SUPERIOR COURT OF CALIFORNIA

COUNTY OF LOS ANGELES

Case No: JCCP 4574

IN RE: BYETTA CASES

ORDER GRANTING DEFENDANTS' MOTION FOR SUMMARY JUDGMENT BASED ON PREEMPTION

I. INTRODUCTION

There are hundreds of pending coordinated tort claims alleging a failure to warn of the risk of pancreatic cancer if a patient ingests Byetta® or its pharmacological incretin-mimetic counterparts, such as Januvia® or Victoza®. Defendants are the various manufacturers of the prescription drugs, which are subject to extensive regulation as to labeling and in other regards by the United States Food and Drug Administration ("FDA") pursuant to the Food, Drug & Cosmetics Act, 21 U.S.C. § 301 et seq. In *Wyeth v. Levine* (2009) 555 U.S. 555, the Supreme Court held that FDA's broad authority over label regulation did not, however, preclude states from continuing to exercise their police powers to authorize common-law tort compensation for

plaintiffs injured due to inadequate labeling unless there was "clear evidence" that the FDA would not have allowed a manufacturer to add the missing warnings which plaintiff at trial claims should have been included to provide a non-negligent (i.e. full and complete) warning.

Defendants here assert that at all relevant times the FDA would not have allowed any of these manufacturers to implement a *sua sponte* label change through the FDA's "change being effected" ("CBE") process to add any warning of a risk of pancreatic cancer associated with use of the drug in question.

For reasons more fully discussed below, the Court holds: (a) the determination of whether or not federal preemption applies in these cases is a matter to be resolved solely by the judge without any involvement by a jury to determine disputed preliminary factual matters, and (b) defendants are correct as a matter of law that on the record before this Court in the context of the current motions, the many plaintiffs' claims based on alleged failure to warn are precluded by the application of federal preemption pursuant to the United States Constitution Art. VI, § 2.

For this reason, defendants' motion is granted, and judgment will be entered for defendants for all pending claims in this coordinated proceeding for alleged failure to warn regarding pancreatic cancer which involved ingestion of the drugs in question on or before October 8, 2015, the date that the record closed for this Motion.

II. PROCEDURAL HISTORY

To the best of this Court's understanding, the first case in this now coordinated proceeding was filed in the Los Angeles Superior Court by plaintiff Sandy Crabb on December 16, 2008 in BC403946 against Amylin Pharmaceuticals Inc. and Eli Lilly & Co., who at the time were jointly marketing the prescription drug Byetta®, a drug intended to help patients with diabetes

Type 2 in control of their blood sugar. Many additional cases against these defendants were filed in various Superior Courts in California, and defendants filed a Petition For Coordination on February 11, 2009. The petition was granted on July 2, 2009, and the coordinated proceeding was named "*In re Byetta Cases*" since all or virtually all of the cases at that time arose out of use of this specific drug.[1]

As noted below in the factual discussion, Amylin and Eli Lilly eventually encountered competition in the diabetes Type 2 treatment field as other manufacturers brought competing drugs to market with similar characteristics in terms of their therapeutic value and thus similar characteristics (at least from plaintiffs' viewpoint) in terms of the potentiality to cause pancreatic cancer. Patients often take a series of different prescription drugs according to their treating physician's best judgment, so many plaintiffs have a fact pattern where they have taken two or more of the drugs at issue.

As time progressed, additional manufacturers found themselves named in these cases, and these claims were added to the coordinated proceeding as Add-On's pursuant to California Rule of Court 3.531 although the docket title was not updated. To the best of this Court's knowledge a total of 129 separate cases have been brought into this coordinated proceeding (some now resolved insofar as the claims only involved pancreatitis). The most recent Add-On Petition pursuant to CRC 3.531 was the 60th such petition. Based on the most current list of pending plaintiffs and the nature of their alleged diseases, there appear to be at least 287 individual plaintiffs before the Court alleging tort damages flowing from pancreatic cancer. There are other plaintiffs alleging other diseases who will be not impacted by this motion and the ruling thereon,

[1] Many of the original cases in this coordinated proceeding, e.g., plaintiff Crabb's claim, were brought by patients who suffered pancreatitis, not pancreatic cancer, as such. These cases were resolved in due course by various global settlements, and few or no new cases involving claims arising out of only pancreatitis have been filed in recent years, perhaps because the label was changed in 2007 to more directly warn of this potential side effect.

e.g. plaintiffs alleging they have suffered thyroid cancer as a consequence of one or more defendants' failure to warn.

Concurrent with the litigation in this proceeding, certain otherwise similar cases were removed to federal court from California state courts and from other state courts.[2] New cases were also filed directly in federal court involving the same basic theory of tort liability for failure to warn of pancreatic cancer. On or about August 26, 2013, the federal Multi-District Litigation ("MDL") Panel ordered the creation of a MDL for *In re Incretin-Mimetic Cases* (MDL # 2452) and assigned the cases to the Hon. Anthony Battaglia in the Southern District of California. Judge Battaglia and Judge Highberger have made continuing efforts to coordinate the discovery as between the two cases to avoid redundant work by the parties and to minimize or eliminate inconsistent rulings regarding the extent of discovery required. They also, with the consent of all relevant parties, held an off-the-record Joint Science Day in Judge Battaglia's court on February 5-6, 2014.

Defendants first filed a motion for summary judgment in the MDL action on April 17, 2014 based on a theory of federal preemption pursuant to *Wyeth v. Levine, supra.* Defendants' motion was denied without prejudice, and plaintiffs were permitted to take focused discovery specific to this issue over a period of over a year, largely under the supervision of Judge Battaglia. Defendants filed a superseding motion for summary judgment in federal court based on preemption on June 19, 2015. Plaintiffs' Opposition in the federal action was filed on July 17, 2015, and defendants' Reply was filed in federal court on August 7, 2015. In the federal MDL,

[2] Not every case removed to federal court stayed there. See generally, *Briggs v. Merck Sharp & Dohme* (August 6, 2015) 796 F.3d 1038, a case remanding various incretin-mimetic MDL matters back to state court.

the plaintiffs also brought a cross-motion for summary adjudication that this affirmative defense should be stricken although no such companion motion was filed in this coordinated proceeding.

