UNITED STATES DISTRICT COURT
FOR THE
DISTRICT OF VERMONT

KEVIN DRAKE and LORI DRAKE, individually and as next friend of J.D. Plaintiffs, v. ALLERGAN, INC. Defendant.	:	Case No. 2:13-cv-234

Opinion and Order

Plaintiff J.D. is a minor whose parents, Kevin and Lori Drake, filed claims individually and as next friend of J.D. against Defendant Allergan, Inc. ("Allergan"), the manufacturer of Botox. J.D. has cerebral palsy. His doctor injected Botox into his calves to treat his lower limb spasticity. The Plaintiffs claimed that these injections caused J.D. to develop a seizure disorder.

After a thirteen-day trial, the jury found that the Plaintiffs had proven that Allergan was negligent and that J.D. suffered injuries as a result of that negligence. ECF No. 201 (jury verdict form). The jury also found that punitive damages should be awarded. *Id.* The jury did not find, however, that the Plaintiffs had proven that Allergan violated the Vermont Consumer Fraud Act. *Id.*

The parties have filed post-trial motions. Plaintiffs move for judgment incorporating the jury's verdict. ECF No. 206. Allergan renews its motion for judgment as a matter of law or, in the alternative, moves for a new trial. ECF No. 207. For the reasons described in detail below, the Court **grants** Plaintiffs' motion and **denies** Allergan's motions. The Court will enter judgment in favor of the Plaintiffs incorporating the jury's verdict.

I. Relevant Background

Allergan manufactures Botox, an injectable prescription drug that includes botulinum toxin type A as its active ingredient. When injected into a muscle, Botox temporarily blocks the nerve impulses that trigger muscle contractions.

Individuals with cerebral palsy often experience spasticity, or tightness in their limbs. The Food and Drug Administration ("FDA") has not approved Botox as a treatment for pediatric spasticity. Any administration of Botox for that purpose is known as "off-label" use. Doctors are free to prescribe drugs for off-label use but pharmaceutical companies are generally prohibited from promoting off-label uses of their products. Allergan pled guilty to a criminal prosecution by the United States government in 2010 for promoting Botox for off-label uses in the years 2000 to 2005. Technically Allergan was charged with misbranding, which is how off-label promotion can

be prosecuted. Juvenile cerebral palsy and spasticity were two of the off-label indications to which Allergan pled guilty.

J.D. was born in 2006 with cerebral palsy. He has experienced mild to moderate spasticity in his lower limbs. When J.D. was about two, his parents took him to see Dr. Scott Benjamin at Fletcher Allen Health Care. Dr. Benjamin is a doctor of physical medicine and rehabilitation, also known as a physiatrist. J.D. saw Dr. Benjamin every three or four months after his initial visit.

Dr. Benjamin first treated J.D. with Botox on April 22, 2010 when J.D. was three-and-a-half years old. At that time, he selected a dose of either 6.5 or 6.7 u/kg and injected it into J.D.'s calves. Mrs. Drake testified that she did not think that the initial Botox injections resulted in much improvement or benefit for J.D. ECF No. 161 at 40. On April 25, 2012, when J.D. was almost five-and-a-half years old, Dr. Benjamin suggested additional Botox treatments at a higher dose. J.D.'s parents agreed to the treatment and on May 24, 2012 Dr. Benjamin injected J.D. with a dose of either 12.33 or 12.6 u/kg.

The next day J.D. experienced facial swelling and reddening but it seemed to improve after Mrs. Drake gave J.D. some Benadryl. The day after that his ears were also red. Eventually, J.D.'s head dropped and his tongue darted around his mouth extremely quickly. Mrs. Drake also noticed thick saliva

coming out of his mouth. Next, J.D. vomited and different parts of his body began to twitch, including his eyes. He became unresponsive and was diagnosed as status epilepticus when the Drakes brought him to the emergency room. Status epilepticus is a seizure or series of seizures that lasts for more than thirty minutes. After being discharged from the hospital, J.D. eventually returned to normal.

J.D. had another odd episode in August of 2012 that included red ears. The next major event was in September of 2012 when J.D. had red ears and swollen cheeks. In October of 2012 the Drakes brought J.D. to the emergency room after he vomited. J.D.'s doctors eventually put him on anti-seizure medications and diagnosed him with epilepsy after an EEG revealed significant seizure activity. There was also one other incident in February 2013.

When patients experience an adverse event while taking a prescription drug they are encouraged to report it to the FDA, whether or not they or their doctors believe that it is related to the drug or caused by the drug. Anyone can submit an adverse event report, including drug manufacturers, doctors, and individual patients. Dr. Benjamin reported J.D.'s reaction.

Plaintiffs filed their Complaint on September 3, 2013. ECF No. 1. Although they initially alleged claims for strict liability failure to warn, negligence, strict liability design

defect, breach of implied warranties, and violation of the Vermont Consumer Fraud Act ("VCFA"), Plaintiffs dropped their design defect and implied warranty claims shortly before the trial began.

The first day of trial was November 3, 2014. Plaintiffs finished their case-in-chief on November 12, 2014. On the same day, Allergan moved to strike the testimony of Dr. Anna Hristova, the Plaintiffs' medical causation expert, ECF No. 177, and moved for judgment as a matter of law, ECF No. 178. The Court denied both motions and Allergan proceeded with its case. Allergan renewed its motion for judgment as a matter of law on November 16, 2014, which the Court again denied. ECF No. 187. Plaintiffs dropped their strict liability failure to warn claim during the charge conference. The Court charged the jury only on Plaintiffs' claims for negligence and violation of the VCFA. ECF No. 191.

