Docket No. 10-1524

In the

Supreme Court of the United States

April Term, 2010

Dan Cooks*, et al.*,

***Petitioner*,**

v.

Carolina Laboratories, Inc.,

***Respondent*.**

On Writ of Certiorari to the
United States Court of Appeals for
the Thirteenth Circuit

Brief for Respondent

Team 16

QUESTIONS PRESENTED

I. Whether a state court jury's case-by-case determination of design defect undermines Congress' intent, in passing the National Childhood Vaccine Injury Act, to protect manufacturers from uncertain tort liability and place vaccine decisions within a federally regulated scheme?

II. Whether a complaint must allege enough facts to be plausible on its face after this Court's decisions in *Bell Atlantic v. Twombly* and *Ashcroft v. Iqbal*?

TABLE OF CONTENTS

PAGE

TABLE OF AUTHORITIES

PAGE

UNITED STATES SUPREME COURT CASES

CIRCUIT COURT CASES

US CIRCUIT COURTS

STATE COURT CASES

UNITED STATES CONSTITUTION

FEDERAL STATUTES

FEDERAL RULES AND REGULATIONS

SECONDARY SOURCES

OPINIONS BELOW

The opinion of the United States Court of Appeals for the Thirteenth Circuit is reproduced at R. 9-13. The decision and order of the United States District Court, District of Grace is reproduced at R. 1-8.

CONSTITUTIONAL AND STATUTORY PROVISIONS

This case involves questions related to the Supremacy Clause of the United States Constitution, particularly preemption, contained in the U.S. Const. Article VI cl. 2. This case also presents issues pertaining to the interpretation of Rule 8 of the Federal Rules of Civil Procedure. The full text of these provisions are set forth in the appendices.

STATEMENT OF THE CASE

Carolina Laboratories is a manufacturer of children's vaccines with its principal place of business in New Jersey. (R. at 2.) At some point between March 1996 and October 1998 the petitioner's daughter was injected with a combination DPT vaccine manufactured by Carolina Laboratories. The vaccine contained thimerosal, a mercury-containing compound used as a preservative. (R. at 1.) The petitioner's daughter suffers from developmental delays, social delays, learning disabilities, impairment of her motor skills, gastrointestinal illness and immune system dysfunction. The petitioner claims that these injuries were caused by his daughter's vaccination. (R. at 1.) Nobody disputes that the product administered to the petitioner's daughter contained thimerosal or that it is a vaccine recognized under the Vaccine Act. Further, it is stipulated that there were no defects in the preparation or manufacture of the vaccine and that the warning supplied by Carolina Laboratories was adequate. (R. at 1-2.) On January 14, 2004, the petitioners opted out of the National Vaccine Injury Compensation Program. Over three years later, on March 14, 2007, the petitioners brought this action alleging that Carolina Laboratories

was negligent in failing to adequately test the vaccine and that the vaccine was defective in design. (R. at 2.) Petitioners asserted that a safer alternative design existed, however, they could not articulate what it was. (R. at 3.)

SUMMARY OF THE PROCEEDINGS

Petitioners, on behalf of their daughter, initiated these proceedings by filing a petition with the National Vaccine Injury Compensation Program ("NVICP") on September 3, 2001. (R. at 1.) As authorized by the NVICP, they filed a notice of withdrawal on November 5, 2003, which was entered by the Clerk of the U.S. Court of Federal Claims on January 14, 2004. (R. at 2.) The petitioners then elected to file a civil action, which was commenced on March 14, 2007, over three years after their notice of withdrawal was granted. (R. at 2.) Their complaint was initially filed in Wicked County Court, but was correctly removed, pursuant to diversity jurisdiction, to the District Court for the District of Grace. (R. at 2.)

Carolina Laboratories moved for summary judgment on two grounds: first, that § 22(b)(1) of the Vaccine Act imposes a total bar on design defect claims arising from vaccine-related injuries and second, that petitioners failed to allege facts sufficient to state a claim for design defect under Grace law. (R. at 2-3.) The District Court granted summary judgment based on the first argument, holding that a "case-by-case determination of whether a vaccine was unavoidably unsafe would defeat the protection the Vaccine Act was intended to provide vaccine manufacturers." (R. at 7.) The order of summary judgment, dismissing all claims against Carolina Laboratories was issued on March 25, 2008. (R. at 7-8.)

Petitioners appealed the decision of the District Court to the U.S. Court of Appeals for the Thirteenth Circuit. (R. at 9.) The Thirteenth Circuit addressed two issues: (1) whether the Vaccine Act preempted design defect claims and (2) whether the petitioner's complaint

successfully met the heightened pleadings standards in light of this Court's decision in *Bell Atlantic v. Twombly* and *Iqbal v. Ashcroft*. (R. at 10.) In addressing these issues the Thirteenth Circuit held that § 22(b)(1) failed to preempt all design defect claims against manufacturers. (R. at 11.) The Thirteenth Circuit also held that petitioner's complaint "alleges nothing more than conclusions of law and fails to state any scientifically reliable evidence to support their allegations…." (R. at 13.) Finally, based on petitioner's failure to meet the sufficiency standards in both *Twombly* and *Iqbal*, the court affirmed the District Court's dismissal of petitioner's case. (R. at 13.)

SUMMARY OF ARGUMENT

The Thirteenth Circuit's final judgment and its holding in regard to the applicable pleading standard should be affirmed. The Thirteenth Circuit decided that the petitioner's complaint should be dismissed. It reached this conclusion by finding that the complaint did not plead enough facts to make it plausible under this Court's recent decision in *Twombly*. The Thirteenth Circuit also held that § 22 of the National Childhood Vaccine Injury Act does not preempt state design defect claims. Although respondent asks that the final judgment of the Thirteenth Circuit be affirmed, respondent asks that this holding be reversed.

I. The National Childhood Vaccine Injury Act preempts state suits for design defect.

Congress passed the Vaccine Act in 1986 with two prominent objectives: (1) stabilize the vaccine market by protecting manufacturers from uncertain tort liability and (2) provide adequate, fair compensation to those children who are injured by vaccines. Congress believed that vaccinations were one of the most successful health initiatives this country has ever undertaken. However, Congress recognized the danger that uncertain tort liability could have on the vaccine market, including the risk of a vaccine shortage caused by manufacturers leaving the

market. To ameliorate this situation, Congress promulgated § 22 of the Vaccine Act, which contains language that limits state tort claims against vaccine manufacturers.

This language states that a vaccine manufacturer is not liable for a vaccine related injury as long as the vaccine was properly prepared and contained adequate warnings. Although Congress left open the possibility for failure to warn or manufacturing defect claims in state court, it effectively shut the door to the third type of products liability claim, design defect. A design defect claim is generally based on a risk-utility analysis, which is a set of factors a jury will consider to determine if a product was defectively designed. In passing the Vaccine Act, Congress intended to keep this tremendous power from a state jury and replace it with a federally regulated scheme in charge of vaccine design and certification.

The Thirteenth Circuit's holding, allowing a jury to make a case-by-case determination on design defect claims, undermines Congress' intent in passing the Vaccine Act. First, it is a clear misreading of the language Congress utilized in § 22 of the Vaccine Act. Second, it violates the structure of the Vaccine Act as read against the background of products liability law. Third, it is further contrary to Congress' intent, as evidenced by the relevant legislative history. Finally, it undermines the policy behind the Vaccine Act, to stabilize the vaccine market by protecting manufacturers from uncertain liability.

II. Application of *Twombly*'s two-part sufficiency test to the petitioner's complaint results in its dismissal.

In *Bell Atl. Corp. v. Twombly,* this Court announced a two-part test used to analyze the sufficiency of a plaintiff's complaint. Further, in *Iqbal v. Ashcroft,* this Court held that *Twombly*'s two-part sufficiency test applied to all federal complaints. The Thirteenth Circuit properly applied both parts of that test to the petitioner's complaint, holding that the complaint did not allege enough facts to make it plausible on its face, as *Twombly* requires. The Thirteenth

Circuit's holding not only properly applies *Twombly*; it also reinforces this Court's previous policy considerations at issue in *Twombly*.

Therefore, respondent begs this Court to affirm the final judgment of the Thirteenth Circuit, dismissing the petitioner's complaint. Respondent also asks this Court to affirm the Thirteenth Circuits holding that the petitioner's complaint failed to state a plausible claim under *Twombly*, and to reverse its holding that § 22 of the Vaccine Act does not preempt state design defect claims.

ARGUMENT

I. THE NATIONAL CHILDHOOD VACCINE INJURY ACT PREEMPTS STATE SUITS FOR DESIGN DEFECT

The National Childhood Vaccine Injury Act, (hereinafter "Vaccine Act") when read as a whole, reflects Congress' intent to preempt state lawsuits for design defect against vaccine manufacturers. The Vaccine Act, passed in 1986, was intended to provide "optimal prevention of human infectious diseases through immunization and to achieve optimal prevention against adverse reactions to vaccines." 42 U.S.C § 300aa-1 (2006). In order to compensate those who may have been injured by a vaccine, Congress created the National Vaccine Injury Compensation Program (hereinafter "NVICP"), which established a mandatory forum for administration of claims against manufacturers. *Id*. at § 300aa-11. To file a successful claim, a petitioner merely has to show that: (1) the affected person received a vaccine covered under the Act, (2) the affected person suffered an injury listed on the "vaccine table," and (3) it cannot be shown by a preponderance of the evidence that the injuries or death were caused by something other than the vaccine. *Id*. at §§ 300aa-11, 300aa-13, 300aa-14. A petitioner has no duty to prove a defect in the vaccine or any fault of the manufacturer.

Following an order of final judgment from the United States Court of Federal Claims (hereinafter "Vaccine Court"), a petitioner is entitled to either accept the judgment and waive their rights to any remaining tort action, or reject the judgment, and pursue certain, limited claims. *Id*. at § 300aa-21. Section 22 of the Vaccine Act qualifies the causes of action a petitioner is allowed to pursue, should they choose to reject the judgment of the Vaccine Court.

The Thirteenth Circuit's holding, promulgating a case-by-case analysis for state design defect suits, incorrectly interprets the language of the Vaccine Act. (R. at 11.) First, this holding is inconsistent with the language of § 22, which expressly preempts design defect claims. Second, the structure of § 22(b), when read against the backdrop of products liability law, reflects Congress' intent to bar design defect suits against vaccine manufacturers. Third, the relevant legislative history reflects Congress' intent to establish a federally regulated vaccine program, designed to protect manufacturers from the uncertainties of the tort system by barring certain causes of action. Finally, the case-by-case analysis, promulgated by the Thirteenth Circuit, would undermine the purpose and policy behind the Vaccine Act, allowing juries to adversely affect the market for vaccines, a product that Congress considered to be socially beneficial. Accordingly, this Court should reverse the Thirteenth Circuit's judgment and affirm the District Court's decision, holding that the Vaccine Act preempts state product liability suits for design defect.

A. Standard of review

Determining the standard a court should apply when deciding whether state law is preempted by federal statute is a question of law, reviewed *de novo*. *Howlett v. Rose*, 496 U.S. 356 (1990).