Defendants filed a motion for summary judgment (i.e. the motion at issue here) before this Court on June 19, 2015; plaintiffs filed their Opposition on July 17, 2015, and moving parties' Reply was filed August 7, 2015. By agreement of the parties and the judges involved, the oral argument for all the preemption motions was held in Judge Battaglia's courtroom in San Diego on September 11, 2015 with both Judge Battaglia and Judge Highberger presiding.[3]

On September 15, 2015, this Court asked counsel for further briefing on a predicate question which had been aired in oral argument but which was not addressed in the original round of briefing: Was the resolution of the applicability of a potential federal preemption affirmative defense in these cases a "question of law" reserved exclusively to judicial authority for resolution or was it potentially a "question of fact" for resolution by a jury if there were disputed material facts. Two rounds of concurrent supplemental briefs on this topic were filed by both sides on September 28, 2015 and October 8, 2015. This Court has been advised that the same or substantially similar briefs were filed with Judge Battaglia in the MDL proceeding. On November 9, 2015, Judge Battaglia released an order granting defendants' motions based on preemption.

While the parties contested the merits of the motion, there was no request pursuant to C.C.P. § 437c(h) by plaintiffs for a continuance to obtain additional discovery. It is unlikely additional discovery would yield anything as plaintiffs conducted focused discovery on this specific issue

[3] While the hearing was held jointly, this Court has individually decided and reasoned this decision without any collaboration with Judge Battaglia. Furthermore, this decision was drafted before Judge Battaglia released his order on November 9, 2015. Revisions to the draft of this opinion have been made after a review of Judge Battaglia's order.

for more than one year and the most relevant factual material for the analysis required by *Wyeth v. Levine, supra,* are the public statements of the FDA, which are readily obtainable without need for subpoena. Even so, a continuance to subpoena the FDA would be fruitless, pursuant to 21 C.F.R. § 20.1(a):

> No officer or employee of the Food and Drug Administration or of any other office or establishment in the Department of Health and Human Services, except as authorized by the Commissioner of Food and Drugs pursuant to this section or in the discharge of his official duties under the laws administered by the Food and Drug Administration, shall give any testimony before any tribunal pertaining to any function of the Food and Drug Administration or with respect to any information acquired in the discharge of his official duties.

Pursuant to *Buckman Co. v. Plaintiffs' Legal Committee* (2001) 531 U.S. 341, the parties are unable for force the FDA and its responsible officials to respond as a third-party to subpoenas issued out of this coordinated proceeding (or out of the MDL proceeding) to explain their actions or inaction. In this regard, the FDA is something analogous to a "black box," i.e. "a usually complicated electronic device whose internal mechanism is usually hidden from or mysterious to the user; *broadly*: anything that has mysterious or unknown internal functions or mechanisms." MERRIAM-WEBSTER ON-LINE DICTIONARY.

Both sides supplemented the record regarding authorized public statements from the FDA with expert opinions and the scientific papers on which such competing expert opinions were based. These will be discussed further in the course of the Legal Analysis and are much more fully discussed in Judge Battaglia's decision, which is fully incorporated by this reference except as noted below.

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III. ISSUES PRESENTED

As noted in the Introduction, resolution of the pending motion for summary judgment requires consideration and resolution of two related questions: (a) whether determination of the question of federal preemption is a matter to be resolved solely by the judge without any involvement by a jury to determine disputed preliminary factual matters, and (b) whether defendants are correct as a matter of law that the plaintiffs' claims based on alleged failure to warn of a risk of pancreatic cancer are precluded by the application of federal preemption pursuant to the United States Constitution Art. VI, § 2 due to "impossibility preemption." The motion is brought "against all Plaintiffs alleging pancreatic cancer." Notice of Motion, filed June 19, 2015 at 1, ll. 8-9.

IV. RELEVANT FACTUAL RECORD

A. Motion Presented As Motion For Summary Judgment:

The motion before the Court is presented as a motion for summary judgment pursuant to C.C.P. § 437c so the normal modes of proof and for framing of the issues have been used by the parties.[4] Accordingly, there are voluminous declarations and supporting exhibits and excerpts of discovery depositions and exhibits thereto. There are, in turn, various evidentiary objections to portions of the proffered evidence. While the Court will rule on each of them, given the gravity of the relief now requested, the Court does not believe that the outcome of such rulings have any impact on the actual outcome.

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[4] As noted previously, this Court has reviewed and now incorporates by reference Judge Battaglia's November 9, 2015 ruling addressing the same factual and legal issues. Because these JCCP cases are controlled by C.C.P. § 437c, not Rule 56, F.R.C.P., Judge Battaglia's references to Rule 56 on page 4, lines 4-16 of his decision, are not incorporated into this decision.

Moving parties have submitted a Separate Statement Of Undisputed Material Facts ("UMF") with their motion, listing 12 UMF's, all of which are related to actions or statements by the FDA. Plaintiffs concede one of the 12 UMF's, but they dispute the rest for various reasons, including that they are "irrelevant," "incomplete" and "legal conclusion about who 'published' the article." Plaintiffs also offer 49 "Additional Disputed And Undisputed Facts In Opposition," e.g. # 41: "Defendants' regulatory expert agrees that if the sponsors failed to disclose information, that could have change the FDA's assessment contained in the NEJM article."

B. Demand For New Diabetes Type 2 Drug Treatments:

Turning to the relevant facts and the context in which these issues arise, the Court notes the following. Diabetes Type 2 (basically adult onset diabetes) is a public health problem of increasing gravity as more and more Americans (and humans worldwide) develop this condition. Insulin has been a recognized therapeutic drug for treatment of the blood sugar imbalance caused by diabetes (both Type 1 and Type 2), but continued use of that drug can have negative impacts on a patient. Accordingly, pharmaceutical manufacturers have worked hard to develop alternatives to insulin. A biguanide known generically as metformin has been used for some years as an alternative to insulin. Sulfonylurea medications exist as an alternative to metformin and insulin. Other products, such as Actos® (generic name: piglitazone), have been developed to be taken with products such as metformin or sulfonylurea.

Side-effects of those medications in certain patients have prompted researchers to try to develop alternative drug therapies which will help a body regulate its internal production of insulin so that blood sugar is properly absorbed by the cells. As noted previously, Amylin and Eli Lilly (acting jointly) first marketed Byetta®, an incretin mimetic (generic name: exenatide).

