction is not restricted to color or population density. Undersigned counsel suggests that selecting the Melvin Price Federal District Courthouse in East St. Louis, Illinois as the venue for one of the bellwether-class action trials will support global resolution by reinforcing the notion that opioid epidemic affects every demographic segment of the United States.

Scope and Sequencing of Test Cases

Undersigned counsel suggests the entry of a Case Management Order in which discovery, class certification and dispositive motion practice be presided over by Judge Polster in Cleveland after which point the cases would be transferred back to their respective venues of origination for trial on the merits.

Discovery

Undersigned counsel suggest that a Case Management Order be entered which streamlines the discovery process as follows:

- Allow Use of Discovery Responses from Other MDL Cases- As the Court pointed out in its February 4, 2018 order there seem to exist common issues of fact and law among claims as diverse as governmental claims and individual wrongful death claims. Rather than force the Defendants to defend duplicative depositions and answer repetitive written discovery responses, undersigned counsel suggest that discovery responses from other MDL cases be available for use in the NAS Class Actions. Federal District Judge John T. Copenhaver, USDC S.D.W.V., implemented a similar process in a recent class action in which attorneys litigating claims in a parallel action before West Virginia's Mass Litigation Panel were permitted to participate in depositions noticed pursuant to the parallel federal action. *Good v. American Water, et al,* 2:14-cv-1374, (USDC, S.D.W.V.)

- Limitations on Depositions Taken by Plaintiffs During Class Certification Phase- If the Plaintiffs in the NAS Class Actions are given the opportunity to use deposition testimony and written discovery responses adduced in other MDL cases, then limiting non-expert depositions of Defendant personnel to only a single 30(b)(6) corporate deposition of each Defendant would do no prejudice to the Plaintiffs and create efficiencies inuring to the benefit of all parties.

- Expedited Discovery of the CDC- Upon information and belief, undersigned counsel posit that the United State Centers of Disease Control is in possession of evidence going to class issues of ascertainability, numerosity, predominance and superiority. While it is anticipated that Plaintiffs' Counsel in other cases before

the MDL will conduct vigorous discovery of other federal agencies, CDC is believed to possess critical evidence involving issues of epidemiology and medicine that will be much more probative of the issues presented by the NAS Class Actions than the issues presented by the governmental entity and hospital parties.

Motion Practice

Undersigned Counsel suggest that the Court enter a Case Management Order setting forth a briefing schedule for the following motions:

- Motion for Appointment of Interim Class Counsel- Undersigned Counsel intends to file a motion for appointment of Interim Class Counsel so that the interests of this unique class are represented by attorneys who have already been working with experts and developing evidence in support of certifying NAS Class Actions.
- Motion for Class Certification- Given the Court's Order of February 4, 2018 already explored the idea that there are issues of common fact and law relating to the Defendants' liability, litigating the issue of Class Certification before Judge Polster is compatible with the fact that such common issues exist across the various types of plaintiffs before the Court.
- Motion for Partial Summary Judgment- A great deal of evidence has already been collected that would support a motion for partial summary judgment. Undersigned Counsel suggests that the CMO include a briefing schedule to run concurrently with the Class Certification briefing schedule.

Schedule

Undersigned Counsel suggests the following schedule:

Class Discovery Cut-off-	September 1, 2018
Class Certification Brief Due-	October 1, 2018
Partial Summary Judgment Motion Due-	October 1, 2018
Class Certification Response Due-	November 1, 2018
Partial Summary Judgment Response Due-	November 1, 2018
Class Certification Reply Due-	November 15, 2018
Partial Summary Judgment Reply Due-	November 15, 2018
Class Certification Hearing-	December 15, 2018
Partial Summary Judgement Hearing-	December 15, 2018

Bellwether Class Action Trials

Undersigned Counsel suggest that in the event that the Plaintiffs are successful in certifying the West Virginia and Illinois Trials that those two cases be transferred to their respective transferor courts for limited merits discovery, final dispositive motions and trial.

IV. CONCLUSION

Considering the foregoing, we respectfully ask this Court for special consideration of classes of individuals who through no fault of their own suffer some of the most egregious injuries arising out of the opiate epidemic. The circumstances of these enfants and children are unique and call for expedited consideration of this Honorable Court.

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EXPERT REPORT OF
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(A) Background and Qualifications

I am a pediatrician specialized in the care of critically ill newborns and children. For more than 30 years, I have conducted intensive research and study on the development of pain/ stress in human newborns, their development during early childhood, and long-term outcomes.