B. The language of § 22 demonstrates Congress' intent to bar state tort claims for design defect.

The preemption doctrine is derived from the Supremacy Clause of the United States Constitution. *Bruesewitz v. Wyeth Inc.*, 561 F.3d 233, 238 (3d Cir. 2009). It allows Congress to "supersede state law in several different ways." *Hillsborough County, Fla. v. Automated Med. Labs, Inc.*, 471 U.S. 707, 713 (1985). Congress' ability to supersede has been delineated into three subsections: express preemption, implied conflict preemption, and field preemption. *Id*. Express preemption occurs when Congress abrogates state action through the plain language of a federal statute. *Lorillard Tobacco Co. v. Reilly*, 533 U.S. 525, 541 (2001) (holding that the Federal Cigarette Labeling and Advertising Act expressly preempted Massachusetts from imposing further advertising and labeling restrictions on cigarette manufacturers). Essentially, express preemption is an "explicit statutory command that state law be displaced." *St. Thomas-St. John Hotel & Tourism Ass'n, Inc. v. Gov't of the U.S.V.I.*, 218 F.3d 232, 238 (3d Cir. 2000).

In interpreting the language of Congress, this Court has long recognized that "'[t]he purpose of Congress is the ultimate touchstone' in every preemption case." *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 485 (1996) (quoting *Retail Clerks v. Schermerhorn*, 375 U.S. 96, 103 (1963)). However, a preemption statute that treads on traditional state police powers must be read with a presumption against preemption. *Cipollone v. Liggett Group, Inc.*, 505 U.S. 504, 518 (1992). The starting point of every statutory analysis is the plain language of the text. *Cmty. for Creative Non-violence v. Reid*, 490 U.S. 730, 739 (1989). This is accomplished by giving the plain meaning to the words as they are written. *U.S. v. Am. Trucking Ass'ns*, 310 U.S. 534, 543 (1940).

But, a court should also be guided by "the structure and purpose of the statute as a whole, as revealed not only in the text, but through the reviewing court's reasoned understanding of the

way in which Congress intended the statute and its surrounding regulatory scheme to affect business, consumers, and the law." *Medtronic, Inc.*, 518 U.S. at 486. A court should not be unduly influenced by a single sentence or even a single word, but must look to the objectives and policy of the statute as a whole. *Pilot Life Ins. Co. v. Dedeaux*, 481 U.S. 41, 51 (1987). As a final guide, a court should consider legislative history, especially if the language of the text has more than one reasonable interpretation. *BedRoc Ltd., LLC v. U.S.* 541 U.S. 176, 187 (2004).

1. Congress utilized language of express preemption in crafting § 22 of the Vaccine Act.

In interpreting the language of § 22, the Third Circuit's analysis in *Bruesewitz* is instructive. In *Bruesewitz*, the plaintiff brought a design defect suit against Wyeth, a vaccine manufacturer, alleging that their minor child received the DPT vaccination series and was subsequently injured. *Bruesewitz*, 561 F.3d at 236. The Third Circuit held that § 22 of the Vaccine Act bars design defect claims against vaccine manufacturers in both strict liability and negligence. *Id*. at 251. Further, the Third Circuit reasoned that the text of § 22(b)(1) was necessarily Congressional language of express preemption. *Id*. at 242.

In reaching this conclusion, the Third Circuit relied heavily on a decision of this Court, *Lorillard Tobacco Co. v. Reilly*. *Id.* In *Lorillard*, this Court addressed whether § 1334 of the Federal Cigarette Labeling and Advertising Act (hereinafter "FCLAA") preempted certain state restrictions on cigarette advertising. *Lorillard Tobacco Co.*, 533 U.S. at 540. The language of § 1334(a) of the FCLAA states that "…no statement relating to smoking and health, other than the statement required by § 1333 of this title, shall be required on any cigarette package." 15 U.S.C. § 1334(a) (2006). This Court characterized this language as expressly carving out an area where states may not regulate, even though Congress failed to use language such as "no state shall" or "state law is preempted." *Lorillard Tobacco Co.*, 533 U.S. at 542. This Court reasoned that the

language used showed that "Congress unequivocally preclude[d] the requirement of any additional statements on cigarette packages beyond those provided in §1333." *Bruesewitz*, 561 F.3d at 242 (quoting *Lorillard Tobacco Co.*, 533 U.S. at 542).

Similar to the statutory language analyzed *Lorillard*, § 22(a) of the Vaccine Act says that "except as provided in subsection (b), (c), and (e) of this section State law shall apply to a civil action brought for damages for vaccine-related injury or death." 42 U.S.C. §§ 300aa-22(a). Again, although Congress failed to use the "key words" of express preemption mentioned above, based on this Court's analysis of § 1334 of the FCLAA, § 22 of the Vaccine Act demonstrates Congress' unequivocal intent to preclude state law from applying in certain delineated areas regarding vaccinations. *Bruesewitz*, 561 F.3d at 242.

2. Section 22(b)(1) explicitly preempts state tort suits for design defect, while leaving open the possibility of state suits for failure to warn or manufacturing defect.

Section 22(b)(1) states:

> no vaccine manufacturer shall be liable in a civil action for damages arising from a vaccine-related injury or death associated with the administration of a vaccine after October 1, 1988, if the injury or death resulted from side effects that were unavoidable even though the vaccine was properly prepared and was accompanied by proper directions and warnings.

42 U.S.C. § 300aa-22(b)(1).

The Third Circuit recognized the scope of this express preemption provision as the crux of preemption analysis. *Bruesewitz* 561 F.3d at 243. However, the Thirteenth Circuit's interpretation of this preemptive scope was incorrect, in that it held that subsection (b)(1) allows for a case-by-case determination of unavoidable side effects. (R. 11.) Further, the Thirteenth Circuit also incorrectly assumed that use of the word "unavoidable" meant that certain side effects were avoidable. (R. 11.)

Respondent concedes that the words "design defect" are not included in the text. However, subsection (b) implicitly recognizes design defect claims, "as evidenced by the use of a subordinate clause introduced by 'even though' to reference claims that might arise from a manufacturing defect or warning defect." *Bruesewitz*, 561 F.3d at 245. Congress crafted this language to specifically leave two causes of action within State law authority: manufacturing defect and failure to warn. *Blackmon v. Am. Home Prods. Corp.*, 328 F.Supp.2d 659, 664 (S.D. Tex. 2004). Thus, if "the alleged defect that caused the injury does not fall into one of these two enumerated categories, the defect is considered 'unavoidable,' and the claimant's tort claim is barred." *Id*. Reading the language of subsection (b) in concert with subsection (a) illustrates the clear intent of Congress to exempt manufacturers from design defect liability. *Bruesewitz*, 561 F.3d at 245.

C. The structure of the Vaccine Act, read against the backdrop of products liability law, expressly bars design defect claims.

The structure of the Vaccine Act, read as a whole, bars state design defect claims. The Vaccine Act established the National Vaccine Program, which is under the supervision of a director, task force, and two other commissions. *See* 42 U.S.C. §§ 300aa 1, 2, 5, 19, 27. This regulatory system put the Food and Drug Administration (hereinafter "FDA") in charge of "design and distribution of prescription drugs, including vaccines." *Sykes v. Glaxo-SmithKline*, 484 F.Supp.2d 289, 301 (E.D. Penn. 2007) (citing 21 U.S.C. §§ 301-393). Manufacturers must submit a formal Product License Application, which contains information about vaccine safety, efficacy, labeling, and manufacturing, to the FDA, before being allowed market any vaccine. *See* 42 U.S.C. § 262(a).

The FDA is in charge of individual vaccine licenses based on each vaccine's specific formula and labeling information. *See* 21 C.F.R. §§ 601.2, 601.12 (2010). This type of analysis

requires the FDA to employ extremely "specialized experience in assessing risks and control measures" of vaccines, which the state tort system is "ill-equipped to handle." Victor E. Schwartz & Phil Goldberg, *A Prescription for Drug Liability and Regulation*, 58 Okla. L. Rev. 135, 136 (2005). Once the FDA has concluded its rigorous vaccine review process, a manufacturer is restricted from changing the formula or label of that vaccine. *Sykes*, 484 F.Supp.2d at 301. Because the Vaccine Act delegates questions of safety to the Secretary of Health and Human Services, an individual challenge to an FDA approved design would undermine the FDA's authority in setting the standards for childhood vaccine safety. *Id*.

A case-by-case determination, supported by the Thirteenth Circuit's holding, would allow juries to hold manufacturers "liable for design defects in drugs approved by the FDA." *Id*. The consequence of this type of case-by-case determination, discussed below, is another factor consistent with the conclusion that "§ 22(b) directs the evaluation of vaccine design exclusively to the FDA." *Id*.

D. The relevant legislative history reflects Congress' intent to preempt design defect claims.

This Court, in *Cipollone*, recognized that a statute should be read as a whole, keeping its purpose in mind, including reference to legislative history. *Cipollone*, 505 U.S. at 519. In reviewing relevant legislative history, the authoritative source is the Committee Report on the bill that became law. *Garcia v. U.S.*, 469 U.S. 70, 76 (1984). The legislative history surrounding the Vaccine Act reflects Congress' conviction of the social benefit of vaccinations as an effective means to combat disease. It further reflects Congress' deep concern with the instability of the vaccine market and the realization that some vaccines, although extremely beneficial, are incapable of being made any safer.

1. Congress understood the overwhelming social benefit associated with vaccinations.

Congress passed the Vaccine Act with two primary goals: (1) compensating individuals injured by vaccines and (2) safeguarding manufacturers against uncertain liability, while encouraging development of new, improved vaccines. *Bruesewitz*, 561 F.3d at 247. As long as manufacturers met the product specifications regulated by the FDA, they were to be exempt from tort liability. *Sykes*, 484 F. Supp. 2d at 302. Congress, medical doctors, and the public all understood that vaccinations were the most effective means of reducing the incidence of communicable diseases. Elizabeth A. Breen, *A One Shot Deal: The National Childhood Vaccine Injury Act*, 41 Wm. & Mary L. Rev. 309, 311-312 (1999). Congress specifically stated that "vaccinations of children against deadly, disabling, but preventable infectious diseases [have] been one of the most spectacularly effective public health initiatives this country has ever undertaken." H.R. Rep. No.99-108 at 4 (1986), *reprinted in* 1986 U.S.C.C.A.N. 6344, 6345.

Every state now requires children to be immunized prior to attending public schools. Derry Ridgway, *No-Fault Vaccine Insurance: Lessons From the National Vaccine Injury Compensation Program*, 24 J. Health. Pol. Pol'y & L. 59, 60 (1999). Vaccines have vastly reduced the number of communicable diseases. For example, smallpox was prevalent at the turn of the twentieth century, but in 1980, the World Health Organization "declared that smallpox had been totally eradicated…" no longer requiring routine vaccinations. United States Center for Disease Control, *Historical Perspectives Notifiable Disease Surveillance Statistics – United States, June 1946 and June 1996*, 45 Morbidity & Mortality Wkly. Rep. (June 28, 1996) *available at* http://www.cdc.gov/MMWR/preview/mmwrhtml/00042744.htm (last visited Feb. 26, 2010). Although vaccines were highly effective, they did pose a risk of side effects to a small number of children. Paula Jacobi, *Pharmaceutical Tort Liability: A Justifiable Nemesis to*

Drug Innovation and Access?, 38 J. Marshall L. Rev. 987, 989 (2005). These side effects led to lawsuits, and lawsuits led to the disruption of the vaccine market. *Id*.

2. Prior to passing the Vaccine Act, Congress was acutely aware of the instability of the vaccine market, due to the rising cost of tort litigation.