FDA approval for commercial use was first obtained in 2005 with a first-generation label. The label for Byetta® has evolved over time (in ways directly relevant to failure-to-warn litigation regarding pancreatitis) but the label has consistently avoided any reference to pancreatic cancer up to the present time.[5] A longer acting variant branded as Bydureon® was brought to market in 2012 with FDA approval of the associated label. The joint venture between Amylin and Eli Lilly has now terminated as a consequence of the acquisition of Amylin by AstraZeneca.

Byetta® had competitors in next-generation drug therapies in due course. In 2010, Merck Sharp & Dohme Corp. obtained FDA approval to sell a dipeptidyl peptidase 4 inhibitor branded as Januvia® (generic name: sitagliptin). In 2010 NovoNordisk obtained FDA approval to sell a similar product branded as Victoza® (generic name: liraglutide). As in the case of Byetta® and Bydureon®, the labels approved by the FDA for both Januvia® and Victoza® contain no reference to risk of pancreatic cancer.

C. FDA Classifies All Drugs At Issue As Incretin-Mimetic Therapies But Does Not Require Any Label Reference To Pancreatic Cancer:

While the drugs at issue in this litigation are sufficiently different that each has patent protection as a separate product, their mode of operation in the human body is sufficiently similar that they are all considered to be glucagon-like peptide-1 receptor agonists ("GLP-1 receptor agonists" or more succinctly "incretin mimetics"). The FDA has seen fit to classify all

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[5] Package inserts for FDA-regulated prescription drugs can alert a treating physician and an interested patient in possible side-effects with varying degrees of certitude, from a mere reference to a possible "association" of drug use with onset of a side effect (without a finding of a causative link) to much more robust warnings, leading up to a "black box" warning calling out the hazard with graphic, dramatic emphasis.

these drugs as drugs in the "incretin mimetic" class.[6] Therefore, the balance of this discussion will treat them as equivalent for purposes of analyzing whether or not the FDA would approve a CBE label change to include reference to pancreatic cancer. As noted previously, a common fact for all the drugs at all relevant times is that there is no reference to pancreatic cancer. Plaintiffs' theory of the case is that the failure to include some such warning is actionable negligence.

D. Evidentiary Objections:

Defendants' specific objections to various items offered by plaintiff are all overruled. The Court gives no weight, however, to proffered items which were not in the public domain or not shown to be information submitted to the FDA some time prior to the February 2014 issuance of the NEJM article based on *Buckman Co. v. Plaintiffs' Legal Committee, supra.* Plaintiffs' specific objections to various items offered by defendants are all overruled.

E. Nature Of Factual Question Presented:

The question before this Court is whether there is "clear evidence" pursuant to *Wyeth v. Levine, supra,* that the FDA would not have approved a CBE label change request to add any kind of reference of a risk of pancreatic cancer. The parties dispute whether or not the factual record now before this Court (and also before the federal court in the MDL companion cases) supports such a conclusion. It should be clearly noted that the question posed by *Wyeth v. Levine* is NOT to second guess whether the FDA should have allowed such a CBE, NOR whether or not the FDA of its own accord should have required a label change to add such a warning. Further,

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[6] *See* Deborah Hinnen, *ARNP, BC-ADM, CDE, FAAN,* Loretta L. Nielsen, *PhD,* Amy Waninger, *BS and* Pamela Kushner, *MA, MD Incretin Mimetics and DPP-IV Inhibitors: New Paradigms for the Treatment of Type 2 Diabetes,* JOURNAL OF THE AMERICAN BOARD OF FAMILY MEDICINE (2006), *available at* http://www.jabfm.org/content/19/6/612.full.

the question presented is not whether or not there is admissible scientific evidence that one of these drugs causes pancreatic cancer, which is a different question.

As is implicit in the nature of the question presented for resolution and as discussed at greater length in the legal analysis following, the factual dispute, such as it is, is a dispute regarding a "legislative fact," not an "adjudicative fact."[7] It is a legislative fact because the outcome generally applies to the claims of all the plaintiffs (since the dispute only turns of the actions and inactions of the FDA), and it is not a "adjudicative fact," such as would require analysis of a specific plaintiff's claim (e.g. a learned intermediary defense based on a given treating physician's testimony or question of whether a specific plaintiff actually ever took a specific drug exposure).

The only prism through which the adequacy of the label is to be examined for federal preemption purposes is via the action or inaction of the FDA such that one can conclude that a CBE would have been rejected (or was rejected in actual fact) by the FDA during the relevant period. Further, and as discussed below, one can only extrapolate the FDA's likely behavior based on how they acted on the information known to them at all relevant times. For this reason and consistent with *Buckman Co. v. Plaintiffs' Legal Committee, supra* (prohibiting litigation of a "fraud on the FDA tort theory for public policy reasons), this Court must disregard this portion of plaintiffs' factual showing as preempted by *Buckman Co.*

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[7] *Franz v. Board of Medical Quality Assurance* (1982) 31 Cal.3d 124, 140 n 6.

F. The Role Of The FDA In Supervising Product Labeling:

Prescription drugs, also known as "ethical" drugs, have been sold in this country and elsewhere long before the FDA was established by Congress in 1906 to improve standards and to protect public safety. Accordingly, the several states have had police power jurisdiction since the creation of the republic to regulate the same field via the common law of torts and otherwise. As noted in *Wyeth v. Levine,* the states retain these powers subject to limited federal preemption if the tort plaintiff's "failure to warn" theory would have required the use of a label on a prescription drug which the FDA itself would have prohibited. This leaves the plaintiff some running room to show that a given defendant manufacturer's label was negligently incomplete and recognizes the manufacturer's continuing obligation under the relevant federal laws to use adequate warning labels and to update such labels on their own initiative as and when a manufacturer obtains additional information showing that the status quo label is inadequate.

In simple terms, the FDA has a "veto" power over a proposed label change, but one will not see this veto exercised directly if no CBE request for a label change is presented by a manufacturer. (Other parties can submit a "citizens' petition" requesting FDA administrative action so there are other circumstances when a label-propriety question may be raised in actual fact.) The FDA has its own legitimate reasons to limit the practice of "over-warning" (a phenomenon of which any resident of or visitor to California is quite aware in other contexts) since doing so will diminish the utility of valid warnings to treating physicians and interested patients.