I received a M.B.B.S. (Bachelor of Medicine/Bachelor of Surgery, equivalent to an M.D.) from Mahatma Gandhi Memorial Medical College in Indore, India. After post-doctoral training in Pediatrics, I received a Rhodes Scholarship to University of Oxford, UK, where I received the degree of D.Phil. (Doctor of Philosophy) for my scientific research on hormonal and metabolic responses of newborns to the pain/stress caused by surgical operations and effects of anesthesia. Additional post-doctoral training was acquired at the John Radcliffe Hospital in Oxford, at the Children's Hospital in Boston, and at Massachusetts General Hospital in Boston, including a pediatric residency and fellowship training in neonatal and pediatric critical care medicine.

Since then, I have held academic appointments at the University of Oxford, Harvard Medical School, Emory University School of Medicine, University of Arkansas for Medical Sciences, University of Tennessee Health Science Center and Stanford University School of Medicine, where I served as Division Chief of Pediatric Critical Care, Department of Pediatrics (2015-2016) and where I remain presently employed. From University of Arkansas I received the Morris & Hettie Oakley Endowed Chair in Pediatric Critical Care Medicine and from University of Tennessee Health Science Center I received the St. Jude Chair for Excellence in Critical Care Medicine. I serve as a fully tenured Professor of Pediatrics, Anesthesiology, Perioperative & Pain Medicine at Stanford University School of Medicine, and as Director of the Pain/Stress Neurobiology Laboratory at Children's Hospital Research Institute. I have received competitive grant funding for my research from the U.S. National Institutes of Health, the European Economic Commission, and other grant funding agencies. My clinical appointment at Lucile Packard Children's Hospital, as an Attending Physician, allows me to provide care for the patients admitted to the Pediatric Intensive Care Unit. I am a diplomate of the American Board of Pediatrics and the Sub-Board of Pediatric Critical Care Medicine, and licensed to practice medicine in the States of California and Tennessee; I have previously held medical licenses in the States of Massachusetts, Georgia, and Arkansas, and in the United Kingdom and India.

I have authored 311 scientific publications (125 in the last 10 years), edited 9 books, and received numerous professional awards. These include the Dr. Michael Blacow Award from the British Paediatric Association (1986), Pediatric Resident Research Award from the American Academy of Pediatrics (1992), the *inaugural* Young Investigator Award in Pediatric Pain from the International Association for the Study of Pain (1994), the Jeffrey Lawson Award from the American Pain Society (2000), the Windermere Honorary Lectureship from Royal College of Paediatrics and Child Health (2004), the Joan M. Cranmer *"Mentor of the Year"* Award (2007) from University of Arkansas, the Nils Rosén von Rosenstein Award from the Swedish Academy of Medicine and Swedish Paediatric Society (2009), the 9th Annual "In Praise of Medicine" Keynote Award for the Centennial Ceremony of Erasmus University Medical Center (2013), and the Nightingale Excellence Award for Physicians (2016) from Stanford Children's Healthcare. For community service, I have received the Father Joseph Biltz Award (2007) from the National Conference for Community & Justice (NCCJ) and the Dr. Martin Luther King "Salute to Greatness" Individual Award (2008) from the State of Arkansas, recognition from the Rotary Club International

and numerous other civic bodies. Attached as Appendix A are my Curriculum Vitae and a brief Biosketch, which list the additional details of my academic background, positions, research and publications.

(B) Summary of Opinion

1. Immediate Hospitalization

The neonatal abstinence syndrome (NAS) is a generalized multi-system disorder that produces a constellation of symptoms in neonates, and results from abrupt discontinuation of opioids consumed by the mother during pregnancy at the infant's birth. Approximately 13,500 infants born in the US each year develop NAS, and this number has increased nearly 5-fold between 2000 and 2012[1], with continued increases since then. The period of hospitalization for NAS averages 16 days[2] and hospital costs for a typical newborn with NAS are $159,000-$238,000 greater than those of healthy newborns**.**

At-risk neonates remain in the hospital for observation, supportive care and opioid replacement therapy. All infants born to mothers with opioid use disorders are at high risk for developing NAS and there are no well-defined strategies to prevent NAS from occurring in at-risk infants. Supportive measures are the standard of care, and pharmacotherapy is often initiated to treat their inability to sleep, lack of weight gain, inadequate caloric intake, extreme irritability, seizures and hypertonicity. If a neonate is treated with an opioid, the drug has to be gradually tapered as the infant regains the capacity for self-regulation.