In the half-decade prior to the passage of the Vaccine Act, claims against vaccine manufacturers reached more than $3.5 billion. Ridgway, *No-Fault Vaccine Insurance*, 24 J. Health Pol. Pol'y & L. at 60-61. As the civil tort verdicts began to mount, vaccine manufacturers began to stop their vaccine research and production, and many began exiting the market entirely. Jacobi, *Pharmaceutical Tort Liability*, 38 J. Marshall L. Rev. at 989. For example, early 1980's tort litigation increased the price of DPT vaccine from "11 cents in 1982 to $11.40 in 1986, with $8 of this price going towards liability insurance." Deborah J. La Fetra, *Freedom, Responsibility, and Risk: Fundamental Principles Supporting Tort Reform*, 36 Ind. L. Rev. 645, 650 (2003). Ultimately, this increasing tort liability became such a burden, that "ten of the thirteen companies producing vaccines for five serious childhood diseases left the market." *Id.*at 649.

In an attempt to ease the burdens of uncertain, skyrocketing tort ligation against manufacturers, and a dwindling supply of childhood vaccines, Congress passed the National Childhood Vaccine Injury Act in 1986. Kapil Kumar Bhanot, *What Defines a Public Health Emergency? An Analysis of the Strategic National Stockpile and the National Childhood Vaccine Injury Act: The Need for Prevention of Nonterror National Medical Emergencies*, 21 Contemp. Health L. & Pol'y 137, 140-41 (2004). Specifically, Congress stated that "the loss of any of the existing manufacturers of childhood vaccines at this time could create a genuine public health hazard in this country," and that "the withdrawal of even a single manufacturer would present the very real possibility of vaccine shortages, and, in turn, increasing numbers of unimmunized

children, and, perhaps, a resurgence of preventable diseases." H.R. Rep. No 99-908, at 6, *reprinted in*1986 U.S.C.C.A.N 6344, 6347. Although socially beneficial, Congress recognized that a small number of children would be seriously injured in the process of vaccination. H.R. Rep. No 99-908, at 5-6, *reprinted in*1986 U.S.C.C.A.N 6344, 6346. Therefore, Congress utilized the language of comment k to section 402A of the Restatement (Second) of Torts, in clarifying its direction under § 22(b) of this Act. *See* H.R. Rep. No 99-908, at 25-26, *reprinted in*1986 U.S.C.C.A.N 6344, 6366-67.

3. Congress intended Restatement (Second) of Torts section 402A comment k, to apply to § 22(b)(1) of the Vaccine Act, effectuating an intent to bar design defect suits.

Congress specifically stated that certain provisions within § 300aa-22 would "change most state laws." H.R. Rep. No 99-908, at 25, *reprinted in*1986 U.S.C.C.A.N 6344, 6366. However, this change was fair, given the availability of an ample compensation system. *Id.* Specifically addressing subsection (b), Congress utilized the language of comment k of the Restatement (Second) of Torts section 402A . *Id*. at 25-26. Comment k stands for the principle that certain products are inherently beneficial to society although it is impossible to make these products safer. *Id*. at 26. Specifically, comment k states that

> the seller of such products, again with the qualification that they are properly prepared and marketed, and proper warning is given, where the situation calls for it, is *not to be held to strict liability for unfortunate consequences attending their use, merely because he has undertaken to supply the public with an apparently useful and desirable product, attended with a known but apparently reasonable risk.*

Restatement (Second) of Torts § 402A cmt. k (emphasis added).

Congress fully understood the emotional overtones associated with the childhood vaccination issue, stating that

> even if the defendant manufacturer may have made as safe a vaccine as anyone reasonably could expect, a court or jury undoubtedly will find it difficult to rule in favor of the "innocent" manufacturer if the equally "innocent" child has to bear the risk of loss with no other possibility of recompense.

H.R. Rep. No 99-908, at 26, *reprinted in* 1986 *U.S.C.C.A.N.* 6344, 6367. Analogous to § 22(b),

> comment k distinguishes the three heads of products liability – design defect, manufacturing defect, and warning defect – and rejects the notion of defective design in the context of products with certain known and inherent risks that have nonetheless been accepted as a matter of policy given the benefit provided and the grim consequences that would follow if the product were not available.

Sykes 484 F.Supp.2d 300.

That is why Congress stated that if an injured person "cannot demonstrate under applicable law either that a vaccine was improperly prepared or that it was accompanied by improper directions or inadequate warnings" they "should pursue recompense in the compensation system, not the tort system." H.R. Rep. No. 99-908, at 26, *reprinted in* 1986 U.S.C.C.A.N. 6344, 6367. This regulatory system would allow an individual to obtain fair compensation even if the manufacturer could not have made the vaccine any safer. *Id.* This legislative history "indicates rather clearly the Committee's intent to relegate design defect claims to the compensation system, provided that the injury-producing vaccine was manufactured and distributed according to applicable federal standards." *Blackmon* 328 F. Supp. 2d at 665.

The Thirteenth Circuit's opinion correctly acknowledges that states have applied comment k in a more limited way, establishing a case-by-case analysis to determine if a product was unavoidably unsafe. (R. 10.) However, it erroneously held that Congress intended comment k to be applied using a case-by-case analysis.

First, the Thirteenth Circuit ignores that "courts in a significant minority of states have held that comment k preempts strict liability design defect claims against FDA-approved drugs."

Bruesewtiz, 561 F.3d at 248 (FN 9). In *Brown v. Superior Court*, the Supreme Court of California rejected the risk-utility or consumer expectation analysis as applied to prescription drugs, holding that comment k barred design defect claims against manufacturers. 751 P.2d 470, 480 (Cal. 1988); *See also Young for Young v. Key Pharms., Inc.*, 922 P.2d 59, 64 (Wash. 1996) (Supreme Court of Washington rejecting a case-by-case determination of whether a product is unavoidably unsafe); *Grundburg v. Upjohn Co.*, 813 P.2d 89, 95 (Utah 1991) (Supreme Court of Utah agreeing with the analysis of the *Brown* decision, believing that this application was in line with the public policy considerations in the area of pharmaceutical design). The Court recognized that "[p]ublic policy favors the development and marketing of beneficial new drugs, even though some risks, perhaps serious ones, might accompany their introduction, because drugs can save lives and reduce pain and suffering." *Id.* at 1063

Second, the Vaccine Act was passed in 1986, and current interpretations of comment k yield little guidance on what Congress knew in the mid 1980's. *Bruesewitz*, 561 F.3d at 248 n.9. Even today there is very little uniformity in the application of comment k, as well as much uncertainty and fear that applying the case-by-case analysis will create a disincentive for manufacturers in developing new pharmaceuticals. *Grundberg*, 813 P.2d at 94-95. However, after reviewing the legislative history, purpose, and structure of the Vaccine Act, it is clear that Congress' adoption of comment k closely parallels the "product availability-over product safety" reasoning in *Brown.* Three policies outline this reasoning: (1) society has greater interest in the availability of beneficial drugs, (2) a state design defect suit, based on a risk-utility analysis, exposes manufacturers to uncertain liability, decreasing the incentives to produce new, beneficial drugs, and (3) increase of tort suits for design defect leads to higher priced vaccines due to the increased need for liability insurance. *Brown*, 751 P.2d at 479.

E. A case-by-case analysis of design defect suits frustrates the intent of Congress by replacing a sophisticated regulatory scheme with the whims of state court juries.

Allowing a state jury to decide when a vaccine is unavoidably dangerous would undermine not only the language of the Vaccine Act, but also the regulatory scheme that Congress established. Congress intended to vest the determinative power of vaccine design safety in a number of federal agencies by establishing a regulatory scheme to control the makeup and marketing of vaccines. Further, the vast majority of courts have recognized that Congress intended the power of vaccine design to be vested within federal agencies, rejecting a case-by-case approach as undermining that intent.

1. Congress intended specific federal agencies to govern vaccine design, not the juries of fifty different states.

Congress intended the federal agencies listed within the language of the Vaccine Act, with their experience and expertise, to control the design of vaccinations, not juries. *Sykes*, 484 F.Supp.2d 299. Allowing juries "in each state to pass judgment on the design of childhood vaccines could interfere with the federal government's efforts to establish a uniform national standard for childhood vaccines." *Id*. at 301. Congress designated a number of entities to control the licensing, distribution and safety evaluation of vaccines. *See generally* 42 U.S.C. §§ 300aa-1, 2. These entities include the FDA's Office of Biologics Research and Review, the National Institute of Health, and the Centers for Disease Control and Prevention. *See* 42 U.S.C. § 300aa-2. Specifically, Congress mandated that the Secretary of Health and Human Services "promote the development of childhood vaccines that result in fewer and less serious adverse reactions than those vaccines on the market on December 27, 1987, and promote refinement of vaccines." 42 U.S.C. § 300aa-27(a)(1). It is the Secretary, not the jury, who is in charge of

assuring improvements in licensing, manufacturing, processing, testing, labeling, warning, and research of more effective, improved vaccines. *Id*.

The essence of a design defect claim is a risk-utility analysis. (R. 4.) A design defect suit allows the jury to consider several factors, giving them great power in determining the social utility of a product. Specifically, the jury is allowed to consider the "gravity and severity of the danger caused by the design, the avoidability of the danger, and the ability to eliminate the danger without impairing the product's usefulness." (R. 4.) Allowing a jury to consider these factors would undermine the Vaccine Act's regulatory scheme, as established by Congress. Elissa Levy, *The Health Act's FDA Defense to Punitive Damages*, 74 Fordham L. Rev., 2425, 2435 (2006). Congress passed § 22(b)(1), utilizing the language of comment k to prevent courts from "co-regulating" vaccines on a case-by-case basis. *Id*. Specifically, Congress was worried that courts, especially sympathetic juries, would focus on a specific injury by a specific plaintiff when they impose liability. *Id*. This type of piecemeal state tort regulation subject's vaccine manufacturers to numerous different tort standards, the very problem the Vaccine Act was designed to prevent. *Id.* at 2449-50.

The purpose of the Vaccine Act was to "free manufacturers from the specter of large, uncertain tort liability, and thereby keep vaccine prices fairly low and keep manufactures in the market." *Schafer v. Am. Cyanamid Co.*, 20 F.3d 1, 4 (1st Cir. 1994). This type of case-by-case analysis would defeat the protection the Vaccine Act was intended to provide, again subjecting manufacturers to the "unpredictability and expense of the tort system" causing them exit the market. *Sykes*, 484 F.Supp.2d at 302. The Thirteenth Circuit's holding that "unavoidably unsafe products" should be evaluated on a case-by-case basis is not only inconsistent with the "policy behind the Vaccine Act; it strips the passage of all meaning." *Blackmon*, 328 F.Supp.2d at 665.