In this context, logic would suggest that the test of the adequacy of a prescription drug's label would reduce to an analysis of whether or not a manufacturer had duped the government agency

with misinformation in order to use a more commercially valuable label (presumptively a label with fewer side effect warnings and contraindications). For valid reasons of public policy, however, this line of inquiry has been fenced off by the United States Supreme Court in its decision in *Buckman Co. v. Plaintiffs' Legal Committee, supra.* The understandable concern is that allowing a private right of action for "fraud on the FDA" would embroil the agency's staff, particularly its scientific staff, in court litigation to the derogation of their performance of their primary duties. This would result both from the consumption of time in litigation activity and from a concern that their routine duties, decision-making processes and public communications would all have to be vetted with litigation avoidance in mind. "Applicants would then have an incentive to submit a deluge of information that the Administration neither wants nor needs, resulting in additional burdens on the FDA's evaluation of an application." *Id* at 351.

The upshot, however, is that some of the most logically relevant arguments are off limits when a failure-to-warn case is at issue in private litigation. Therefore, the holding in *Buckman* prevents the Court and parties from second guessing what the FDA relied on, creating a de facto privilege prohibiting the "should have submitted" line of inquiry and argument.

Further adding to the limits on meaningfully assessing the correctness of the FDA's performance of its duties in approving or disapproving a given label, there are limits on the extent to which parties in private litigation can obtain information from the FDA and its employees via subpoena. Federal regulations set forth at 21 C.F.R. § 20.1(a) further support the holding in *Buckman* that courts should not try to determine the information and evidence the FDA relied on in reaching its conclusions.

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In conclusion, the FDA has a central role in regulating the labels on prescription drugs, but it has not been given field-preclusive exclusive jurisdiction by Congress. Some states' laws structure their failure-to-warn test in terms which require proof that the manufacturer misled the FDA, a formulation which has led to the conclusion that such laws (and thus such claims) are preempted by federal law. *Lofton v. McNeil Consumer & Specialty Pharmaceuticals* (2012) 672 F.3d 372 (Texas tort reform law preempted for this reason).[8] But there is no requirement that a state defer to the FDA's actions regarding labeling, allowing states like Vermont (the locus of *Wyeth v. Levine*), California and many other states to preserve common-law tort remedies for negligent failure to warn.

Mindful that the FDA could, however, bar a particular CBE label change in any particular circumstance and thus deny to a manufacturer the ability to add an additional warning as proposed by plaintiff in tort litigation in support of his or her request for damages, the Supreme Court has recognized that "impossibility" preemption exists to allow a defendant the chance to offer an affirmative defense that the label change on which plaintiff relies in pursuit of recovery would have been prohibited by the FDA in its lawful exercise of federal power.

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[8] *Lofton v. McNeil Consumer & Specialty Pharmaceuticals* (2012) 672 F.3d 372 (holding that federal law preempted failure to warn state statute unless FDA itself found fraud); *see also Lashley v. Pfizer, Inc.* (5th Cir. 2014) 750 F.3d 470; *Gonzalez v. Bayer Healthcare Pharmaceuticals, Inc.* (S.D. Tex. 2013) 930 F.Supp.2d 808, 821; *Garcia v. Wyeth-Ayerst Laboratories* (6th Cir. 2004) 385 F.3d 961 (preempting state statute that permitted tort claim if information was withheld from the FDA); *Marsh v. Genentech, Inc.* (6th Cir. 2012) 693 F.3d 546.

G. FDA Consideration Of Possible Label Changes For Incretin-Mimetic Drugs:

The FDA was never presented with a CBE (Change Being Effected) request from a drug manufacturer asking to add a warning regarding pancreatic cancer to an incretin-mimetic product. The FDA did receive a series of requests from the defendants herein to approve labels for various incretin-mimetic products over the years which omitted any reference to pancreatic cancer, and the FDA uniformly approved those labels.

The FDA was made aware of concerns by certain researchers in the field of public health and medicine that there might be an association between use of an incretin mimetic and onset of pancreatic cancer (the lowest threshold that might warrant some label disclosure of "association" without disclosure of "causation," as such). In 2012, a citizen petition requested that the incretin-mimetic drug Victoza® be removed from the market because of an alleged increased risk of pancreatic cancer. The petition caused the FDA to issue a drug safety communication associating incretin mimetics with pancreatic cancer, which the FDA further evaluated before coming to a final conclusion.

The FDA and its European counterpart (the European Medicines Agency) authorized various trusted scientists on staff to investigate the question, which is consistent with each agency's continuing duty to ensure that labels in use are adequate whether or not a manufacturer has submitted a CBE request for label change. The outcome of this process was the publication in the NEW ENGLAND JOURNAL OF MEDICINE on February 27, 2014 of an article by Amy G. Egan, M.D., M.P.H., Eberhard Blind, M.D., Ph.D., Kristina Dunder, M.D., Pieter A. de Graeff, M.D., B. Timothy Hummer, Ph.D., Todd Bourcier, Ph.D., and Curtis Rosebraugh, M.D., M.P.H., entitled "Pancreatic Safety of Incretin-Based Drugs — FDA and EMA Assessment." The

authors were described as "From the Office of New Drugs, Center for Drug Evaluation and Research, Food and Drug Administration, Silver Spring, MD (A.G.E., B.T.H., T.B., C.R.); the European Medicines Agency, London (E.B.); Läkemedelsverket, Uppsala, Sweden (K.D.); and the Dutch Medicines Evaluation Board, Utrecht, the Netherlands (P.A.G.)." A copy of the article is attached hereto and incorporated by this reference.