Morphine and methadone are the most commonly used agents for opioid replacement therapy. When methadone is used for treatment of NAS, newborns are exposed to an opioid with a long half-life. The cytochrome P450 liver enzymes (CYP3A4, CYP2B6 and CYP2D6) that metabolize methadone are immature at birth, but the measured half-life of methadone in neonates is similar to that of adults.[3] Because of its shorter half-life, morphine can be administered every 3 to 4 hours, which enables rapid dose adjustments in response to changes in the severity of NAS. Methadone and morphine use in neonates are associated with reduced brain and somatic growth[4], intractable nystagmus, altered visual evoked potentials and a delayed encephalopathy. Morphine therapy is associated with respiratory depression, bradycardia, hypotension, urinary retention, reduced gut motility, emesis, or other adverse effects; but these occur less frequently in opioid-tolerant neonates presenting with NAS.

2. NAS Increases Risk to the Infant:

Major risks from prenatal opioid exposure include birth defects (early pregnancy), altered brain development (throughout pregnancy) and NAS (late pregnancy). Recent evidence shows that long-term cognitive development is impaired in children born to opioid-addicted mothers[5]. Therefore, the long-term care and therapy required for NAS infants cannot be underestimated.

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[1] Patrick SW, Dudley J, Martin PR, et al. Prescription opioid epidemic and infant outcomes. *Pediatrics*. 2015; 135(5):842-850.

[2] Patrick SW, Schumacher RE, Benneyworth BD, Krans EE, McAllister JM, Davis MM. Neonatal abstinence syndrome and associated health care expenditures: United States, 2000-2009. *JAMA.* 2012;307(18): 1934-1940

[3] Ward RM, Drover DR, Hammer GB, et al. The pharmacokinetics of methadone and its metabolites in neonates, infants, and children. *Paediatr Anaesth.* 2014;24(6):591-601

[4] Welle-Strand GK, Skurtveit S, Jones HE, et al. Neonatal outcomes following in utero exposure to methadone or buprenorphine: a Noational Cohort Study of opioid-agonist treatment of Pregnant Women in Norway from 1996 to 2009. *Drug Alcohol Depend*. 2013; 127(1-3): 200-206

[5] Nygaard E, Moe V, Slinning K, Walhovd KB. Longitudinal cognitive development of children born to mothers with opioid and polysubstance use. *Pediatr Res.* 2015;78(3):330-335.

Opioid use in pregnancy is associated with increased preterm labor, early onset delivery, poor fetal growth, prematurity and stillbirth.[6] Another study found increased odds of intrauterine growth restriction (2·7-fold), placental abruption (2·4-fold), preterm labor (2·1-fold), oligohydramnios (1·7-fold), stillbirth (1·5-fold), and premature rupture of membranes (1·4-fold) associated with illicit opioid use.[7] Preterm birth occurred 3 times more commonly in primiparous mothers hospitalized for opioid abuse (± other drugs) and their babies were 6 times more likely to require NICU admission.[8] Improved neonatal outcomes can result from structured treatment programs.[9]

Animal studies suggest an association of prenatal opioids with increased incidence of neural tube defects.[10] One large, multicenter study found severe heart defects (conoventricular septal defects: odds ratio 2.7, atrioventricular septal defects: odds ration 2.0, hypoplastic left heart syndrome: odds ratio 2.4), spina bifida (OR, 2.0), and gastroschisis (OR, 1.8) in infants associated with maternal intake of opioids.[11] Buprenorphine is considered an attractive alternative, partly due to more favorable neonatal brain growth patterns[11], but its long-term use has been associated with poor child outcomes to 3 years of age.[12] A population-based study from Finland found birth defects in 10% of children from mothers receiving buprenorphine in pregnancy; mostly involving congenital heart disease, urinary collecting system defects, ophthalmic and maxillofacial defects.[13]

Prenatal opioid exposure impair nerve myelination by disrupting oligodendrocyte development,[14] decrease dendritic growth[15] and branching patterns of cortical neurons, lower cell proliferation and neuronal migration to the cortical plate. These effects reduce regional brain volumes in the basal ganglia[16] and other brain areas,[17] with long-term changes in subsequent behavior,[18] autonomic

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[6] Whiteman VE, Salemi JL, Mogos MF, Cain MA, Aliyu MH, Salihu HM. Maternal opioid drug use during pregnancy and its impact on perinatal morbidity, mortality, and the costs of medical care in the United States. *Journal of pregnancy.* 2014;2014:906723.

[7] Maeda A, Bateman BT, Clancy CR, Creanga AA, Leffert LR. Opioid abuse and dependence during pregnancy: temporal trends and obstetrical outcomes. *Anesthesiology.* 2014;121(6):1158-1165.

[8] Bonello MR, Xu F, Li Z, Burns L, Austin MP, Sullivan EA. Mental and behavioral disorders due to substance abuse and perinatal outcomes: a study based on linked population data in New South Wales, Australia. *International journal of environmental research and public health.* 2014;11(5):4991-5005.