This interpretation of the statute would protect manufacturers "from liability only on meritless claims." *Id.* Further, it would take the authority away from the FDA where Congress designated it, and allow juries to hold manufacturers liable for design defect suits even though they met the stringent requirements of FDA approval. *Id.*

2. A case-by-case analysis of § 22(b)(1) has been rejected by an overwhelming majority of courts.

The Georgia Supreme Court is the only court to hold that § 22(b)(1) must be determined through a case-by-case analysis. *Am. Home Prods. Corp. v. Ferrari*, 668 S.E.2d 236, 242 (Ga. 2008). Conversely, two district courts and the Third Circuit Court of Appeals have all rejected this approach, holding that a design defect claim is expressly preempted under the language of § 22(b)(1) of the Vaccine Act. *See Bruesewitiz*, 561 F.3d at 255; *Sykes* 484 F.Supp.2d at 303; *Blackmon*, 328 F.Supp.2d at 666. Further, the opinion of the Georgia Supreme Court is erroneous for three reasons. First, the court placed undue emphasis on the conditional nature of the word "unavoidable" in § 22(b)(1). *Ferrari*, 668 S.E.2d at 240. The court believed this conditional nature implied that some vaccine injuries or deaths could be avoided. *Id*. Second, the court placed undue influence on the current status of comment k, as adopted by the states. *Id.* at 239. It noted that a majority of the states permit design defect claims under comment k. *Id.* However, the current state of affairs with regard to comment k speaks little as to Congressional intent surrounding the 1986 adoption of the Vaccine Act. *Bruesewitz*, 561 F.3d at 248 n.9.

Second, the court discounted a significant minority of states who have held that a case-by-case determination of design defect suits for unavoidably dangerous products undermines the purpose of comment k; most notably, the California Supreme Court, which adopted an express preemption of design defect suits against prescription drug manufacturers in 1988, just two years after the Vaccine Act was passed. *See Brown v. Superior Court*, 751 P.2d at 480. Finally, a

case-by-case determination would undermine each of the objectives in the Committee Report, which set up an alternative compensation system, stressed the importance of vaccine development, and expressed concern about the rising cost of tort litigation and the adverse effects of losing just one manufacturer from the market. *Bruesewitz*, 561 F.3d at 248-249. Accordingly, this Court should reverse the Thirteenth Circuit, and hold that § 22(b)(1) of the Vaccine Act expressly preempts state tort suits for design defect.

II. APPLICATION OF THE *TWOMBLY* PLEADING STANDARD RESULTS IN DISMISSAL OF PETITIONER'S COMPLAINT.

Federal Rule of Civil Procedure 12(b)(6) allows for dismissal of a complaint "for failure to state a claim upon which relief can be granted." While a complaint does not need detailed factual allegations to survive a 12(b)(6) motion, it must assert enough factual material to make the claim plausible and raise "it above the speculative level." *Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 555 (2007). A mere formal recitation of the elements of a cause of action without factual support is insufficient. *Id.* The U.S. Supreme Court recently explained that this standard applies to all civil litigation, resulting in an affirmative requirement that a complaint allege enough factual information to make it plausible on its face. *Ashcroft v. Iqbal*, 129 S. Ct. 1937, 1949 (2009). A claim is only facially plausible when it pleads enough facts to allow the court to draw the *reasonable* inference that the defendant is liable for the alleged misconduct. *Id*. at 1949.

When deciding a 12(b)(6) motion a court must construe the complaint in the light most favorable to the plaintiff and must accept all factual allegations as true. *Id*. However, this does not hold true for legal conclusions which the court may freely reject. *Id*.

A. Standard of review.

In reviewing a District Court's decision on a motion to dismiss pursuant to 12(b)(6) this Court reviews *de novo*. *See Mylan Labs., Inc. v. Matkeri*, 7 F.3d 1130, 1134 (4th Cir. 1993).

B. Application of *Twombly's* two-part test set forth by this Court and followed by all federal courts results in dismissal of Petitioner's complaint.

Since this Court's decision in *Twombly*, a two-part test is used to analyze the sufficiency of a complaint. The first step is to identify any conclusory allegations. *Ashcroft v. Iqbal*, 129 S.Ct. 1937, 1950 (2009). "Threadbare recitals of the elements of a cause of action, supported by mere conclusory statements, do not suffice." *Id.* at 1949 (citing *Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 555 (2007)). When reviewing a motion to dismiss the court must accept well-pleaded factual allegations of the complaint as true but is "not bound to accept as true a legal conclusion couched as a factual allegation." *Id.*

After assuming the veracity of all well-pleaded factual allegations and striking those allegations which are merely conclusory, the court engages in the second step: determining whether the complaint pleads "a claim to relief that is plausible on its face." *Iqbal*, 129 S.Ct. at 1949-50 (citing *Twombly*, 550 U.S. at 556) (rejecting the traditional 12(b)(6) standard set forth in *Conley v. Gibson*, 355 U.S. 41, 45-46 (1957) that a complaint should not be dismissed "unless it appears beyond doubt that the plaintiff can prove no set of facts in support of his claim which would entitle him to relief."). A claim is facially plausible when the plaintiff "pleads factual content that allows the court to draw the reasonable inference that the defendant is liable for the misconduct alleged." *Id.* at 1949 (citing *Twombly*, 550 U.S. at 556). The standard for plausibility is not akin to a "probability requirement," but requires "more than a sheer possibility that a defendant has acted unlawfully." *Id.*

In *Twombly*, plaintiffs brought suit alleging anti-trust violations by Bell Atlantic Corporation. *Twombly*, 550 U.S. at 549-551. The principle allegation in the complaint hinged

on the assertion that Bell had engaged in parallel conduct with several of its competitors. *Id.* The Court noted that while parallel conduct may be offered as circumstantial evidence of a conspiracy it did not establish the "contract, combination, or conspiracy" required by the anti-trust act. *Id.* at 554 (citing 6 P. Areeda & Hovenkamp, Antitrust Law ¶ 1433a, p. 236 (2d ed. 2003)). The complaint further failed to show that any of the alleged parallel conduct was in fact consistent with conspiracy. *Id*. This Court reasoned that on its face the alleged parallel conduct could be "just as much in line with a wide swath of rational and competitive business strategy unilaterally prompted by common perceptions of the market." *Id*. It went on to state that factual allegations must be above the speculative level. *Id*. at 555. This Court noted several policy reasons for its decision, mainly, that without this sort of new backstop to litigation, plaintiffs armed only with speculative claims will continue to take up judicial and economic resources by pursuing liability that does not exist. *Id*. at 557-559.

Two leading cases in the area of products liability apply and explain the practical application of the *Twombly* pleading standard. The first is *Frey v. Novartis Pharms. Corp.*, 642 F.Supp.2d 787 (S.D. Ohio 2009). In *Frey*, the plaintiff alleged, among other claims, defect in design of the drug Trileptal. *Id*. at 790. The plaintiff made factual allegations that Trileptal had previously been linked to "several severe and life threatening medical disorders" and that a practical and feasible "alternative design was available which would have prevented the harm alleged without substantially impairing the product's usefulness or intended purpose." *Id*. at 789-790. However, the plaintiff also alleged that they could not particularly allege why the scientific make-up of the drug was defective without conducting discovery. *Id*. at 792. The court held that the design defect claim must be dismissed because it failed to allege any facts that would make the claim plausible under *Twombly*. *Id*. at 795. Even though the complaint stated

that some reasonable alternative design existed, it failed to state any actual design defect which could have been the proximate cause of the plaintiff's injuries. *Id*.

The Western District of Louisiana was confronted with a similar claim in *Ivory v. Pfizer Inc.*, 2009 WL 3230611 (W.D. La. 2009). This decision is particularly insightful because it illustrates what must be pled in order to be considered sufficient under *Twombly's* plausibility standard. The plaintiff in *Ivory* claimed that the anti-smoking drug Chantix was defective in construction and alternatively in design. *Id*. at *1. The complaint at issue made a hundred and four factual averments including allegations that medical reports as early as 1972 documented the risks involved with Chantix, that there had been numerous adverse event reports from the FDA, and that regulatory action and reviews from the FDA indicated increased risks. *Id*. at *2. The court held that this was sufficient to raise a right to relief above the speculative level making the complaint plausible as to defect in construction. *Id*. However, in regard to the design defect claim, the court was left with no choice but to dismiss based on the plaintiff's failure to plead that there was a reasonable alternative design that would have prevented the harm caused, a requirement under Louisiana law. *Id*. at *3.

1. Application of the first part of *Twombly*'s two-part test eliminates all conclusory allegations from the petitioner's complaint.

Similar to the plaintiffs in *Ivory*, petitioner alleged negligence in testing and defect in design under Grace law. (R. at 2.) The first count of petitioner's complaint, negligence in failing to test, is simply a recitation of the elements of the cause of action. (R. at 4.) It alleges no factual information about causation except the conclusory statement that "as a result of the mercury exposure, Estella Marie suffered neurological injuries." (R. at 4, n.7.) Any information in regard to causation is totally void, that is, how any testing or lack of testing could have contributed or caused the damages claimed. Because causation has not been pled, the statement

alleging damages becomes wholly conclusory and should be stricken from the complaint altogether. Again, this Court should be mindful that "threadbare recitals of the elements of a cause of action, supported by mere conclusory statements, do not suffice." *Iqbal*, 129 S. Ct. at 1949 (citing *Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 555 (2007)).

Count one of the petitioner's complaint alleges that Carolina Laboratories negligently failed to conduct adequate safety tests to determine if thimerosal was safe and nontoxic to humans in the doses administered. (R. at 2.) The first part of *Twombly's* two-part test demands that unsupported legal conclusions be eliminated from the complaint. Assuming, *arguendo*, that the statements in the complaint are not legal conclusions, count one of the complaint is still defective because it is void of any supportive facts. The complaint fails to allege what tests were accomplished, why those tests were not adequate or what testing would have been adequate. The complaint fails to define what acceptable results from testing would have been. Finally, petitioner concedes that there was no defect with the preparation or manufacture of the vaccine and that the warnings supplied were adequate. (R. at 2, n.5.) In light of these deficiencies, the Thirteenth Circuit was left with only one choice, dismissing this count. (R. at 13.)

The second count of the complaint, defective design, is similarly flawed. Grace law employs an in-depth risk-utility analysis when determining whether a product is defective. (R. at 4.) This analysis looks to a number of factors such as the gravity and severity of the danger caused by the vaccines design, the avoidability of that danger, and the ability to eliminate the danger without impairing the product's usefulness i.e., the availability of a reasonable alternative design. (R. at 4.) The only risk-utility factor alleged in the complaint is that a reasonable alternative design existed. (R. at 2.) Although that is one of the applicable standards to evaluate whether a product is defective in Grace, the petitioners have failed to allege factually what that

design would have been. Nor were they, at anytime, able to provide this information by amending their complaint. This complaint is also void of any mention of the other elements of design defect such as the gravity and severity of the danger caused by the design of the vaccine and the avoidability of danger. Further, this count is defective in that it fails to allege any sort of causal link between exposure to the vaccine and illness besides a conclusory allegation with no scientific factual support. (R. at 4, n.7.) After striking these conclusory statements from the complaint as the first part of the sufficiency test under *Twombly* and *Iqbal* requires, the only remaining facts are that the respondent manufactured the vaccine at issue, the petitioner was vaccinated, and the petitioner is ill.

After striking all conclusory allegations contained in count two of the complaint the only thing that could possibly survive is the allegation that a reasonable alternative design exists. (R. at 2.) The petitioner also states that they cannot plead their specific allegations more particularly without conducting discovery. (R. at 3.) This is remarkably similar to the plaintiffs in *Frey*. The court there found that the assertion that a reasonable alternative design existed without more was not enough to elevate the claim above the speculative level. This Court in *Twombly* reached the same conclusion in regard to whether the bare factual allegation of parallel conduct was enough to make a claim for conspiracy plausible. In no way do the petitioner's allegations rise to the level of those made by the plaintiff in *Ivory*. The complaint in *Ivory* contained one hundred and four factual allegations that listed detailed facts and data in regard to the problems discovered by the FDA and other medical studies regarding Chantix. *Ivory*, 2009 WL 3230611 at *2. The court held that those facts directly supported their defect in composition claim and raised it above the speculative level. *Id*.