After deliberating for several days the jury returned its verdict in favor of the Plaintiffs on their negligence claim and in favor of Allergan on the Plaintiffs' VCFA claim. It also found that punitive damages were warranted. The jury awarded

$2,778,881.35 in total compensatory damages and $4,000,000.00 in punitive damages.[1]

II. Allergan's Motion for Judgment as a Matter of Law

A. Legal Standard

Allergan renews its motion for judgment as a matter of law pursuant to Federal Rule of Civil Procedure 50. To succeed on a Rule 50 motion, the moving party must show that, after a full hearing on an issue at trial, "'there is no legally sufficient evidentiary basis for a reasonable jury' to resolve the issue in favor of the non-moving party." *Cross v. New York City Transit Authority*, 417 F.3d 241, 247 (2d Cir. 2005) (quoting Fed. R. Civ. P. 50(a)(1)). In reviewing a Rule 50 motion, a court must "'draw all reasonable inferences in favor of the nonmoving party'" and "'may not make credibility determinations or weigh the evidence.'" *Id.* (quoting *Reeves. v. Sanderson Plumbing Products, Inc.*, 530 U.S. 133, 150 (2000)).

A movant's burden in securing Rule 50 relief is "particularly heavy" after a jury has deliberated and returned its verdict. *Id.* at 248. The motion must be denied unless "'the evidence is such that, without weighing the credibility of the

[1] The jury awarded compensatory damages as follows: J.D. was entitled to $2,500,000.00 in compensatory damages, Lori Drake and Kevin Drake were entitled to $28,881.35 in compensatory damages, and Lori Drake and Kevin Drake were entitled $250,000.00 in mental anguish damages.

evidence, there can be but one conclusion as to the verdict that reasonable [persons] could have reached.'" *Id.* (quoting *Samuels v. Air Transp. Local 504*, 992 F.2d 12, 14 (2d Cir. 1993)). In other words the court may only grant a Rule 50 motion in this posture if there is "'such a complete absence of evidence supporting the verdict that the jury's finding could only have been the result of sheer surmise or conjecture'" or there is "'such an overwhelming amount of evidence in favor of the movant that reasonable and fair minded men [and women] could not arrive at a verdict against him.'" *Id.* (quoting *Song v. Ives Labs., Inc.*, 957 F.2d 1041, 1046 (2d Cir. 1992)).

B. Discussion

Allergan argues that the Court should enter judgment as a matter of law in its favor on the Plaintiffs' negligence claim because the Plaintiffs failed to provide sufficient evidence to support a finding of causation. Allergan also argues that the jury could not have reasonably found that the evidence demonstrated the culpability required to impose punitive damages. The Court examines each of these arguments, with Allergan's "heavy" burden in mind below. *Cross*, 417 F.3d at 248.

1. Causation

The Court charged the jury, without objection, to consider whether Allergan's "act or omission played a substantial part in

bringing about or actually causing the injury" when evaluating causation. ECF No. 191 at 11. To meet their burden, the Plaintiffs had to prove 1) that Botox was the cause of J.D.'s seizure disorder and 2) that negligence by Allergan caused Dr. Benjamin to prescribe Botox to J.D. in the dose selected. The Plaintiffs presented sufficient evidence for a reasonable jury to find in their favor on both aspects of causation.

a. Medical Causation

Dr. Anna Hristova was the Plaintiffs' medical causation expert. Prior to trial Allergan moved to exclude her testimony under Federal Rule of Evidence 702 and *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993). ECF No. 93. The Court denied that motion, ECF No. 134, as well as Allergan's subsequent motion to strike her testimony after it was completed, ECF Nos. 177, 183. Allergan now argues that no reasonable jury could have found that Botox caused J.D.'s seizure disorder, primarily because one piece of evidence on which Dr. Hristova relied, the Albavera-Hernández study,[2] was discredited during cross-examination.

The Court initially noted that the Albavera-Hernández study was an important piece of epidemiological evidence in its

[2] Tr. Ex. 108, Cidronio Albavera-Hernández et al., *Safety of Botulinum Toxin Type A among Children with Spasticity Secondary to Cerebral Palsy: A Systematic Review of Randomized Clinical Trials*, 23 Clinical Rehabilitation 394 (2009).

Opinion and Order denying Allergan's pretrial motion to exclude Dr. Hristova's testimony. ECF No. 134. Although Allergan effectively discredited the study during cross-examination, that does mean that no reasonable jury could have found that Botox caused J.D.'s seizures or that Dr. Hristova's opinions were too unreliable to be presented to the jury. In its initial Opinion and Order, the Court explicitly noted that an expert is not required to back her opinion with published studies that unequivocally support her position. ECF No. 134 at 15 (citing *Amorgianos v. Nat'l Railroad Passenger Corp.*, 303 F.3d 256 (2d Cir. 2002)). And, importantly, another court had found that case reports, prevalence studies, adverse event reports, animal studies, and a hypothesis about a potential mechanism through which the drug supposedly caused the alleged injury were sufficiently reliable to permit an expert to testify. *Id.* (citing *In re Fosamax Products Liability Litig.*, 645 F. Supp. 2d 164 (S.D.N.Y. 2009)).

The Court denied Allergan's motion to strike Dr. Hristova's testimony because she relied on the "totality of circumstances." ECF No. 184 at 5. Allergan argues that according to *Hollander v. Sandoz Pharms. Corp.*, 289 F.3d 1193, 1216 n.21 (10th Cir. 2002) this is not a sufficiently reliable approach. The *Hollander* court observed:

> The Hollanders also suggest that a totality of the circumstances approach establishes that there are controverted issues of material fact. In essence they maintain that even though each individual category of evidence may be insufficient, all of the evidence considered as a whole raises factual questions as to whether Parlodel caused her stroke. The Hollanders cite no legal authority in support of this approach, and in our view, this argument is inconsistent with *Daubert.* To suggest that those *individual categories of evidence deemed unreliable by the district court* may be added to form a reliable theory would be to abandon "the level of intellectual rigor" of the expert in the field.

Id. (emphasis added) (citation omitted). Dr. Hristova's testimony is distinguishable because the district court in *Hollander* found that the individual categories of evidence related to the particular drug and injuries at issue were unreliable. Here the Court did not find the individual categories of evidence to be unreliable, nor did they present "too great an analytical gap between the data and the opinion proffered." *Id.* at 1205 (quoting *General Elec. Co. v. Joiner*, 522 U.S. 136, 146 (2002)). Rather, some pieces of evidence that may have been insufficient to support a finding of causation in isolation could be sufficient when considered together.