The article shows that possible association between use of these drugs and pancreatic cancer was directly at issue:

> Both the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) are committed to ensuring the safety of drug products marketed for the treatment of diabetes, and **postmarketing reports of** pancreatitis and **pancreatic cancer in patients taking certain antidiabetic medications have been of concern to both agencies.** (emphasis added)

Having reviewed the available scholarship, the two agencies' scientists concluded that there is no persuasive showing of an association of usage of the drug with pancreatitis (a label change which had been implemented after litigation regarding alleged failure-to-warn of pancreatitis had been pressed) but that the current label, which indicates that there may be such an association, could remain in place. Notably, however, they confirmed that the current labels' silence regarding pancreatic cancer was correct based on currently available information and that no revision was warranted:

> Both agencies agree that **assertions concerning a causal association between incretin-based drugs and pancreatitis or pancreatic cancer, as expressed recently in the scientific literature and in the media, are inconsistent with the current data.** The FDA and the EMA have not reached a final conclusion at this time regarding such a causal relationship. Although the totality of the data that have been reviewed provides reassurance, pancreatitis will continue to be considered a risk associated with these drugs until more data are available; both agencies continue to investigate this safety signal. **The FDA and the EMA believe that the current knowledge is adequately reflected in the**

> **product information or labeling,** and further harmonization among products is planned in Europe. (emphasis added)

As noted in more detail in defendants' brief and Separate Statement, the FDA has also approved labels for GLP-1 drugs without requiring a warning for pancreatic cancer in a series of decisions, and in March 2014 it rejected the citizen petition seeking the removal of Victoza® from the market, a petition based in part on the assertion that the drug increases the risk of pancreatic cancer. In 2014, the FDA also provided a Briefing Book to an Advisory Committee assessing a higher-dose version of a GLP-1 drug which stated:

> Risk for pancreatic cancer has more recently emerged as a concern with GLP-1-based therapies, including liraglutide. … However, animal, observation, and clinical trial data review by FDA to date have not supported a causal association.

Exhibit C to Laurendeau Declaration. Fairly read, the moving parties' evidence shows that the FDA was aware of and considered the risk of pancreatic cancer as a consequence of patient use of a GLP-1 drug and has not found a basis for stating that a causal association has been shown, for which reason it has never required a disclosure of a possible risk of pancreatic cancer for this class of drugs. Plaintiffs' heavy reliance on the adverse event reporting is misplaced because the public record shows that the FDA acknowledged and took account of the adverse event reports in its conclusion to reject the citizen petition and publish its finding in the NEW ENGLAND JOURNAL OF MEDICINE. Adverse event reporting does not automatically validate data; anyone, including plaintiffs' lawyers, can submit an adverse event report.[9] While adverse event reports are undoubtedly useful as early warnings for potential problems, as applied in this case, they are not

[9] "Reporting of adverse events and medication errors by healthcare professionals and consumers is voluntary in the United States. FDA receives some adverse event and medication error reports directly from healthcare professionals (such as physicians, pharmacists, nurses and others) and consumers (such as patients, family members, lawyers and others)." FDA Adverse Event Reporting System (FAERS), *available at* http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/.

particularly useful to prove causation, and the FDA took them into account in its conclusions. For a more detailed account of the record before the FDA and this Court, see Judge Battaglia's order.

V. LEGAL ANALYSIS

A. Application Of "Impossibility" Preemption Under *Wyeth v. Levine* Is A Question Of Law Reserved Exclusively For Judicial Resolution:

1. There Is No Controlling Precedent On Point

Having reviewed the briefs filed post-argument, the parties have not cited this Court to any controlling precedent which overtly raises and resolves the question of whether or not a jury should have any role in deciding the question framed by *Wyeth v Levine*.[10] Although Justice Stevens chose to state the test in *Wyeth v. Levine*, using the words "clear evidence," he never suggested a jury had a role. Thus, this Court concludes that there is no California or Supreme Court decision that directly addresses the "question of law" versus "question of fact" issue.

It should also be noted that the label "question of law" is a simplistic formulation which consigns a given decision-making process to the judge to the exclusion of any prospective jury. The label does not preclude resolution of disputed "preliminary" facts since judges do this routinely in various contexts, including (a) preliminary facts ("[d]etermination of issues of fact preliminary to the admission of evidence are to be decided by the court…" Cal. Evid. Code, § 310), (b) in personam jurisdiction ("[w]hen there is conflicting evidence, the trial court's factual determinations are not disturbed on appeal if supported by substantial evidence." *Vons*

[10] In ruling in favor of preemption, a District Court found that the preemption motion "presents only a legal question for the court." *Dobbs v. Wyeth* (2011 W.D. Okla) 797 F.Supp.2d 1264, 1267.

Companies, Inc. v. Seabest Foods, Inc. (1996) 14 Cal.4th 434, 449), and (c) whether or not privileges are validly invoked (2 Witkin, CAL. EVID. 5TH (2012) Witnesses, § 90, p. 382).

2. The Courts Handling *Wyeth v. Levine* Each Handled The Issue As A Question Of Law

While the U.S. Supreme Court and the Vermont Supreme Court did not expressly speak to the issue now before this Court, it is obvious from the record disclosed in the published opinions that those two courts as well as the trial court in Vermont all treated the question as one reserved for a judge. The Vermont jury did have a factual question to resolve: "Was the label's omission of a warning against intravenous use of the drug inadequate?" But it was only AFTER they had rendered an affirmative verdict for plaintiff that the judge in post-trial motions considered and rejected defendant's "impossibility" preemption defense. Notably, the preemption defense had been attempted pre-trial via an unsuccessful motion for summary judgment, so the potential relevance of this defense was known to both the lawyers and the trial judge long before the jury was empaneled and charged.

On appeal, the defendant manufacturer argued that the case should never have been submitted to the jury, but no one argued that the asserted "impossibility" preemption defense presented a question suitable for jury resolution.

3. All The Cases Decided Since *Wyeth v. Levine* Have Treated The Preemption Question As A Question Of Law

Although the assignment of this class of decision-making work to the judge and not to a jury has not been expressly addressed in the dozen or so district court cases cited by the parties as applications of the *Wyeth v. Levine* test to various product labels, it is notable that the decisions

have always been made by the judge, typically via a motion for summary judgment, and not via fact-finding by a jury.