[9] McCarthy JJ, Leamon MH, Willits NH, Salo R. The effect of methadone dose regimen on Neonatal Abstinence Syndrome. *Journal of addiction medicine.* 2015.

[10] McCarthy JJ, Leamon MH, Willits NH, Salo R. The effect of methadone dose regimen on Neonatal Abstinence Syndrome. *Journal of addiction medicine.* 2015. Yazdy MM, Mitchell AA, Tinker SC, Parker SE, Werler MM. Periconceptional use of opioids and the risk of neural tube defects. *Obstet Gynecol.* 2013;122(4):838-844.

[11] Broussard CS, Rasmussen SA, Reefhuis J, et al. Maternal treatment with opioid analgesics and risk for birth defects. *Am J Obstet Gynecol.* 2011;204(4):314 e311-311.

[12] Kivisto K, Tupola S, Kivitie-Kallio S. Prenatally buprenorphine-exposed children: health to 3 years of age. *Eur J Pediatr.* 2015.

[13] Kivisto K, Tupola S, Kivitie-Kallio S. Prenatally buprenorphine-exposed children: health to 3 years of age. *Eur J Pediatr.* 2015

[14] Vestal-Laborde AA, Eschenroeder AC, Bigbee JW, Robinson SE, Sato-Bigbee C. The opioid system and brain development: effects of methadone on the oligodendrocyte lineage and the early stages of myelination. *Dev Neurosci.* 2014;36(5):409-421.

[15] Lu R, Liu X, Long H, Ma L. Effects of prenatal cocaine and heroin exposure on neuronal dendrite morphogenesis and spatial recognition memory in mice. *Neurosci Lett.* 2012;522(2):128-133.

[16] Yuan Q, Rubic M, Seah J, et al. Do maternal opioids reduce neonatal regional brain volumes? A pilot study. *J Perinatol.* 2014;34(12):909-913.

[17] Walhovd KB, Moe V, Slinning K, et al. Volumetric cerebral characteristics of children exposed to opiates and other substances in utero. *Neuroimage.* 2007;36(4):1331-1344

[18] Conradt E, Sheinkopf SJ, Lester BM, et al. Prenatal substance exposure: neurobiologic organization at 1 month. *J Pediatr.* 2013;163(4):989-994 e981. Coyle MG, Salisbury AL, Lester BM, et al. Neonatal neurobehavior effects following buprenorphine versus methadone exposure. *Addiction.* 2012;107 Suppl 1:63-73. Fodor A, Timar J, Zelena D. Behavioral effects of perinatal opioid exposure. *Life Sci.* 2014;104(1-2):1-8.

regulation,[19] visual-motor,[20] strabismus,[21] or swallowing[22] dysfunctions and lower developmental potential.[23] Thus, infants, toddlers, and children diagnosed with NAS in the newborn period will require comprehensive therapy from physicians and nurses, speech and language therapists, physical and occupational therapists, early enrichment programs, special education programs, and later assistance with job or vocational training.

Many newborns are exposed to repetitive or continuous pain because of their prolonged hospitalizations and associated comorbidities, which accentuates their suffering from NAS. Drug abusing mothers are often abandoned by their families, criminalized by society and burdened with a social stigma. The mother-infant dyads often face an unstable social environment. Even social and healthcare workers may treat them with contempt and may be unwilling to offer the most effective NAS treatments to their infants in the hospital or the clinic. These barriers to improving their medical care contribute to poor knowledge uptake and practice changes by health-care providers, nursing, and family members.[24]

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I certify under penalty of perjury that the forgoing curriculum vitae of Kanwaljeet S. Anand is true and correct.

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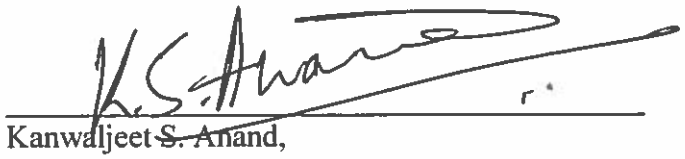

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I certify under penalty of perjury that the forgoing expert report, prepared by Kanwaljeet S. Anand, M.B.B.S., D.Phil., FAAP, FCCM, FRCPCH, is true and correct.

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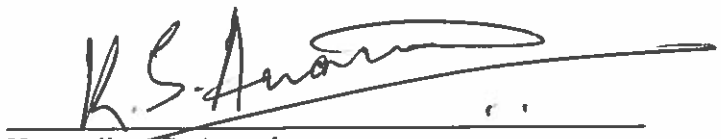

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