The First Circuit reversed a trial court's decision to exclude testimony from an expert under similar circumstances. The trial court failed to appreciate that the expert inferred causality "from the accumulation of multiple scientifically acceptable inferences from different bodies of evidence." *Milward v. Acuity Specialty Products Group, Inc.*, 639 F.3d 11,

26 (1st Cir. 2011). It is valid for an expert to infer causation based on the totality of evidence when combined it supports such an inference. *Id.* at 23.

Plaintiffs presented a significant amount of evidence, including other aspects of Dr. Hristova's testimony, from which reasonable jurors could have inferred that it was more likely than not that Botox was to blame for J.D.'s seizures. As described below, the Plaintiffs' evidence included: the seizure rates in Allergan's clinical trials; the Graham study; adverse event and anecdotal reports; biological plausibility and theoretical mechanisms of action; FDA guidance and the Botox label; and the timing and lack of alternative explanation for J.D.'s seizures. Although no single piece of evidence necessarily may have been conclusive in isolation, together it paints a picture sufficient to support the jury's finding on medical causation.

i. Seizure Rates in Clinical Trials

First, Plaintiffs presented evidence suggesting that the overall rate of seizures in Allergan's clinical trials was higher in Botox groups than in placebo groups and that Allergan may have selected favorable data to make this fact less obvious in its reports to the FDA. Exhibit 112 is a series of internal Allergan emails from February of 2009. In one of these emails, an Allergan employee states that the number of seizures reported

in double blind placebo controlled studies was 0.61% for Botox groups and 0.37% for placebo groups, or in his words, "[a]lmost twice the rate" for participants receiving Botox. Tr. Ex. 112 at AGN2164348.

However, in Allergan's 2012 report to the FDA titled Seizure Disorder Safety Analysis Allergan reported that the "convulsion" rates for clinical trials were 0.7% for Botox and 0.6% for placebo. Tr. Ex. 143 at AGN1735510. The report explains that "upper limb spasticity appeared imbalanced" so "the raw adverse event frequencies from the pooled data were not used for statistical comparisons." *Id.* The jury could have reasonably inferred that Allergan reported the data in a way that made the disparity in seizure rates across groups less obvious.

The jury also reasonably may have inferred that Allergan changed the way it reported its data to obscure the total number of positive rechallenges. A positive rechallenge means that the seizures ceased when Botox was withheld but then reoccurred when Botox was reintroduced. The number of positive rechallenges was included in the 2004 report but is absent from the 2012 report. *Compare* Tr. Ex. 40 *with* Tr. Ex. 143.

ii. The Graham Study

Next, Dr. Hristova relied on the Graham study.[3] Participants in this study received either Botox and hip bracing or no injections and no bracing. The jury could have reasonably given this study significant weight because participants in the treatment group received an average dose of 13.9 u/kg of Botox. This dose was higher than the highest dose of 8 u/kg Allergan had studied in its clinical trials and was more consistent with the dose J.D. received. The Graham study reported that two children in the Botox group died. None in the control group died. The authors reported that the autopsy findings suggested that the deaths resulted from "asphyxiation related to epilepsy." Tr. Ex. 752 at 29. The authors claimed that the two deaths were not thought to be injection-related but provided no further analysis. *Id.*

Dr. Hristova testified that these two deaths were statistically significant according to her calculations and that the study was sponsored by Allergan. ECF No. 172 at 76. She also testified that other studies show that when drug manufacturers sponsor research, the experiments conducted tend to have poorer controls and tend to favor the drug. Dr.

[3] Tr. Ex 752, H. Kerr Graham et al., *Does Botulinum Toxin A Combined with Bracing Prevent Hip Displacement in Children with Cerebral Palsy and "Hips at Risk"?*, 90 J. Bone Joint Surg. Am. 23 (2008).

Hristova concluded that the number of deaths from epilepsy in the Graham study is much higher than would be expected in the background population. *Id.* Thus the jury could have found that the Graham study supported Dr. Hristova's conclusions.

iii. Adverse Event and Anecdotal Reports

Next, Dr. Hristova relied on adverse event reports submitted to the FDA. She explained that people typically take the time to submit adverse event reports only when they believe that there is some relationship between a particular drug and an event, especially busy doctors. ECF No. 172 at 80. The fact that many of the reports Dr. Hristova analyzed were medically confirmed gave her greater confidence in inferring that Botox was the potential cause. *See* ECF No. 172 at 85. Dr. Hristova also analyzed individual seizure reports including, for example, one pediatric report in which a child experienced seizures immediately after receiving Botox and was subsequently diagnosed with epilepsy based on positive EEG and MRI findings. Tr. Ex. 198; ECF No. 176 at 12-13.

At least one doctor, Dr. Mark Gormley, a frequent Botox injector, also directly raised some concerns to Allergan employees about the connection between Botox and seizures when eight of his patents experienced seizures after Botox. Tr. Ex. 21. One patient experienced a positive rechallenge. *Id.* Allergan may have declined to investigate these reports because

one employee could "not see a good outcome from poking around in this subject." *Id.* at AGNRVB0384912. Dr. Gormley later reported yet another first time seizure that he admitted could be coincidental but "certainly seem[ed] related" in his view. Tr. Ex. 24 at AGNRBV038374.

The jury could have inferred that the medically confirmed reports and positive rechallenges should be given greater weight than other adverse event and anecdotal reports. *See Glastetter v. Novartis Pharm. Corp.*, 252 F.3d 986, 990 (8th Cir. 2001) (noting that positive rechallenge data is "substantially more valuable than run-of-the-mill case reports because a patient's reactions are measured against his own prior reactions"). While caution may be advised when attributing causation solely on the basis of these kinds of reports, the jury could properly consider them to be a relevant factor.

iv. Biological Plausibility and Theoretical Mechanism of Action

Next, the Plaintiffs presented evidence from which a jury reasonably could have inferred that it is biologically plausible that Botox can cause seizures. Plaintiffs also presented evidence describing theories about how it might do so. Biological plausibility takes on greater significance when epidemiological evidence is lacking or inconclusive. *See Fosamax*, 645 F. Supp. 2d at 181.