2. With all conclusory allegations removed, the second part of *Twombly*'s two-part test determines whether the remnants of the complaint make it plausible.

Moving to the second part of *Twombly* and *Iqbal's* two-part test the court looks at what is left of the complaint and determines if it states a claim that is plausible on its face. *Iqbal*, 129 S.Ct. at 1949, 1950 (citing *Twombly*). Again, the only factual allegations remaining after the first part of the test are that the petitioner's daughter received a vaccine, the vaccine was manufactured by Carolina Laboratories, and the petitioner's daughter is ill. The illness suffered in this case is analogous to the parallel conduct alleged in *Twombly*. There, this Court concluded that, after striking conclusory allegations, the remaining factual allegations simply were not plausible because, while parallel conduct might be circumstantial evidence of conspiracy at trial, the complaint failed to show that any of the alleged parallel conduct was in fact consistent with conspiracy. *Twombly*, at 554. The facts in this case similarly do not demonstrate how this illness is consistent with either a design defect or a failure to test. Because petitioner's complaint fails to allege sufficient facts, similar to those alleged in *Ivory*, the Thirteenth Circuit, applying *Twombly*, was left with only one choice, dismissal of the petitioner's complaint. (R. at 13.)

3. The District Court applied what is now bad law.

The District Court reached the wrong conclusion because its analysis was flawed from the outset. The judge's analysis rests on the proposition that it may be difficult for a plaintiff to know the source of defect responsible for the harm caused. (R. at 4.) She concluded that because Carolina Laboratories was on notice of the plaintiff's accusations, the pleadings were satisfactory. *Id*. The District Court's opinion cites to what is now bad law when it quotes *Iqbal v. Hasty*, 490 F.3d 143 (2d Cir. 2007), *rev'd, Iqbal v. Ashcroft*, 129 S.Ct. at 1954. This analysis fails to apply *Twombly*'s two-part test. Because the Thirteenth Circuit correctly applied

Twombly and concluded that the complaint was not plausible, we ask this Court to affirm that decision. (R. at 12-13.)

C. Public policy supports a heightened pleading standard when the initiation of a potentially frivolous lawsuit has a regulatory effect on the vaccine market.

In *Cippollone v. Ligget*, this court recognized the regulatory effect of lawsuits. 505 U.S. 504 (1992) (holding that the federal Public Health Cigarette Smoking Act preempted state law failure to warn claims). A manufacturer found liable for products liability claims is presented with a myriad of decisions. *Id.* at 536. The manufacturer can alter the product, provide better warnings, choose to stop selling the product, or accept payment of damages awards as the cost of doing business. *Id.* When a high profile lawsuit is filed the media takes notice, stock prices fluctuate and public speculation sets in. Sharon Sobczak, *To Seal or Not to Seal, In Search of Standards*, 60 DEFCJ 406, 411 (1993).

Cippollone involved cigarette manufacturers. The case at bar is fundamentally more important because it involves the manufacturers of vaccines. Although vaccines are effective, they do pose a risk of side effects to a small number of children. Paula Jacobi, *Pharmaceutical Tort Liability: A Justifiable Nemesis to Drug Innovation and Access?*, 38 J. Marshall L. Rev. 987, 989 (2005). These vaccine side effects have led to lawsuits that have led to disruptions of the vaccine market. *Id*. With mounting litigation costs several vaccine manufacturers stopped vaccine research and began exiting the market altogether. *Id*.

Nobody benefits from the disruptions caused by the filing of frivolous suits built only on allegations unsupported by any set of plausible facts. *Twombly's* plausibility standard effectively allows a 12(b)(6) motion to test the sufficiency of the complaint at an early stage. Thus, manufacturers do not have to bear the regulatory burden of a lawsuit when there has been no finding of wrongdoing but merely a speculative allegation. Parents do not have to live with the

day-to-day bombardment of the media crying wolf simply because a suit is filed without factual support. After *Twombly,* potential plaintiffs should understand that a reasonable investigation must be completed before filing to ensure that their allegations are plausible.

D. The continued application of *Twombly* to all federal complaints advances judicial policy by increasing district court discretion.

Rule 12(i) of the Federal Rules of Civil Procedure states that any defense listed in Rule 12(b)(1)-12(b)(7) must be heard and decided before trial unless the court orders a deferral until trial. Fed. R. Civ. Pro. 12(i). This expressly empowers a trial judge with the ability to defer ruling on a 12(b)(6) motion until the eve of trial or during trial itself. Edward Hartnett, *Taming Twombly Even After Iqbal*, 158 U. Pa. L. Rev. 473, 511 (2010) *quoting* Charles Clark, *Handbook of the Law of Code Pleading 2d ed.* vii-viii (1947). Either way, additional discovery is available to the plaintiff when a trial judge feels that there is a reasonable expectation that discovery will raise the complaint from the speculative to the plausible level. *Id*. at 511-512. This gives a District Court a wide range of latitude in deciding which complaints are so flawed on their face that no amount of investigation or discovery will be able to cure the defect and which complaints appear questionable but may be corrected through amendment after reasonable discovery. Exercise of a District Court judge's discretion in such matters is largely unreviewable as it is not a final order that would be appealable. *Id*. at 513.

CONCLUSION

For the foregoing reasons, Petitioners respectfully request that this Court affirm in part and reverse in part the judgment of the Court of Appeals for the Thirteenth Circuit.

Appendix A

U.S. Const. Article VI cl. 2

This Constitution, and the Laws of the United States which shall be made in Pursuance thereof; and all Treaties made, or which shall be made, under the Authority of the United States, shall be the supreme Law of the Land; and the Judges in every State shall be bound thereby, any Thing in the Constitution or Laws of any State to the Contrary notwithstanding.

Appendix B

15 U.S.C. § 1334

a) Additional statements

Except to the extent the Secretary requires additional or different statements on any cigarette package by a regulation, by an order, by a standard, by an authorization to market a product, or by a condition of marketing a product, pursuant to the Family Smoking Prevention and Tobacco Control Act (and the amendments made by that Act), or as required under section 387c(a)(2) of Title 21 or section 387t(a) of Title 21, no statement relating to smoking and health, other than the statement required by section 1333 of this title, shall be required on any cigarette package.

(b) State regulations

No requirement or prohibition based on smoking and health shall be imposed under State law with respect to the advertising or promotion of any cigarettes the packages of which are labeled in conformity with the provisions of this chapter.

(c) Exception

Notwithstanding subsection (b), a State or locality may enact statutes and promulgate regulations, based on smoking and health, that take effect after the effective date of the Family Smoking Prevention and Tobacco Control Act, imposing specific bans or restrictions on the time, place, and manner, but not content, of the advertising or promotion of any cigarettes

42 U.S.C. §§300aa-1 Establishment

The Secretary shall establish in the Department of Health and Human Services a National Vaccine Program to achieve optimal prevention of human infectious diseases through immunization and to achieve optimal prevention against adverse reactions to vaccines. The Program shall be administered by a Director selected by the Secretary.

42 U.S.C. §§300aa-2 Program Responsibilities

(a) The Director of the Program shall have the following responsibilities:

(1) Vaccine research

The Director of the Program shall, through the plan issued under section 300aa-3 of this title, coordinate and provide direction for research carried out in or through the National Institutes of Health, the Centers for Disease Control and Prevention, the Office of Biologics Research and Review of the Food and Drug Administration, the Department of Defense, and the Agency for International Development on means to induce human immunity against naturally occurring infectious diseases and to prevent adverse reactions to vaccines.

(2) Vaccine development

The Director of the Program shall, through the plan issued under section 300aa-3 of this title, coordinate and provide direction for activities carried out in or through the National Institutes of Health, the Office of Biologics Research and Review of the Food and Drug Administration, the Department of Defense, and the Agency for International Development to develop the techniques needed to produce safe and effective vaccines.

(3) Safety and efficacy testing of vaccines

The Director of the Program shall, through the plan issued under section 300aa-3 of this title, coordinate and provide direction for safety and efficacy testing of vaccines carried out in or through the National Institutes of Health, the Centers for Disease Control and Prevention, the Office of Biologics Research and Review of the Food and Drug Administration, the Department of Defense, and the Agency for International Development.

(4) Licensing of vaccine manufacturers and vaccines

The Director of the Program shall, through the plan issued under section 300aa-3 of this title, coordinate and provide direction for the allocation of resources in the implementation of the licensing program under section 263a of this title.

(5) Production and procurement of vaccines

The Director of the Program shall, through the plan issued under section 300aa-3 of this title, ensure that the governmental and non-governmental production and procurement of safe and effective vaccines by the Public Health Service, the Department of Defense, and the Agency for International Development meet the needs of the United States population and fulfill commitments of the United States to prevent human infectious diseases in other countries.

(6) Distribution and use of vaccines

The Director of the Program shall, through the plan issued under section 300aa-3 of this title, coordinate and provide direction to the Centers for Disease Control and Prevention and

assistance to States, localities, and health practitioners in the distribution and use of vaccines, including efforts to encourage public acceptance of immunizations and to make health practitioners and the public aware of potential adverse reactions and contraindications to vaccines.

(7) Evaluating the need for and the effectiveness and adverse effects of vaccines and immunization activities

The Director of the Program shall, through the plan issued under section 300aa-3 of this title, coordinate and provide direction to the National Institutes of Health, the Centers for Disease Control and Prevention, the Office of Biologics Research and Review of the Food and Drug Administration, the National Center for Health Statistics, the National Center for Health Services Research and Health Care Technology Assessment, and the Centers for Medicare & Medicaid Services in monitoring the need for and the effectiveness and adverse effects of vaccines and immunization activities.

(8) Coordinating governmental and non-governmental activities

The Director of the Program shall, through the plan issued under section 300aa-3 of this title, provide for the exchange of information between Federal agencies involved in the implementation of the Program and non-governmental entities engaged in the development and production of vaccines and in vaccine research and encourage the investment of non-governmental resources complementary to the governmental activities under the Program.

(9) Funding of federal agencies

The Director of the Program shall make available to Federal agencies involved in the implementation of the plan issued under section 300aa-3 of this title funds appropriated under section 300aa-6 of this title to supplement the funds otherwise available to such agencies for activities under the plan.

(b) In carrying out subsection (a) of this section and in preparing the plan under section 300aa-3 of this title, the Director shall consult with all Federal agencies involved in research on and development, testing, licensing, production, procurement, distribution, and use of vaccines.

42 U.S.C. §§300aa-5 National Vaccine Advisory Committee

(a) There is established the National Vaccine Advisory Committee. The members of the Committee shall be appointed by the Director of the Program, in consultation with the National Academy of Sciences, from among individuals who are engaged in vaccine research or the manufacture of vaccines or who are physicians, members of parent organizations concerned with immunizations, or representatives of State or local health agencies or public health organizations.

(b) The Committee shall--

(1) study and recommend ways to encourage the availability of an adequate supply of safe and effective vaccination products in the States,

(2) recommend research priorities and other measures the Director of the Program should take to enhance the safety and efficacy of vaccines,

(3) advise the Director of the Program in the implementation of sections 300aa-2, 300aa-3, and 300aa-4 of this title, and

(4) identify annually for the Director of the Program the most important areas of government and non-government cooperation that should be considered in implementing sections 300aa-2, 300aa-3, and 300aa-4 of this title.