4. Federal Preemption Is Normally Considered A Question Of Law

As a general proposition, there is law on point in California state cases and elsewhere that the existence or absence of a valid federal preemption defense under Art. VI, § 2 of the United States Constitution is a "question of law." *Farm Raised Salmon Cases* (2008) 42 Cal.4th 1077, 1089; *Spielholz v. Superior Court* (2001) 86 Cal.App.4th 1366, 1372. One must start by recognizing that federal preemption defenses arise in three different contexts, which are certainly not identical in terms of the decision-making process involved. They are:

- Express Field Preemption
- Implied Preemption Via Obstacle Preemption
- Implied Preemption Via Impossibility Preemption

In basic terms the task(s) involved are as follows, category by category:

Express Field Preemption: Analyze the legislative text and legislative history of federal legislation to determine if Congress has expressly intended to "occupy" a field of regulation, thus ousting the opportunity for states to regulate via legislation or the common law. A classic example is Congress' enactment of field preemption in ERISA § 502(a)(1)(B), 29 U.S.C. § 1132(a)(1)(B).

Implied Preemption Via Obstacle Preemption: Analyze the legislative text and legislative history of federal legislation to determine if the challenged state law (created by statute or by case law) is an obstacle to the accomplishment and execution of the full

purposes and objectives of Congress. A timely example is the jurisprudence under the Federal Arbitration Act § 2, 9 U.S.C. § 2, striking down inconsistent state-law rules regulating enforcement of arbitration agreements. *AT&T Mobility LLC v. Concepcion* (2011) 563 U.S. 333. This requires both a legalistic analysis of Congress' intent and an analysis of the effects of the challenged state law in the context of a given case.

Implied Preemption Via Impossibility Preemption: Whether or not a defendant asserting the affirmative defense can show a broad-brush policy reason why the state law must accede to a contrary or inconsistent objective of federal law, a defendant is entitled to avoid liability if he, she or it can show that it was prevented from complying with state law (including tort exposure flowing from state common law) due to an operative federal law. This concededly can arise in a multitude of contexts, making it fundamentally different, analytically, from the thought processes involved in resolving the first two categories of potential preemption analysis.

The instant case is an example of "impossibility" analysis since Congress has not expressly occupied the field of drug label regulation, and *Wyeth* forecloses an argument for implied preemption via "obstacle preemption." For this reason, the parties deserve a focused analysis of why impossibility preemption should still be considered a judicial "question of law," not a "question of fact" amenable to submission to a jury.

Mindful of how the Courts have tried this question to date (headings 2 & 3 above) and of the considerations listed below, the Court does hold that in the context of this case that the question can and should be resolved exclusively by the judge, even if there are preliminary disputed facts which have to be resolved before the ultimate "question of law" can be fully and finally resolved.

5. Treating Drug Labeling "Impossibility" Preemption As A Question Of Fact For The Jury Would Likely Create Unacceptable Inconsistent Outcomes

The record in this case aptly shows the nature of the "impossibility" preemption analysis required here and its impact on multiple litigants. Thousands, indeed hundreds of thousands or millions, of prescriptions for these incretin-mimetic prescription drugs were filled during the relevant period, and hundreds of plaintiffs have now submitted claims in this coordinated proceeding, each of which asserts that the various labels – each of which was silent on the matter of pancreatic cancer – was tortuously negligent. If a drug manufacturer has a valid defense under *Wyeth v. Levine* that it could not have revised the label in the fashion sought by a given plaintiff and his/her counsel in litigation, that defense should be equally operative as to all similarly situated plaintiffs.

This outcome favoring consistency can only be had if the question is viewed as a question of law to be decided by the trial judge in the first instance subject to appellate review and then applied broadly to all similarly situated litigants once and for all. If an outcome in a given case is considered to turn on a finding of fact, there are no consequences for a different litigant with a factually similar tort claim, subject only to the potential for a second plaintiff's use of offensive collateral estoppel once the first outcome has ripened into a final, non-reviewable judgment. *Cf. Parklane Hosiery Co. v. Shore* (1979) 439 U.S. 322; RESTATEMENT (SECOND) JUDGMENTS § 29. Conversely, if an outcome is had in a given litigation by reason of a ruling on a question of law, e.g. the running of a statute of limitations, then all similarly situated litigants are bound if that ruling is reflected in a controlling published appellate opinion. *Auto Equity Sales, Inc. v. Superior Court* (1962) 57 Cal.2d 450, 455.

In other words, this Court is analyzing legislative and administrative "facts," not adjudicative facts, which must be given to a jury. The predicate factual findings made herein are done to interpret and apply the law, namely preemption analysis. Respect for the law requires a fair consistency of outcomes when the same legal issue is tested. For this reason, it is important as a matter of public respect for the law (and for judicial efficiency) that the existence or non-existence of federal preemption be resolved in a process which has broad applicability, not as a one-off factual question subject to the happenstance of how a given jury takes to a presentation of disputed facts and arguments.

6. *Boyle v. United Technologies Corp.* Does Not Dictate A Contrary Ruling

Plaintiff appropriately calls the Court's attention to the federal preemption analytical process used and endorsed in *Boyle v. United Technologies Corp.* (1988) 487 U.S. 500, and cited with approval in *Oxford v. Foster Wheeler LLC* (2009) 177 Cal.App.4th 700. The federal preemption affirmative defense applicable there applied to military contractors who supply weapons and associated components to the United States government in accordance with government blueprints and specifications. This absolves contractors from tort liability if they supplied the product according to the government's own design, leaving the injured soldier or bystander to whatever remedy, if any, he or she may have against the government itself. This immunity reduces the cost of military procurement and broadens the field of willing contractors and also allows the government to obtain products according to its own best design judgment without undue second-guessing by the contractor involved.

The product-specific inquiry analysis leads, however, to a need to resolve in a given case whether or not the allegedly defective design giving rise to a pending state-law tort claim is

foreclosed by federal preemption. This, in turn, requires the legal system to resolve the extent to which, if at all, the allegedly defective design was mandated by the government or was a choice made unilaterally by the contractor. This is such a different, factually driven process from the instant case, which is deducing on a systemic basis whether or not the FDA would have approved a CBE label change, that this Court finds *Boyle* and its progeny factually distinguishable.

7. The Task Required Here Is An Inherently Judicial Function

By comparison to the fact-finding needed in *Boyle* to apply (or not apply) the military contractor affirmative defense, the process here is a variant on engaging in an analysis of legislative or administrative-law history and intent, where the words used by various actors in the historic record are the touchstone (particularly if they become the text of a statute or regulation). The oddity here is that the words are those of an agency which approves or disapproves labels presented and which, on rare occasion, makes additional public pronouncements. This all has the look and feel of an analytical process where legal training and experience add value and where a jury's unique ability to test credibility is not as useful or material to the actual project at hand.