Dr. Roger Aoki, before retiring, was Allergan's Vice President of Neurotoxin Research Program and had many years of experience studying Botox. In 2001 Dr. Brin received Dr. Gormley's reports described above and asked Dr. Aoki for the first time whether there is a mechanism by which Botox can cause seizures. ECF No. 176 at 97. In his deposition many years later, Dr. Aoki testified that injections like the ones J.D. received could plausibly cause seizures. Aoki Dep. Tr. 32:20-23 (Q "[M]y question is is triggering of seizures due to peripheral BOTOX injections biologically plausible? A Yes."). At trial, however, Dr. Aoki qualified the statement in his deposition and stated that after examining whether it is possible he "would have to reject that hypothesis and say it can't trigger –- a peripheral administrative botulinum toxin would not trigger a seizure." ECF No. 176 at 76. The jury could have credited his statement in his deposition rather than his testimony at trial.

Dr. Hristova's testimony and article[4] describing potential mechanisms of how Botox might spread, including to the brain

[4] Tr. Ex. 140, Anna H. Hristova et al., *Severe Nervous System Complications after Botulinum Type A Therapy: Three Case Reports with Reviews of FDA-Reported Nervous System Effects*, 4 PM&R 613 (Aug. 2012).

further, support an inference of biologic plausibility.[5] *See* ECF No. 172 at 33-38, Tr. Ex. 140. Dr. Hristova testified about research by Flavia Antonucci[6] and Matteo Caleo[7] and others suggesting that Botox may travel by retrograde axonal transport. In 1991, many years before he became an Allergan employee, Dr. Brin co-wrote a paper stating that "after peripheral administration [botulinum toxin] can enter the central nervous system." Tr. Ex. 3, Joseph Jankovic & Mitchell F. Brin, *Therapeutic Uses of Botulinum Toxin*, 324 New England J. of Med. 118 (1991); *see also* Tr. Ex. 5 at AGN210341 ("Animal studies have clearly demonstrated that BTX can reach the central nervous system from inoculations of muscles."). Dr. Brin later recanted this position. Tr. Ex. 190, Brin Dep. 120:18-121:2; 123:3-10. Even Dr. Aoki admitted that retrograde axonal transport may "possibly" occur and that it is a "valid theory." ECF No. 176

[5] Dr. Hristova's peer-reviewed article reflects her theories of how Botox may spread beyond the site of injection, including in the bloodstream or by retrograde axonal transport. While it does not specifically focus on how botulinum toxin A might spread to the brain and then cause a seizure, little is understood about the mechanism of action for any seizure. Dr. Hristova's theories about how Botox spreads are relevant because it is more likely that Botox can seizures if there is a plausible theory as to how it might reach the brain.

[6] Tr. Ex. 78, Flavia Antonucci et al, *Long-Distance Retrograde Effects of Botulinum Neurotoxin A*, 28(14) J. of Neuroscience 3689 (April 2, 2008).

[7] Tr. Ex. 107, Matteo Caleo et al, *A Reappraisal of the Central Effects of Botulinum Neurotoxin Type A: By What Mechanism?*, 109 J. of Neurochemistry 15 (2009).

at 85-86. The Plaintiffs' evidence thus included both a statement from an Allergan scientist about biological plausibility and a theoretical mechanism of action the jury could have reasonably relied on.

v. FDA Guidance and the Botox Label

Next, the FDA's own guidance supports an inference that there is some relationship between Botox and seizures. In 2010 Allergan put a warning regarding seizures in the Post-Marketing Experience section of the Botox label. Tr. Ex. 133 at 6.3 ("New onset or recurrent seizures have also been reported, typically in patients who are predisposed to experiencing these events."). Although the label states that the exact relationship of these events to the botulinum toxin has not been established, adverse reactions are selected for inclusion on the label when "there is some basis to believe there is a causal relationship between occurrence of an adverse event and the use of a drug." Tr. Ex. 199 at 8. While this guidance is not binding on drug companies, it is an additional factor supporting the jury's finding.

vi. Temporality and Lack of Alternative Explanations

Finally, the temporality and lack of alternative explanations for J.D.'s seizures support an inference that the Botox injections he received were the cause of J.D.'s seizures. Dr. Benjamin testified that he thought that whatever had

happened to J.D. was the result of the Botox because of timing of the events. ECF No. 170 at 15. As of the date of trial Dr. Benjamin still thought it was possible that Botox caused J.D.'s seizures and stated that he would not give J.D. any more Botox. ECF No. 170 at 16.

The Second Circuit affirmed an expert's opinion that relied in part on the progression and timing of the development of a disease to support an inference of causality. *Zuchowicz v. United States*, 140 F.3d 381, 390 (2d Cir. 1998); *see also Westberry v. Gislaved Gummi AB*, 178 F.3d 257, 265 (4th Cir. 1999) (explaining that under some circumstances "a temporal relationship between exposure to a substance and the onset of a disease or a worsening of symptoms can provide compelling evidence of causation"); *Heller v. Shaw Indus., Inc.*, 167 F.3d 146, 154 (3d Cir. 1999) (noting courts "have looked favorably on medical testimony that relies heavily on a temporal relationship between an illness and a causal event").

The defense's theory at trial was that J.D.'s seizures developed simply by chance because he is at greater risk for seizures in general due to his cerebral palsy. However, Dr. Hristova's testimony suggested this would be an extremely unlikely coincidence. She testified that only 21% of individuals with spastic diplegia, a milder form of cerebral palsy, develop seizures. ECF No. 172 at 49-51. Other evidence

suggested that of cerebral palsy patients who experience a seizure in their lives, over two thirds of them experience their first seizure by age two. Tr. Ex. 208. Thus Dr. Hristova testified that the odds of developing a seizure disorder for the first time after the age of 5 with a relatively mild form cerebral palsy was very small. Moreover, she testified that J.D.'s seizures are autonomic, a much rarer kind of seizure, and that other features of his experience were unusual. ECF No. 172 at 69-70, ECF No. 173 at 87-93. This suggests that J.D.'s unusual seizure was not a natural occurrence but rather caused by the Botox.