42 U.S.C. §§300aa-19 Advisory Committee on Childhood Vaccines

(a) Establishment

There is established the Advisory Commission on Childhood Vaccines. The Commission shall be composed of:

(1) Nine members appointed by the Secretary as follows:

(A) Three members who are health professionals, who are not employees of the United States, and who have expertise in the health care of children, the epidemiology, etiology, and prevention of childhood diseases, and the adverse reactions associated with vaccines, of whom at least two shall be pediatricians.

(B) Three members from the general public, of whom at least two shall be legal representatives of children who have suffered a vaccine-related injury or death.

(C) Three members who are attorneys, of whom at least one shall be an attorney whose specialty includes representation of persons who have suffered a vaccine-related injury or death and of whom one shall be an attorney whose specialty includes representation of vaccine manufacturers.

(2) The Director of the National Institutes of Health, the Assistant Secretary for Health, the Director of the Centers for Disease Control and Prevention, and the Commissioner of Food and Drugs (or the designees of such officials), each of whom shall be a nonvoting ex officio member.

The Secretary shall select members of the Commission within 90 days of October 1, 1988. The members of the Commission shall select a Chair from among the members.

(b) Term of office

Appointed members of the Commission shall be appointed for a term of office of 3 years, except that of the members first appointed, 3 shall be appointed for a term of 1 year, 3 shall be appointed for a term of 2 years, and 3 shall be appointed for a term of 3 years, as determined by the Secretary.

(c) Meetings

The Commission shall first meet within 60 days after all members of the Commission are appointed, and thereafter shall meet not less often than four times per year and at the call of the chair. A quorum for purposes of a meeting is 5. A decision at a meeting is to be made by a ballot of a majority of the voting members of the Commission present at the meeting.

(d) Compensation

Members of the Commission who are officers or employees of the Federal Government shall serve as members of the Commission without compensation in addition to that received in their regular public employment. Members of the Commission who are not officers or employees of

the Federal Government shall be compensated at a rate not to exceed the daily equivalent of the rate in effect for grade GS-18 of the General Schedule for each day (including traveltime) they are engaged in the performance of their duties as members of the Commission. All members, while so serving away from their homes or regular places of business, may be allowed travel expenses, including per diem in lieu of subsistence, in the same manner as such expenses are authorized by section 5703 of Title 5 for employees serving intermittently.

(e) Staff

The Secretary shall provide the Commission with such professional and clerical staff, such information, and the services of such consultants as may be necessary to assist the Commission in carrying out effectively its functions under this section.

(f) Functions

The Commission shall--

(1) advise the Secretary on the implementation of the Program,

(2) on its own initiative or as the result of the filing of a petition, recommend changes in the Vaccine Injury Table,

(3) advise the Secretary in implementing the Secretary's responsibilities under section 300aa-27 of this title regarding the need for childhood vaccination products that result in fewer or no significant adverse reactions,

(4) survey Federal, State, and local programs and activities relating to the gathering of information on injuries associated with the administration of childhood vaccines, including the adverse reaction reporting requirements of section 300aa-25(b) of this title, and advise the Secretary on means to obtain, compile, publish, and use credible data related to the frequency and severity of adverse reactions associated with childhood vaccines, and

(5) recommend to the Director of the National Vaccine Program research related to vaccine injuries which should be conducted to carry out this part.

42 U.S.C. §§300aa-22 Standards of Responsibility

a) General rule

Except as provided in subsections (b), (c), and (e) of this section State law shall apply to a civil action brought for damages for a vaccine-related injury or death.

(b) Unavoidable adverse side effects; warnings

(1) No vaccine manufacturer shall be liable in a civil action for damages arising from a vaccine-related injury or death associated with the administration of a vaccine after October 1, 1988, if the injury or death resulted from side effects that were unavoidable even though the vaccine was properly prepared and was accompanied by proper directions and warnings.

(2) For purposes of paragraph (1), a vaccine shall be presumed to be accompanied by proper directions and warnings if the vaccine manufacturer shows that it complied in all material respects with all requirements under the Federal Food, Drug, and Cosmetic Act [21 U.S.C.A. § 301 et seq.] and section 262 of this title (including regulations issued under such provisions) applicable to the vaccine and related to vaccine-related injury or death for which the civil action was brought unless the plaintiff shows--

(A) that the manufacturer engaged in the conduct set forth in subparagraph (A) or (B) of section 300aa-23(d)(2) of this title, or

(B) by clear and convincing evidence that the manufacturer failed to exercise due care notwithstanding its compliance with such Act and section (and regulations issued under such provisions).

(c) Direct warnings

No vaccine manufacturer shall be liable in a civil action for damages arising from a vaccine-related injury or death associated with the administration of a vaccine after October 1, 1988, solely due to the manufacturer's failure to provide direct warnings to the injured party (or the injured party's legal representative) of the potential dangers resulting from the administration of the vaccine manufactured by the manufacturer.

(d) Construction

The standards of responsibility prescribed by this section are not to be construed as authorizing a person who brought a civil action for damages against a vaccine manufacturer for a vaccine-related injury or death in which damages were denied or which was dismissed with prejudice to bring a new civil action against such manufacturer for such injury or death.

(e) Preemption

No State may establish or enforce a law which prohibits an individual from bringing a civil action against a vaccine manufacturer for damages for a vaccine-related injury or death if such civil action is not barred by this part.

42 U.S.C. §§300aa-27 Mandate for safer childhood vaccines

(a) General rule

In the administration of this part and other pertinent laws under the jurisdiction of the Secretary, the Secretary shall--

(1) promote the development of childhood vaccines that result in fewer and less serious adverse reactions than those vaccines on the market on December 22, 1987, and promote the refinement of such vaccines, and

(2) make or assure improvements in, and otherwise use the authorities of the Secretary with respect to, the licensing, manufacturing, processing, testing, labeling, warning, use instructions, distribution, storage, administration, field surveillance, adverse reaction reporting, and recall of reactogenic lots or batches, of vaccines, and research on vaccines, in order to reduce the risks of adverse reactions to vaccines.

(b) Task force

(1) The Secretary shall establish a task force on safer childhood vaccines which shall consist of the Director of the National Institutes of Health, the Commissioner of the Food and Drug Administration, and the Director of the Centers for Disease Control.

(2) The Director of the National Institutes of Health shall serve as chairman of the task force.

(3) In consultation with the Advisory Commission on Childhood Vaccines, the task force shall prepare recommendations to the Secretary concerning implementation of the requirements of subsection (a) of this section.

(c) Report

Within 2 years after December 22, 1987, and periodically thereafter, the Secretary shall prepare and transmit to the Committee on Energy and Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate a report describing the actions taken pursuant to subsection (a) of this section during the preceding 2-year period.

42 U.S.C. §262

(a) Biologics license

(1) No person shall introduce or deliver for introduction into interstate commerce any biological product unless--

(A) a biologics license is in effect for the biological product; and

(B) each package of the biological product is plainly marked with--

(i) the proper name of the biological product contained in the package;

(ii) the name, address, and applicable license number of the manufacturer of the biological product; and

(iii) the expiration date of the biological product.

(2)(A) The Secretary shall establish, by regulation, requirements for the approval, suspension, and revocation of biologics licenses.

(B) Pediatric studies

A person that submits an application for a license under this paragraph shall submit to the Secretary as part of the application any assessments required under section 355c of Title 21.

(C) The Secretary shall approve a biologics license application--

(i) on the basis of a demonstration that--

(I) the biological product that is the subject of the application is safe, pure, and potent; and

(II) the facility in which the biological product is manufactured, processed, packed, or held meets standards designed to assure that the biological product continues to be safe, pure, and potent; and

(ii) if the applicant (or other appropriate person) consents to the inspection of the facility that is the subject of the application, in accordance with subsection (c) of this section.

(D) Postmarket studies and clinical trials; labeling; risk evaluation and mitigation strategy

A person that submits an application for a license under this paragraph is subject to sections 505(o), 505(p), and 505-1 of the Federal Food, Drug, and Cosmetic Act.

(3) The Secretary shall prescribe requirements under which a biological product undergoing investigation shall be exempt from the requirements of paragraph (1).

(b) Falsely labeling or marking package or container; altering label or mark

No person shall falsely label or mark any package or container of any biological product or alter any label or mark on the package or container of the biological product so as to falsify the label or mark.

(c) Inspection of establishment for propagation and preparation

Any officer, agent, or employee of the Department of Health and Human Services, authorized by the Secretary for the purpose, may during all reasonable hours enter and inspect any establishment for the propagation or manufacture and preparation of any biological product.

(d) Regulations governing licenses; recall of product presenting imminent hazard; violations

(1) Upon a determination that a batch, lot, or other quantity of a product licensed under this section presents an imminent or substantial hazard to the public health, the Secretary shall issue an order immediately ordering the recall of such batch, lot, or other quantity of such product. An order under this paragraph shall be issued in accordance with section 554 of Title 5.

(2) Any violation of paragraph (1) shall subject the violator to a civil penalty of up to $100,000 per day of violation. The amount of a civil penalty under this paragraph shall, effective December 1 of each year beginning 1 year after the effective date of this paragraph, be increased by the percent change in the Consumer Price Index for the base quarter of such year over the Consumer Price Index for the base quarter of the preceding year, adjusted to the nearest 1/10 of 1 percent. For purposes of this paragraph, the term “base quarter”, as used with respect to a year, means the calendar quarter ending on September 30 of such year and the price index for a base quarter is the arithmetical mean of such index for the 3 months comprising such quarter.

(e) Interference with officers

No person shall interfere with any officer, agent, or employee of the Service in the performance of any duty imposed upon him by this section or by regulations made by authority thereof.

(f) Penalties for offenses

Any person who shall violate, or aid or abet in violating, any of the provisions of this section shall be punished upon conviction by a fine not exceeding $500 or by imprisonment not exceeding one year, or by both such fine and imprisonment, in the discretion of the court.

(g) Construction with other laws

Nothing contained in this chapter shall be construed as in any way affecting, modifying, repealing, or superseding the provisions of the Federal Food, Drug, and Cosmetic Act [21 U.S.C.A. § 301 et seq.].

(h) Exportation of partially processed biological products

A partially processed biological product which--

(1) is not in a form applicable to the prevention, treatment, or cure of diseases or injuries of man;

(2) is not intended for sale in the United States; and

(3) is intended for further manufacture into final dosage form outside the United States,

shall be subject to no restriction on the export of the product under this chapter or the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321 et. [FN1] seq.) if the product is manufactured, processed, packaged, and held in conformity with current good manufacturing practice requirements or meets international manufacturing standards as certified by an international standards organization recognized by the Secretary and meets the requirements of section 801(e)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 381(e)).

(i) Definition; application

In this section, the term “biological product” means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings.

(j) Application of Federal Food, Drug, and Cosmetic Act

The Federal Food, Drug, and Cosmetic Act, including the requirements under sections 505(o), 505(p), and 505-1 of such Act, applies to a biological product subject to regulation under this section, except that a product for which a license has been approved under subsection (a) of this section shall not be required to have an approved application under section 505 of such Act.

Appendix C

21 C.F.R § 601.12 – Changes to an approved application

(a)(1) General. As provided by this section, an applicant must inform the Food and Drug Administration (FDA) (see mailing addresses in § 600.2 of this chapter) about each change in the product, production process, quality controls, equipment, facilities, responsible personnel, or labeling established in the approved license application(s).