Since judges have for generations decided preliminary factual matters antecedent to ruling on important matters like in personam jurisdiction, evidentiary and privilege issues, the Court holds that there is no abrogation of these plaintiffs' constitutional right to a jury trial under the federal and state constitution to decide the federal preemption question without use of a jury to resolve disputed preliminary facts. The ultimate question before the Court – the intersection of federal statutory law and state common law – is a jurisprudential question more than it is a truth-finding

process. That a predicate step in the process is an evaluation of competing factual submissions is no different in nature from the approved process by which courts determine whether or not to extend tort liability for "ultra-hazardous activity" to additional activities beyond the categories of activity previously recognized as giving rise to strict liability. See generally, RESTATEMENT OF TORTS § 520, comment l; *Luthringer v. Moore* (1948) 31 Cal.2d 489, 496; *Langan v. Valicopters, Inc.* (Wash. 1977) 88 Wash.2d 855, 861 P.2d 218; *Plourde v. Hartford Electric Lighting Co.* (Super. Ct. Conn. 1974) 31 Conn.Supp. 192, 326 A.2d 848.

The core question presented is very similar to judicial review of the correctness of administrative agency action (or inaction) when the agency itself finds itself caught up in litigation. There is a fairly robust body of law in this field and hardly, if ever, does the review process involve any kind of de novo trial of facts via the jury process.

At the end of the day, this Court is confident that analysis of the federal preemption question under *Wyeth* is a task to be resolved solely by a judge with no jury involvement. This remains so even though the parties have used the normal templates for summary judgment motions, most particularly the submission of a Separate Statement Of Undisputed Facts and plaintiffs' responses thereto. To label the task now before this Court as a "question of law" for these purposes does not foreclose the need for analysis of competing preliminary facts under a standard which does not require the Court to limit its fact-finding to a determination of the existence of an unresolved predicate "material" factual issue. Once the project is assigned to the Court as part of a "question of law," it is the Court's job to resolve the issue on the record presented and not to wait for a "trial," as such, just to complete the project. As noted by the leading scholar in the field of administrative law, Kenneth Culp Davis, in his treatise ADMINISTRATIVE LAW TEXT (1972 ed.):

> That the practical approach as well as the analytical approach to the law-fact distinction is used in the judge-jury context is entirely clear. Even when statutory provisions assign question of fact to juries and question of law to judges, the allocation of functions is usually guided by practical needs and not by analysis of the literal meaning of "law" and "fact." Professor Leon Green, author of a book on Judge and Jury, emphatically asserts the practice approach: "By and large the terms' law' and 'fact' are merely short terms for the respective functions of judge and jury." The same fundamental was neatly expressed by another discerning commentator: "Whether a particular question is to be treated as a question of law or a question of fact is not itself a question of fact, but a highly artificial question of law."

ADMINISTRATIVE LAW TEXT, *supra,* "Scope of Review in Applying Legal Concepts" § 30.02.[11] In sum, insofar as the parties dispute how this Court should deduce the correct conclusion as to what the FDA would or would not have done in a specific circumstance not exactly presented to the FDA, the "legislative fact" dispute is one which this Court can and must resolve now (not at some later event of trial) without regard to the normal constraints and processes contemplated when C.C.P. § 437c is used to test the presence or absence of a disputed issue of material "adjudicative" fact.

B. <u>On The Merits, Defendants' "Impossibility" Preemption Argument Is Correct:</u>

1. The Court Can Resolve A Contested Issue Of Law Via Summary Judgment

The mere fact that defendants have presented these motions via C.C.P. § 437c does not preclude the final resolution of a "question of law" by the judge. While questions of law can also be presented via demurrer or a motion for judgment on the pleadings, neither of those procedures would be suitable for presentation of the extensive extra-pleading information on which both sides rely in contesting the applicability of the "impossibility" defense under *Wyeth*

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[11] The California Supreme Court agreed with Prof. Davis' analysis when it cited favorably to him in *Franz v. Board of Medical Quality Assurance, supra,* 31 Cal.3d 140 n.6: "Davis explains the long-recognized distinction between 'legislative' and 'adjudicative' facts. The latter are 'facts concerning immediate parties' and what happened to them; the former are facts 'utilized for informing a court's [or agency's] legislative judgment on questions of law and policy.'"

to these product labels. While defendants could have, in the alternative, invited the Court to bifurcate a trial to try their affirmative defense first, there was no requirement that they do so.

The record which is now before the Court is similar to what would have been received if the case proceeded as a "trial" rather than on motion practice, and nothing would be gained by denying the instant motion without prejudice only to re-hear the same matter on the same record under the rubric "trial."

Multiple cases have recognized that it is entirely proper to resolve questions of law presented via the motion for summary judgment process under C.C.P. § 437c. *Garofalo v. Princess Cruises, Inc.* (2000) 85 Cal.App.4th 1060 (federal preemption); *Massa v. Southern California Rapid Transit District* (1996) 43 Cal.App.4th 1217 (statutory interpretation); *Hernandez v. Modesto Portuguese Pentecost Ass'n* (1995) 40 Cal.App.4th 1274 (statutory interpretation). This Court is doing no more than that by the evaluation and grant of defendants' motion here.

2. The "Clear Evidence" Test Is Satisfied

As a general proposition, federal preemption is not to be readily assumed. The continuing sovereignty of the several states in tandem with the federal government requires that federal preemption be done sparingly and only on a clear showing. "Congress does not cavalierly preempt state-law causes of action." *Medtronic, Inc. v. Lohr* (1996) 518 U.S. 470, 485. Consistent therewith, the U.S. Supreme Court in the case most relevant to this analysis, *Wyeth v. Levine*, required that the showing in favor of impossibility preemption be done by "clear evidence." Using – by analogy – the terms used to charge a jury in their fact-finding process, "clear evidence" is more than a mere "preponderance." It is, however, less than "evidence beyond a reasonable doubt" or "indisputable" evidence. It is closest to "clear and convincing

evidence." If "clear" could only mean "transparent" evidence (to paraphrase Judge Battaglia's comment during oral argument, when he observed that a government agency such as the FDA can never be considered fully "transparent"), then the Supreme Court has set up an illusory test. The Court does not read the Supreme Court as intending such a foolish project.