Finally, that J.D. and other children with cerebral palsy may be more prone to seizures is not conclusive. The jury needed only to find that Botox was a substantial factor in bringing about the injury. The jury was appropriately instructed that a pre-existing condition that makes the plaintiff more susceptible to the event does not destroy causation. ECF No. 191 at 11. Dr. Hristova testified that it is possible J.D.'s cerebral palsy made him more susceptible to having a Botox-induced seizure. ECF No. 172 at 71. The jury could have reasonably concluded that the Botox either caused the seizure outright or lowered J.D.'s seizure threshold sufficiently to cause the seizure.

In sum the Plaintiffs presented sufficient evidence to support the jury's finding that Botox caused J.D.'s seizures.

b. Negligent Promotion and Proximate Cause

The jury was also required to find that Allergan's promotional activities were the proximate cause of J.D.'s injuries. Allergan argues that proximate cause can only be proven if Allergan caused or played a substantial part in causing Dr. Benjamin to treat J.D. with Botox in May of 2012 and to select a dose above 12 u/kg.

As the Court instructed the jury, without objection, the law "recognizes that there may be more than one proximate cause of an injury" and that "[m]ultiple factors may operate at the same time, or independently, to cause the injury and each may be a proximate cause." ECF No. 191 at 11. Under Vermont law, "'[d]etermination of proximate cause requires a finding by the trier of fact except in rare circumstances.'" *Betz v. Highlands Fuel Delivery, LLC*, No. 5:10-CV-102, 2013 WL 392480, at *8 (D. Vt. Jan. 31, 2013) (quoting *Bloomer v. Gibson*, 2006 VT 104, ¶ 49, 180 Vt. 397, 416, 912 A.2d 424, 437). Here the Plaintiffs presented evidence from which a jury could have reasonably found proximate cause sufficient to find in the Plaintiffs' favor.

Allergan argues that Dr. Benjamin began and continued using Botox to treat juvenile cerebral palsy patients with high doses of Botox because of his training and clinical experience, not

because of anything Allergan said or did or failed to say or do. While this is one possibility, it is not the *only* reasonable conclusion that the jury could have reached. Even if the jurors credited Allergan's theory that Dr. Benjamin relied primarily on his training and experience, they could have nevertheless relied on a variety of evidence to conclude that Allergan's promotional efforts over the years *also* played a substantial part in Dr. Benjamin's choice to treat J.D. with Botox and to select the dose he administered.

First, the Plaintiffs presented evidence that Allergan employees had direct contact with Dr. Benjamin during two separate time periods. An Allergan sales representative, Larry Jackson, called on Dr. Benjamin nineteen times between 2000 and 2002 while Dr. Benjamin was completing his pediatric fellowship at the Kennedy Krieger Institute at Johns Hopkins. Tr. Ex. 20. Dr. Benjamin testified that during his residency and then fellowship there he first learned to inject Botox. ECF No. 170 at 6-7. The jury could have reasonably inferred that Mr. Jackson promoted off-label use of Botox during these calls based on Mr. Jackson's call notes. *See* Tr. Ex. 20.

Next, in 2005 Scott Traub of Allergan called on Dr. Benjamin several times and "renewed [Dr. Benjamin's] interest" in injecting Botox for pediatric cerebral palsy. Tr. Ex. 44 at AGN_DRAKE_00001068. Mr. Traub also apparently talked to Dr.

Benjamin about high dose Botox. *Id.* Dr. Benjamin did not recall the specifics of these conversations. ECF No. 170 at 50. From these interactions with Mr. Jackson and Mr. Traub, the jury could have inferred that Allergan influenced Dr. Benjamin's decisions to treat pediatric spasticity patients with Botox.

The jury also could have reasonably inferred that doctors may be influenced by drug promotion but may not be consciously aware of how the promotion has influenced their behavior. Dr. Benjamin agreed that many doctors might say that they think that drug company promotion influences other doctors but not them. ECF No. 170 at 65. Dr. David Kessler also described a study by the World Health Organization and Health Action International finding promotion influences attitudes more than doctors realize. ECF No. 165 at 46-47

The Plaintiffs elicited testimony suggesting that Dr. Benjamin may have been influenced by medical literature that Allergan had some hand in editing, shaping, directing, or even ghost writing. Tr. Ex. 44; *see also* ECF No. 165 at 50-51, 54-55 (Dr. Kessler describing Allergan's influence over the literature). Dr. Benjamin could not say for sure if he read any item in particular on a list of articles that Allergan was involved with in some way. However, given the sheer number and Dr. Benjamin's testimony that some looked "familiar" and that it is "likely [he] reviewed some of them," it would be reasonable

for the jury to conclude that Allergan's influence reached Dr. Benjamin through the literature. ECF No. 170 at 68.

Dr. Benjamin himself conceded that Allergan's activities affected his practice but could not quantify how much influence Allergan might have had. ECF No. 170 at 65. However, he did testify that Allergan has been a part of all the experiences, influence, and training he has had and that all of that together "would have had some influence in general over the practice." ECF No. 170 at 59.

The jury also could have inferred that Allergan's promotional activities influenced Dr. Benjamin's dosing choices, whether consciously or unconsciously, including the dose he chose for J.D. Dr. Benjamin testified that when he first started injecting he was using a maximum dose of 10 to 12 u/kg. ECF No. 170 at 7-8. While attending the American Academy of Cerebral Palsy and Developmental Medicine there was a breakout session in which doctors discussed the various dosing ranges. Dr. Benjamin testified that pharmaceutical companies, including Allergan, are involved in such conferences and that session influenced his dosing. ECF No. 170 at 9.

Dr. Benjamin also testified that he gave a talk using a slide set put together by WE MOVE. ECF No. 170 at 33-34, 53. WE MOVE is a non-profit organization that Dr. Mitchell Brin founded and used to run before he moved to Allergan. Tr. Ex.