(2) Before distributing a product made using a change, an applicant must assess the effects of the change and demonstrate through appropriate validation and/or other clinical and/or nonclinical laboratory studies the lack of adverse effect of the change on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product.

(3) Notwithstanding the requirements of paragraphs (b), (c), and (f) of this section, an applicant must make a change provided for in those paragraphs in accordance with a regulation or guidance that provides for a less burdensome notification of the change (for example, by submission of a supplement that does not require approval prior to distribution of the product or in an annual report).

(4) The applicant must promptly revise all promotional labeling and advertising to make it consistent with any labeling change implemented in accordance with paragraphs (f)(1) and (f)(2) of this section.

(5) A supplement or annual report must include a list of all changes contained in the supplement or annual report. For supplements, this list must be provided in the cover letter.

(b) Changes requiring supplement submission and approval prior to distribution of the product made using the change (major changes).

(1) A supplement shall be submitted for any change in the product, production process, quality controls, equipment, facilities, or responsible personnel that has a substantial potential to have an adverse effect on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product.

(2) These changes include, but are not limited to:

(i) Except as provided in paragraphs (c) and (d) of this section, changes in the qualitative or quantitative formulation, including inactive ingredients, or in the specifications provided in the approved application;

(ii) Changes requiring completion of an appropriate human study to demonstrate the equivalence of the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product;

(iii) Changes in the virus or adventitious agent removal or inactivation method(s);

(iv) Changes in the source material or cell line;

(v) Establishment of a new master cell bank or seed; and

(vi) Changes which may affect product sterility assurance, such as changes in product or component sterilization method(s), or an addition, deletion, or substitution of steps in an aseptic processing operation.

(3) The applicant must obtain approval of the supplement from FDA prior to distribution of the product made using the change. Except for submissions under paragraph (e) of this section, the following shall be contained in the supplement:

(i) A detailed description of the proposed change;

(ii) The product(s) involved;

(iii) The manufacturing site(s) or area(s) affected;

(iv) A description of the methods used and studies performed to evaluate the effect of the change on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product;

(v) The data derived from such studies;

(vi) Relevant validation protocols and data; and

(vii) A reference list of relevant standard operating procedures (SOP's).

(4) An applicant may ask FDA to expedite its review of a supplement for public health reasons or if a delay in making the change described in it would impose an extraordinary hardship on the applicant. Such a supplement and its mailing cover should be plainly marked: “Prior Approval Supplement–Expedited Review Requested.

(c) Changes requiring supplement submission at least 30 days prior to distribution of the product made using the change.

(1) A supplement shall be submitted for any change in the product, production process, quality controls, equipment, facilities, or responsible personnel that has a moderate potential to have an adverse effect on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product. The supplement shall be labeled “Supplement--Changes Being Effected in 30 Days” or, if applicable under paragraph (c)(5) of this section, “Supplement--Changes Being Effected.”

(2) These changes include, but are not limited to:

(i) [Reserved]

(ii) An increase or decrease in production scale during finishing steps that involves different equipment; and

(iii) Replacement of equipment with that of similar, but not identical, design and operating principle that does not affect the process methodology or process operating parameters.

(iv) Relaxation of an acceptance criterion or deletion of a test to comply with an official compendium that is consistent with FDA statutory and regulatory requirements.

(3) Pending approval of the supplement by FDA, and except as provided in paragraph (c)(5) of this section, distribution of the product made using the change may begin not less than 30 days after receipt of the supplement by FDA. The information listed in paragraph (b)(3)(i) through (b)(3)(vii) of this section shall be contained in the supplement.

(4) If within 30 days following FDA's receipt of the supplement, FDA informs the applicant that either:

(i) The change requires approval prior to distribution of the product in accordance with paragraph (b) of this section; or

(ii) Any of the information required under paragraph (c)(3) of this section is missing; the applicant shall not distribute the product made using the change until FDA determines that compliance with this section is achieved.

(5) In certain circumstances, FDA may determine that, based on experience with a particular type of change, the supplement for such change is usually complete and provides the proper information, and on particular assurances that the proposed change has been appropriately submitted, the product made using the change may be distributed immediately upon receipt of the supplement by FDA. These circumstances may include substantial similarity with a type of change regularly involving a “Supplement--Changes Being Effected” supplement or a situation in which the applicant presents evidence that the proposed change has been validated in accordance with an approved protocol for such change under paragraph (e) of this section.

(6) If the agency disapproves the supplemental application, it may order the manufacturer to cease distribution of the products made with the manufacturing change.

(d) Changes to be described in an annual report (minor changes).

(1) Changes in the product, production process, quality controls, equipment, facilities, or responsible personnel that have a minimal potential to have an adverse effect on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product shall be documented by the applicant in an annual report submitted each year within 60 days of the anniversary date of approval of the application. The Director, Center for Biologics Evaluation and Research or the Director, Center for Drug Evaluation and

Research, may approve a written request for an alternative date to combine annual reports for multiple approved applications into a single annual report submission.

(2) These changes include, but are not limited to:

(i) Any change made to comply with a change to an official compendium, except a change described in paragraph (c)(2)(iv) of this section, that is consistent with FDA statutory and regulatory requirements.

(ii) The deletion or reduction of an ingredient intended only to affect the color of the product, except that a change intended only to affect Blood Grouping Reagents requires supplement submission and approval prior to distribution of the product made using the change in accordance with the requirements set forth in paragraph (b) of this section;

(iii) An extension of an expiration dating period based upon full shelf life data on production batches obtained from a protocol approved in the application;

(iv) A change within the container closure system for a nonsterile product, based upon a showing of equivalency to the approved system under a protocol approved in the application or published in an official compendium;

(v) A change in the size and/or shape of a container containing the same number of dosage units for a nonsterile solid dosage form product, without a change from one container closure system to another;

(vi) The addition by embossing, debossing, or engraving of a code imprint to a solid dosage form biological product other than a modified release dosage form, or a minor change in an existing code imprint; and

(vii) The addition or revision of an alternative analytical procedure that provides the same or increased assurance of the identity, strength, quality, purity, or potency of the material being tested as the analytical procedure described in the approved application, or deletion of an alternative analytical procedure.

(3) The following information for each change shall be contained in the annual report:

(i) A list of all products involved; and

(ii) A full description of the manufacturing and controls changes including: the manufacturing site(s) or area(s) involved; the date the change was made; a cross-reference to relevant validation protocols and/or SOP's; and relevant data from studies and tests performed to evaluate the effect of the change on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product.

(iii) A statement by the holder of the approved application or license that the effects of the change have been assessed.

(4) The applicant shall submit the report to the FDA office responsible for reviewing the application. The report shall include all the information required under this paragraph for each change made during the annual reporting interval which ends on the anniversary date in the order in which they were implemented.

(e) An applicant may submit one or more protocols describing the specific tests and validation studies and acceptable limits to be achieved to demonstrate the lack of adverse effect for specified types of manufacturing changes on the identity, strength, quality, purity, or potency of the product as they may relate to the safety or effectiveness of the product. Any such protocols, or change to a protocol, shall be submitted as a supplement requiring approval from FDA prior to distribution of the product which, if approved, may justify a reduced reporting category for the particular change because the use of the protocol for that type of change reduces the potential risk of an adverse effect.

(f) Labeling changes.

(1) Labeling changes requiring supplement submission--FDA approval must be obtained before distribution of the product with the labeling change. Except as described in paragraphs (f)(2) and (f)(3) of this section, an applicant shall submit a supplement describing a proposed change in the package insert, package label, container label, or, if applicable, a Medication Guide required under part 208 of this chapter, and include the information necessary to support the proposed change. An applicant cannot use paragraph (f)(2) of this section to make any change to the information required in § 201.57(a) of this chapter. An applicant may report the minor changes to the information specified in paragraph (f)(3)(i)(D) of this section in an annual report. The supplement shall clearly highlight the proposed change in the labeling. The applicant shall obtain approval from FDA prior to distribution of the product with the labeling change.

(2) Labeling changes requiring supplement submission--product with a labeling change that may be distributed before FDA approval.

(i) An applicant shall submit, at the time such change is made, a supplement for any change in the package insert, package label, or container label to reflect newly acquired information, except for changes to the package insert required in § 201.57(a) of this chapter (which must be made under paragraph (f)(1) of this section), to accomplish any of the following:

(A) To add or strengthen a contraindication, warning, precaution, or adverse reaction for which the evidence of a causal association satisfies the standard for inclusion in the labeling under § 201.57(c) of this chapter;

(B) To add or strengthen a statement about abuse, dependence, psychological effect, or overdosage;

(C) To add or strengthen an instruction about dosage and administration that is intended to increase the safety of the use of the product; and

(D) To delete false, misleading, or unsupported indications for use or claims for effectiveness.

(E) Any labeling change normally requiring a supplement submission and approval prior to distribution of the product that FDA specifically requests be submitted under this provision.

(ii) Pending approval of the supplement by FDA, the applicant may distribute a product with a package insert, package label, or container label bearing such change at the time the supplement is submitted. The supplement shall clearly identify the change being made and include necessary supporting data. The supplement and its mailing cover shall be plainly marked: “Special Labeling Supplement--Changes Being Effected.”

(3) Labeling changes requiring submission in an annual report.

(i) An applicant shall submit any final printed package insert, package label, container label, or Medication Guide required under part 208 of this chapter incorporating the following changes in an annual report submitted to FDA each year as provided in paragraph (d)(1) of this section:

(A) Editorial or similar minor changes;

(B) A change in the information on how the product is supplied that does not involve a change in the dosage strength or dosage form;

(C) A change in the information specified in § 208.20(b)(8)(iii) and (b)(8)(iv) of this chapter for a Medication Guide; and

(D) A change to the information required in § 201.57(a) of this chapter as follows:

(1) Removal of a listed section(s) specified in § 201.57(a)(5) of this chapter; and

(2) Changes to the most recent revision date of the labeling as specified in § 201.57(a)(15) of this chapter.

(E) A change made pursuant to an exception or alternative granted under § 201.26 or § 610.68 of this chapter.

(1) Removal of a listed section(s) specified in § 201.57(a)(5) of this chapter; and

(2) Changes to the most recent revision date of the labeling as specified in § 201.57(a)(15) of this chapter.

(ii) The applicant may distribute a product with a package insert, package label, or container label bearing such change at the time the change is made.

(4) Advertisements and promotional labeling. Advertisements and promotional labeling shall be submitted to the Center for Biologics Evaluation and Research or Center for Drug Evaluation and Research in accordance with the requirements set forth in § 314.81(b)(3)(i) of this chapter,

except that Form FDA–2567 (Transmittal of Labels and Circulars) or an equivalent form shall be used.

(5) The submission and grant of a written request for an exception or alternative under § 201.26 or § 610.68 of this chapter satisfies the requirements in paragraphs (f)(1) through (f)(2) of this section.

(6) For purposes of paragraph (f)(2) of this section, information will be considered newly acquired if it consists of data, analyses, or other information not previously submitted to the agency, which may include (but are not limited to) data derived from new clinical studies, reports of adverse events, or new analyses of previously submitted data (e.g., meta-analyses) if the studies, events or analyses reveal risks of a different type or greater severity or frequency than previously included in submissions to FDA.