The Court agrees with defendants that the applicable test has been met in this case. The Court reaches this conclusion based on the confluence of:

(a) The fact that agency scientists made a public pronouncement in one of the most respected peer-reviewed medical journals (if not the premier example of such journals) in favor of the current labeling regime as compared to changes thereto of the exact type urged by plaintiffs herein.

(b) The FDA did so in conjunction with the European Medicines Agency, its counterpart agency providing similar regulatory and technical advice to the European Community.

(c) The FDA repeatedly approved labels for new incretin-mimetic drugs which lacked any reference to pancreatic cancer.

Those considerations, by themselves, would be enough to reach this legal conclusion. There is more, however, in support of this conclusion because plaintiffs' own expert, Dr. Thomas Fleming, had to concede how unprecedented it was for the FDA and EMA to make such a full-throated public statement in support of the current label regime. While Dr. Fleming did try to earn his retainer by keeping aloft his own view that a label change was in order, that is not the relevant question. The question is whether there is clear evidence that the FDA would not accept a CBE of the type Dr. Fleming desired:

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> [The paper] involved the nearly unprecedented fact that FDA and EMA had produced it together… *** I can't recall a similar publication. I don't rule out that there haven't been, but this kind of joint collaboration that ends up in a publication like this is, I think, unusual. *** I certainly will say yes to this being an unprecedented article that reflects a very robust evaluation that went on for a significant period of time. I think you are adding a conclusion that I'm not necessarily going to agree with.

Fleming Dep. pp 90-92.

For the same reason, the Court is not persuaded that a private communication to a defendant manufacturer from a different regulator in a different county (i.e. neither from the FDA nor the EMA)(a document filed under seal with court approval) would dictate denial of the motion, with or without prejudice. Under *Wyeth*, the relevant question is what the FDA would do, not the likely behavior of some other government's drug regulators.

Additionally, plaintiffs' effort to rely upon information that was allegedly withheld from the FDA to support its contrary hypothesis of likely agency action is contrary to *Buckman Co.* Because drug manufacturers have a continuing legal duty to update their drug labels, any allegation that information was improperly withheld is a form of fraud, precisely the type of claim that *Buckman Co.* sought to exclude from evidence. All is not lost, since any fraud committed against the FDA is squarely within its jurisdiction, as it has many enforcement options at its disposal. "The FDA thus has at its disposal a variety of enforcement options that allow it to make a measured response to suspected fraud upon the Administration." *Buckman Co., supra,* 531 U.S. at 349.

As previously noted, the Court attaches hereto and incorporates by reference the FDA's public statement on February 27, 2014, in the NEW ENGLAND JOURNAL OF MEDICINE in favor of the current labels. The cautious bureaucratic language of the agency acknowledging that studies

remain under way and that it would entertain new submissions of information does not change the conclusion. The FDA would be remiss if it foreclosed a willingness to consider new information.

Finally and in lieu of a further exegesis of the factual record, this Court fully agrees with Judge Battaglia's analysis that there was "clear evidence" that the FDA would not have approved plaintiff's desired label change. Judge Battaglia's reasoning is therefore incorporated herein.

Litigation is almost always viewed through the rear-view mirror, not with a crystal ball looking to the future,[12] and on the question of federal preemption, the inaction of the FDA in accepting the proposed labels as is and the affirmative action of the FDA in issuing the February 2014 article speak volumes. No one has pointed to any prior case (in litigation or outside litigation) where the FDA has gone to these lengths to publicly convey its views. These were obviously not random or happenstance comments now taken out of context. An article by FDA employees does not get published in a peer-reviewed medical journal without substantial conscious thought and effort.

The one piece of the puzzle arguably lacking is the fact that there was never a CBE request from a manufacturer seeking to add a pancreatic cancer warning, but plaintiffs and their advocates expect too much when they make the assumption that a manufacturer would make an insincere, factually unsound request for a CBE to add an otherwise unjustified warning (unjustified in the view of the manufacturer, that is) just to obtain a denial letter. There is no

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[12] Future damages for economic and non-economic loss being the major exception.

cognizable legal obligation on the defendants to do so as a predicate to invoking impossibility preemption under *Wyeth.*

3. The Evidentiary Objections Could Not Change The Outcome

Simply put, the Court would reach the conclusion that there is "clear evidence" that the FDA would not approve a CBE label change to add reference to pancreatic cancer if the only information in the record was the NEW ENGLAND JOURNAL OF MEDICINE article and the approval of the recent labels for the products in question. Plaintiffs' objections to this form of evidence are entirely without validity since these are the key "legislative facts" relevant to resolution of this motion, and this Court has allowed the entirety of plaintiffs' contrary evidence into the record, subject, however, to the restrictions required by *Buckman Co.* The evidence objections have, therefore, had no practical impact on the outcome of this motion and basically represent wasted lawyer effort.

VI. CONCLUSION

Having held that the Court has the right and duty to decide all questions embedded in defendants' motions for summary judgment, including preliminary questions of disputed facts, the Court now holds that each defendant is entitled to the benefit of federal law preemption on the basis of impossibility under *Wyeth v. Levine* insofar as any plaintiff's claim is predicated on an alleged failure for warn of a risk of pancreatic cancer associated with product use for any products dispensed on or before October 8, 2015.[13] Defendants to prepare [Proposed] Judgment(s) specific to each such defendant's exposure to each named plaintiff who has a case

[13] This preemption finding applies all the way to October 8, 2015 as that was the final date that additional briefing was filed and the date that the record closed.

based only on pancreatic cancer consistent herewith and to submit to Court no later than November 25, 2015.

The case is set for a Further Status Conference on December 3, 2015 at 10 a.m. (concurrent with a pending motion) to discuss how the cases should now progress as to the numerous other plaintiffs whose claims are not limited to or based on pancreatic cancer. Meet and confer in person in advance and submit a Joint Report by November 30, 2015 with a litigation plan (or competing plans) and discuss whether or not there is a role for ADR as to such remaining claims.

Dated: November 13, 2015

William F. Highberger