190, Brin Dep. 61:2-24. Allergan pled guilty to "controll[ing] and fund[ing]" WE MOVE. Tr. Ex. 126 at 13. Allergan influenced the content of the dosing guidelines WE MOVE published. ECF No. 165 at 33-34; Tr. Ex. 32 (email from Dr. Brin concerning language regarding dosing in WE MOVE chapters). The dosing guidelines from 2005 list the lesser of 16 u/kg or 400 units as the maximum dose. Tr. Ex. 52. The guidelines previously listed 12 u/kg as the maximum dose. Tr. Ex. 24 at 139. Dr. Benjamin testified that he used WE MOVE and its website as a resource and that he had seen the WE MOVE guidelines before. ECF No. 170 at 33-34, 112. WE MOVE's high dosing guidelines could have influenced his dosing decisions.

Although Dr. Benjamin could not remember the time frame with precision, he testified that he increased his dosing around eight to ten years ago, which a jury could have inferred was around the time he was talking with Scott Traub in 2005 about high dose Botox. *See* ECF No. 170 at 9-10. Dr. Benjamin explained that any discussion about high dose Botox in the "gestalt of conferences and information and training, et cetera, getting information about higher-dose Botox being used safely would influence my ability to use higher doses." ECF No. 170 at 58-59. 15 u/kg is now his maximum dose. ECF No. 170 at 8. Thus the jury could have inferred that Allergan's influences led

him to move to selecting doses above 12 u/kg, as was the dose he gave J.D.

For the reasons described above the jury could have reasonably concluded that Allergan's promotional activities were a substantial factor influencing Dr. Benjamin's practice. The jury also could have reasonably concluded that Allergan's influence was a substantial factor in Dr. Benjamin's choice to move from doses above 10-12 u/kg to 15 u/kg. Therefore there is no reason to disturb any of the jury's findings on causation.

2. Punitive Damages

Allergan argues that is entitled to judgment as a matter of law on the issue of punitive damages because the evidence was insufficient to support the jury's verdict. The Court disagrees.

The Vermont Supreme Court's jurisprudence on punitive damages, by its own concession, "has not been a model of clarity." *Fly Fish Vermont Inc. v. Chapin Hill Estates*, 2010 VT 33, ¶ 18, 187 Vt. 541, 996 A.2d 1167. However, it is clear that the purpose of punitive damages is to "punish conduct that is morally culpable to the degree of outrage frequently associated with crime." *Id.* ¶ 19. Plaintiffs seeking punitive damages must prove two elements: 1) "wrongful conduct that is outrageously reprehensible" and 2) malice, "defined variously as bad motive, ill will, personal spite or hatred, reckless

disregard, and the like." *Id.* ¶ 18. When evaluating punitive damages, juries may only consider evidence that has "a nexus to the specific harm suffered by the plaintiff." *State Farm. Mut. Auto. Ins. Co. v. Campbell*, 538 U.S. 408, 422 (2003).

Thus, the Plaintiffs were required to prove that Allergan's conduct was outrageously reprehensible and that Allergan acted with malice. It is clear that in this case the Plaintiffs do not allege - nor could they prove – that Allergan had any ill will, personal spite, or hatred towards the Drakes individually. The question then is whether the Plaintiffs proved that Allergan's conduct was outrageously reprehensible and demonstrated a "bad motive" or "reckless disregard" sufficient to constitute malice in the state of Vermont.

Defining the contours of a standard for reckless disregard sufficient to warrant a finding of malice proved to be somewhat slippery for the Vermont Supreme Court. On the one hand, the court had held that in order to qualify for punitive damages the conduct at issue must be more than simply wrongful or unlawful. *Fly Fish*, 2010 VT 33, ¶ 19. And conduct evincing a "mere reckless disregard of the plaintiff's rights" or "a reckless disregard of the right of others" is likewise insufficient. *Id.* ¶¶ 19-20 (discussing *Brueckner v. Norwich University*, 730 A.2d 1086 (Vt. 1999) and *Bolsta v. Johnson*, 848 A.2d 306 (Vt. 2004) (internal quotation omitted)). The court noted that there must

be some kind of bad motive on top of the tort because a threshold of reckless disregard, without more, would be so flexible it could become virtually unlimited in its application. *Fly Fish*, 2010 VT 33, ¶¶ 20-21.

On the other hand, the Vermont Supreme Court had long-recognized the notion of malice arising from acting with a wanton disregard for great harm. *Id.* ¶ 23. When defining the line between "reckless, wanton, or heedless misconduct" sufficient to warrant punitive damages and "mere reckless disregard" the Vermont Supreme Court held:

> the culpability necessary for an award of punitive damages based on reckless or wanton misconduct requires evidence that the defendant acted, or failed to act, in conscious and deliberate disregard of a known, substantial and intolerable risk of harm to the plaintiff, with the knowledge that the acts or omissions were substantially certain to result in the threatened harm.

Id. ¶¶ 19, 21, 25. This is the measure by which reckless misconduct reaches the point of actual malice sufficient to support an award of punitive damages. *Id.* ¶ 25.

There are some circumstances, however, in which no reckless disregard analysis was necessary to find malice when there was either an element of bad motive by definition or otherwise demonstrable malice present. For example, the Vermont Supreme Court explained that an attorney who intentionally misappropriated money from a widowed plaintiff and lied about it in *DeYoung v. Ruggiero*, 2009 VT 9, ¶ 27, 185 Vt. 267, 971 A.2d

627, was egregious enough that malice could be inferred. *Fly Fish*, 2010 VT 33, ¶ 29. In *DeYoung* the court noted that "malice may arise from deliberate and outrageous conduct aimed at securing financial gain or some other advantage at another's expense, even if the motivation underlying the conduct is to benefit oneself rather than harm another." *DeYoung*, 2009 VT 9, ¶ 27. The defendant's admitted motive in *DeYoung* was to enrich himself and promote the interests of his company, which the court found "in and of itself demonstrates a bad motive." *Id.* ¶ 29. It is not necessary to find an intention to do harm to find malice. *Id.* The court also included dicta suggesting that punitive damages should be available against companies that "knowingly [place] dangerous products into the market, hoping that people [will] not get hurt" while ignoring a great risk of harm to increase profits. *Id.*

The other cases in which the court described finding demonstrable malice involved, for example, fraud, *Follo v. Florindo*, 2009 VT 11, 185 Vt. 390, 970 A.2d 1230, a campaign of terror motivated by sectarian and racial bias, *Shahi v. Madden,* 2008 VT 25, 183 Vt. 320, 949 A.2d 1022, and filing a false mechanic's lien on property in an effort to extort right-of-way concessions from owners who had no prior business with the company and owed nothing, *Wharton v. Tri–State Drilling & Boring*, 2003 VT 19, 175 Vt. 494, 824 A.2d 531.