(g) Failure to comply. In addition to other remedies available in law and regulations, in the event of repeated failure of the applicant to comply with this section, FDA may require that the applicant submit a supplement for any proposed change and obtain approval of the supplement by FDA prior to distribution of the product made using the change.

(h) Administrative review. Under § 10.75 of this chapter, an applicant may request internal FDA review of FDA employee decisions under this section.

21 C.F.R. § 601.2 – Application for biologics licenses; procedures for filing

(a) General. To obtain a biologics license under section 351 of the Public Health Service Act for any biological product, the manufacturer shall submit an application to the Director, Center for Biologics Evaluation and Research or the Director, Center for Drug Evaluation and Research (see mailing addresses in § 600.2 of this chapter), on forms prescribed for such purposes, and shall submit data derived from nonclinical laboratory and clinical studies which demonstrate that the manufactured product meets prescribed requirements of safety, purity, and potency; with respect to each nonclinical laboratory study, either a statement that the study was conducted in compliance with the requirements set forth in part 58 of this chapter, or, if the study was not conducted in compliance with such regulations, a brief statement of the reason for the noncompliance; statements regarding each clinical investigation involving human subjects contained in the application, that it either was conducted in compliance with the requirements for institutional review set forth in part 56 of this chapter; or was not subject to such requirements in accordance with § 56.104 or § 56.105, and was conducted in compliance with requirements for informed consent set forth in part 50 of this chapter. A full description of manufacturing methods; data establishing stability of the product through the dating period; sample(s) representative of the product for introduction or delivery for introduction into interstate commerce; summaries of results of tests performed on the lot(s) represented by the submitted sample(s); specimens of the labels, enclosures, and containers, and if applicable, any Medication Guide required under part 208 of this chapter proposed to be used for the product; and the address of each location involved in the manufacture of the biological product shall be listed in the biologics license application. The applicant shall also include a financial certification or disclosure statement(s) or both for clinical investigators as required by part 54 of this chapter. An application for a biologics license shall not be considered as filed until all pertinent information and data have been received by the Food and Drug Administration. The applicant shall also include either a claim for categorical exclusion under § 25.30 or § 25.31 of this chapter or an environmental assessment under § 25.40 of this chapter. The applicant, or the applicant's attorney, agent, or other authorized official shall sign the application. An application for any of the following specified categories of biological products subject to licensure shall be handled as set forth in paragraph (c) of this section:

(1) Therapeutic DNA plasmid products;

(2) Therapeutic synthetic peptide products of 40 or fewer amino acids;

(3) Monoclonal antibody products for in vivo use; and

(4) Therapeutic recombinant DNA–derived products.

(b) [Reserved]

(c)(1) To obtain marketing approval for a biological product subject to licensure which is a therapeutic DNA plasmid product, therapeutic synthetic peptide product of 40 or fewer amino acids, monoclonal antibody product for in vivo use, or therapeutic recombinant DNA–derived product, an applicant shall submit a biologics license application in accordance with paragraph (a) of this section except that the following sections in parts 600 through 680 of this chapter shall

not be applicable to such products: §§ 600.10(b) and (c), 600.11, 600.12, 600.13, 610.11, 610.53, and 610.62 of this chapter.

(2) To the extent that the requirements in this paragraph (c) conflict with other requirements in this subchapter, this paragraph (c) shall supersede other requirements.

(d) Approval of a biologics license application or issuance of a biologics license shall constitute a determination that the establishment(s) and the product meet applicable requirements to ensure the continued safety, purity, and potency of such products. Applicable requirements for the maintenance of establishments for the manufacture of a product subject to this section shall include but not be limited to the good manufacturing practice requirements set forth in parts 210, 211, 600, 606, and 820 of this chapter.

(e) Any establishment and product license for a biological product issued under section 351 of the Public Health Service Act (42 U.S.C. 201 et seq.) that has not been revoked or suspended as of December 20, 1999, shall constitute an approved biologics license application in effect under the same terms and conditions set forth in such product license and such portions of the establishment license relating to such product.

Appendix D

Fed. R. Civ. P. 8

(a) Claims for Relief.

A pleading that states a claim for relief must contain:

(1) a short and plain statement of the grounds for the court's jurisdiction, unless the court already has jurisdiction and the claim needs no new jurisdictional support;

(2) a short and plain statement of the claim showing that the pleader is entitled to relief; and

(3) a demand for the relief sought, which may include relief in the alternative or different types of relief.

(b) Defenses; Admissions and Denials.

(1) In General.

In responding to a pleading, a party must:

(A) state in short and plain terms its defenses to each claim asserted against it; and

(B) admit or deny the allegations asserted against it by an opposing party.

(2) Denials — Responding to the Substance.

A denial must fairly respond to the substance of the allegation.

(3) General and Specific Denials.

A party that intends in good faith to deny all the allegations of a pleading — including the jurisdictional grounds — may do so by a general denial. A party that does not intend to deny all the allegations must either specifically deny designated allegations or generally deny all except those specifically admitted.

(4) Denying Part of an Allegation.

A party that intends in good faith to deny only part of an allegation must admit the part that is true and deny the rest.

(5) Lacking Knowledge or Information.

A party that lacks knowledge or information sufficient to form a belief about the truth of an allegation must so state, and the statement has the effect of a denial.

(6) Effect of Failing to Deny.

An allegation — other than one relating to the amount of damages — is admitted if a responsive pleading is required and the allegation is not denied. If a
responsive pleading is not required, an allegation is considered denied or avoided.

(c) Affirmative Defenses.

(1) In General.

In responding to a pleading, a party must affirmatively state any avoidance or affirmative defense, including:

- accord and satisfaction;
- arbitration and award;
- assumption of risk;
- contributory negligence;
- discharge in bankruptcy;
- duress;
- estoppel;
- failure of consideration;
- fraud;
- illegality;
- injury by fellow servant;
- laches;
- license;
- payment;
- release;
- res judicata;
- statute of frauds;
- statute of limitations; and
- waiver.

(2) Mistaken Designation.

If a party mistakenly designates a defense as a counterclaim, or a counterclaim as a defense, the court must, if justice requires, treat the pleading as though it were correctly designated, and may impose terms for doing so.

(d) Pleading to Be Concise and Direct; Alternative Statements; Inconsistency.

(1) In General.

Each allegation must be simple, concise, and direct. No technical form is required.

(2) Alternative Statements of a Claim or Defense.

A party may set out 2 or more statements of a claim or defense alternatively or hypothetically, either in a single count or defense or in separate ones. If a party makes alternative statements, the pleading is sufficient if any one of them is sufficient.

(3) Inconsistent Claims or Defenses.

A party may state as many separate claims or defenses as it has, regardless of consistency.

(e) Construing Pleadings.

Pleadings must be construed so as to do justice.

Fed R. Civ. P. 12

(a) Time to Serve a Responsive Pleading.

(1) In General.

Unless another time is specified by this rule or a federal statute, the time for serving a responsive pleading is as follows:

(A) A defendant must serve an answer:

(i) within 21 days after being served with the summons and complaint; or

(ii) if it has timely waived service under Rule 4(d), within 60 days after the request for a waiver was sent, or within 90 days after it was sent to the defendant outside any judicial district of the United States.

(B) A party must serve an answer to a counterclaim or crossclaim within 21 days after being served with the pleading that states the counterclaim or crossclaim.

(C) A party must serve a reply to an answer within 21 days after being served with an order to reply, unless the order specifies a different time.

(2) United States and Its Agencies, Officers, or Employees Sued in an Official Capacity.

The United States, a United States agency, or a United States officer or employee sued only in an official capacity must serve an answer to a complaint, counterclaim, or crossclaim within 60 days after service on the United States attorney.

(3) United States Officers or Employees Sued in an Individual Capacity.

A United States officer or employee sued in an individual capacity for an act or omission occurring in connection with duties performed on the United States behalf must serve an answer to a complaint, counterclaim, or crossclaim within 60 days after service on the officer or employee or service on the United States attorney, whichever is later.

(4) Effect of a Motion.

Unless the court sets a different time, serving a motion under this rule alters these periods as follows:

(A) if the court denies the motion or postpones its disposition until trial, the responsive pleading must be served within 14 days after notice of the courts action; or

(B) if the court grants a motion for a more definite statement, the responsive pleading must be served within 14 days after the more definite statement is served.

(b) How to Present Defenses.

Every defense to a claim for relief in any pleading must be asserted in the responsive pleading if one is required. But a party may assert the following defenses by motion:

(1) lack of subject-matter jurisdiction;

(2) lack of personal jurisdiction;

(3) improper venue;

(4) insufficient process;

(5) insufficient service of process;

(6) failure to state a claim upon which relief can be granted; and

(7) failure to join a party under Rule 19.

A motion asserting any of these defenses must be made before pleading if a responsive pleading is allowed. If a pleading sets out a claim for relief that does not require a responsive pleading, an opposing party may assert at trial any defense to that claim. No defense or objection is waived by joining it with one or more other defenses or objections in a responsive pleading or in a motion.

(c) Motion for Judgment on the Pleadings.

After the pleadings are closed but early enough not to delay trial a party may move for judgment on the pleadings.

(d) Result of Presenting Matters Outside the Pleadings.

If, on a motion under Rule 12(b)(6) or 12(c), matters outside the pleadings are presented to and not excluded by the court, the motion must be treated as one for summary judgment under Rule 56. All parties must be given a reasonable opportunity to present all the material that is pertinent to the motion.

(e) Motion For a More Definite Statement.

A party may move for a more definite statement of a pleading to which a responsive pleading is allowed but which is so vague or ambiguous that the party cannot reasonably prepare a response. The motion must be made before filing a responsive pleading and must point out the defects complained of and the details desired. If the court orders a more definite statement and the order is not obeyed within 14 days after notice of the order or within the time the court sets, the court may strike the pleading or issue any other appropriate order.

(f) Motion To Strike.

The court may strike from a pleading an insufficient defense or any redundant, immaterial, impertinent, or scandalous matter. The court may act:

(1) on its own; or

(2) on motion made by a party either before responding to the pleading or, if a response is not allowed, within 21 days after being served with the pleading.

(g) Joining Motions.

(1) Right to Join.

A motion under this rule may be joined with any other motion allowed by this rule.

(2) Limitation on Further Motions.

Except as provided in Rule 12(h)(2) or (3), a party that makes a motion under this rule must not make another motion under this rule raising a defense or objection that was available to the party but omitted from its earlier motion.

(h) Waiving and Preserving Certain Defenses.

(1) When Some Are Waived.

A party waives any defense listed in Rule 12(b)(2)-(5) by:

(A) omitting it from a motion in the circumstances described in Rule 12(g)(2); or

(B) failing to either:

(i) make it by motion under this rule; or

(ii) include it in a responsive pleading or in an amendment allowed by Rule 15(a)(1) as a matter of course.

(2) When to Raise Others.

Failure to state a claim upon which relief can be granted, to join a person required by Rule 19(b), or to state a legal defense to a claim may be raised:

(A) in any pleading allowed or ordered under Rule 7(a);

(B) by a motion under Rule 12(c); or

(C) at trial.

(3) Lack of Subject-Matter Jurisdiction.

If the court determines at any time that it lacks subject-matter jurisdiction, the court must dismiss the action.

(i) Hearing Before Trial.

If a party so moves, any defense listed in Rule 12(b)(1)-(7) whether made in a pleading or by motion and a motion under Rule 12(c) must be heard and decided before trial unless the court orders a deferral until trial.