The Due Process Clause of the United States Constitution limits the scope of evidence juries may properly to consider to conduct with a "nexus" to the specific harm suffered. *State Farm*, 538 U.S. at 422. Therefore the jury could only consider promotional activities that reached Dr. Benjamin in some way.

a. Wrongful and Outrageously Reprehensible Conduct

Allergan pled guilty to a criminal prosecution by the United States government in 2010 for promoting Botox for off-label uses, including pediatric spasticity, from 2000 to 2005. Tr. Ex. 128. The Plaintiffs introduced evidence demonstrating Allergan's promotional activities were aimed at pediatric spasticity and pediatric specialists during this time. *See, e.g.*, Tr. Exs. 27, 28, 34, 86. Sales of Botox for off-label use in pediatric spasticity more than doubled between 2002 and 2007. Tr. Exs. 27, 65.

The Plaintiffs also introduced evidence supporting an inference that doses above 8 u/kg are less safe but Allergan nevertheless promoted higher doses. First, Dr. Brin testified by video deposition that 8 u/kg is the maximum pediatric dose studied and is the dose listed in the Company Core Data Sheet. Tr. Ex. 190, Brin Dep. 12:10-12:20. Of the countries that have approved Botox for pediatric spasticity, 8 u/kg is the maximum dose in every single country. Tr. Ex. 190, Brin Dep. 20:21-21:1; ECF No. 186 at 78-79. Allergan also defined "overdose" in

the context of pediatric use as doses greater than 8 u/kg. Tr. Ex. 190, Brin Dep. at 15:20-16:19; Tr. Ex. 77. Finally, Dr. Brin agreed that "the risk [of possible distant spread of toxin] is higher at doses greater than 8 units per kilogram" and that Allergan considers seizures to be an important potential risk. Tr. Ex. 190, Brin Dep. 95:22-96:3; 118:7-13.

Allergan's animal toxicology data confirms that systemic adverse effects begin to appear at doses of 8 u/kg and higher. Tr. Ex. 145 at AGN4928938. A Botox employee refused to provide free Botox to a researcher who hoped to conduct a clinical trial at higher doses in 2005 because Allergan's "toxicology and safety data (both in house and on file at FDA) cannot not support doses >6-8 units of Botox per Kilo." Tr. Ex. 58 at AGN RVB0150261. A scatterplot that was repeatedly introduced with witnesses and discussed at length at trial plotted the dose that post-marketing pediatric "possible distant spread of toxin" cases received. Tr. Ex. 145 at AGN928944. The scatterplot includes a line labeled "CCDS Maximum Dose" at 8 u/kg and reveals that all of the pediatric cases, save one with special circumstances, occurred above 8 u/kg. *Id*. The Maximum Dose Consideration Review determined that Allergan would keep the pediatric dose at 8 u/kg. Tr. Ex. 201. From this evidence the jury could have reasonably inferred that Allergan had

significant evidence in its possession suggesting that doses above 8 u/kg were more dangerous.

The jury could also have reasonably found that Allergan promoted doses above 8 u/kg. Plaintiffs' evidence suggested that Allergan's marketing personnel and executives sought to increase sales by encouraging doctors to inject patients with higher doses. *See* Tr. Ex. 28 (2001 business planning memorandum identifying "[i]ncreased dosing for pediatric spasticity (from 4-6 units/kg several years ago to 10-20 units/kg now)" as an important factor underlying growth in volume of use by pediatric physiatrists); Tr. Ex 34 (marketing plan reflecting goal of moving the maximum dose to a higher acceptable limit); Tr. Ex. 45 (slide deck prepared by Dr. Edward Goldstein but financed and edited by Allergan stating "20 Units per 'Ki' . . . Is OK by Me!"); Tr. Ex. 50 (email from Allergan CEO David Pyott inquiring whether Allergan was doing any work in the area of dosing as high as 30-35 u/kg).

The jury also could have concluded that Allergan promoted higher doses through its control and influence of WE MOVE. *See* Tr. Ex. 26 at 139 (WE MOVE dosing schedule recommending up to 12 u/kg for total maximum dose per body visit); Tr. Ex. 22 (email to Drake Barborka describing WE MOVE budget proposals for the year); Tr. Ex. 194, Barborka Dep. 54:12-55:16 (Mr. Barborka testified that Allergan paid indirectly for the publication and

dissemination of pediatric dosing charts); Tr. Ex. 192, Traub Dep. 21:6-27:36, 54:5-22 (Mr. Traub testified that he distributed WE MOVE dosing guidelines at conferences, meetings, and talks he gave to doctors). Finally, Allergan CEO David Pyott gave a presentation in which potential reduction of pediatric dose due to FDA safety concerns was a reason why the rate of sales growth of Botox might slow. Tr. Ex. 110.

The jury could also have inferred Allergan's promotional efforts reached Dr. Benjamin. As described above, Larry Jackson called on Dr. Benjamin around the time Allergan's 2001 business planning memorandum was circulated. Mr. Jackson discussed the "dosing trend" with Dr. Benjamin. The jury could have inferred the "dosing trend" was to move from 4-6 u/kg to 10-20 u/kg as described in materials from the marketing department. *See* Tr. Exs. 20, 28. Additionally, around the time that Scott Traub called on Dr. Benjamin and discussed high dose Botox, Mr. Traub had circulated a slide deck by Dr. Goldstein stating 20 u/kg was an acceptable maximum. Tr. Exs. 44, 45. This was about the time that Dr. Benjamin may have increased his maximum dose to 15. The jury also could have inferred Dr. Benjamin was influenced by WE MOVE because he testified that he referred to their website in his practice and had seen the dosing schedule before. ECF No. 170 at 33, 54.

The evidence described above was sufficient to support the jury's conclusion that Allergan's promotional activities were outrageously reprehensible, especially in light of the Plaintiffs' evidence regarding the promotion of higher doses. To begin with, it may have been fair to infer that Allergan's off-label promotion deserved a "degree of outrage frequently associated with crime" because Allergan actually pled guilty to a crime. *Fly Fish*, 2010 VT 33, ¶ 18.

Allergan cites *United States v. Caronia* 703 F.3d 149 (2d Cir. 2012) and argues that its promotional activities may have been legal under federal law. In *Caronia* the Second Circuit held that the misbranding provisions of the Federal Food, Drug and Cosmetic Act do not prohibit or criminalize the truthful off-label promotion of FDA-approved prescription drugs because construing the Act any other way would raise First Amendment concerns. *Id.* at 160, 168. It appears that, like the defendant in *Caronia*, Allergan was prosecuted for its promotional speech. Thus, under this precedent the mere act of off-label promotion through speech may not be illegal.

Regardless of the actual legality or illegality of Allergan's promotional activities, the jury could have nevertheless reasonably concluded that Allergan's conduct was outrageously reprehensible because Allergan did more than simply promote an off-label use. In the light most favorable to the

Plaintiffs, Allergan promoted the use of doses that it knew were risky in order to increase profits. Higher doses meant more product sold. A reasonable jury could have felt morally outraged by a corporation's desire to put its bottom line above children's health, safety, and even lives.

b. Malice

In *DeYoung* the Vermont Supreme Court noted that "malice may arise from deliberate and outrageous conduct aimed at securing financial gain or some other advantage at another's expense, even if the motivation underlying the conduct is to benefit oneself rather than harm another." 2009 VT 9, ¶ 27. The court later explained that malice could be inferred in situations like the one *DeYoung* presented without an analysis of recklessness. *Fly Fish*, 2010 VT 33, ¶ 22. While the court seemed to focus on the unique concerns related to fraud by attorneys and their special fiduciary relationship to clients, it also suggested in dicta that punitive damages should be available in cases in which companies knowingly place dangerous products in the market and hope people do not get hurt. Evidence presented by the Plaintiffs reasonably suggested that Allergan was motived by financial gain and knowingly encouraged risky doses despite the real possibility that children could be injured because the toxin is more likely to spread above 8 u/kg. The facts here appear to present a case in which malice can be inferred.

Even if malice cannot be inferred, however, the Plaintiffs presented sufficient evidence from which a jury could find that Allergan's promotional campaign was undertaken "in conscious and deliberate disregard of a known, substantial and intolerable risk of harm to the plaintiff, with the knowledge that the acts or omissions were substantially certain to result in the threatened harm." *Fly Fish*, 2010 VT 33, ¶ 25. The jury could have reasonably found that promoting doses above 8 u/kg created a substantial and intolerable risk of harm because doses above 8 u/kg were not proven to be safe and effective and nearly every incident in which a child was harmed occurred at a dose above 8 u/kg. While it is a closer question whether Allergan *knew* that promoting Botox at high doses was substantially certain to result in harm to patients, in the light most favorable to the plaintiff that was a reasonable conclusion. The jury could have found that Allergan was aware of the risks of high doses but promoted them anyway in order to reap greater profits.

Thus the Court finds that the Plaintiffs' evidence was sufficient to support the jury's award of punitive damages.

III. Allergan's Motion for a New Trial

In the alternative to its motion for judgment as a matter of law, Allergan argues the Court should order a new trial pursuant to Federal Rule of Civil Procedure 59. A district court may grant a motion for a new trial if it concludes that

the jury has reached a seriously erroneous result or the verdict is a miscarriage of justice. *Manley v. AmBase Corp.*, 337 F.3d 237, 245 (2d Cir. 2003). A new trial may be granted even if there is substantial evidence supporting the jury's verdict. *Id.* Moreover, unlike when deciding whether to grant a Rule 50 motion, courts are free to weigh the evidence and examine it through their "own eyes." *Meloff v. New York Life Ins. Co.*, 240 F.3d 138, 147 (2d Cir. 2001). The Court also need not view the evidence in the light most favorable to the verdict winner. *Id.*

However, Second Circuit precedent admonishes trial judges to "exercise their ability to weigh credibility with caution and great restraint, as a judge should rarely disturb a jury's evaluation of a witness's credibility and may not freely substitute his or her assessment of the credibility of the witnesses for that of the jury simply because the judge disagrees with the jury." *Raedle v. Credit Agricole Indosuez*, 670 F.3d 411, 418 (2d Cir. 2012) (internal citations and quotations omitted). Jury verdicts should be disturbed with great infrequency. *Id.* Moreover, it is "well-settled that Rule 59 is not a vehicle for relitigating old issues, presenting the case under new theories, securing a rehearing on the merits, or otherwise taking a 'second bite at the apple' . . . ." *Sequa Corp. v. GBJ Corp.*, 156 F.3d 136, 144 (2d Cir. 1998).

At trial the parties presented conflicting evidence about all of the questions the jury was asked to answer. It was up to the jury therefore to determine which account was credible. Even when weighing the evidence here, the Court does not conclude that the jury reached a seriously erroneous result or that the verdict was a miscarriage of justice. *Manley*, 337 F.3d at 245 (2d Cir. 2003). The evidence presented was sufficient to sustain the jury's verdict and the Court finds no reason to disturb the jury's credibility determinations in this case by ordering a new trial.

Conclusion

For the reasons described above, the Court **grants** Plaintiffs' motion and **denies** Allergan's motions. The Court will enter judgment in favor of the Plaintiffs incorporating the jury's verdict.

DATED at Burlington, in the District of Vermont, this 22nd day of May, 2015.

/s/ William K. Sessions
William K. Sessions III
District Court Judge