

1 **O'MELVENY & MYERS LLP**
Richard B. Goetz (SBN 115666)
2 Amy J. Laurendeau (SBN 198321)
3 400 South Hope Street
Los Angeles, CA 90071
4 Telephone: (213) 430-6000
Attorneys for Amylin Pharmaceuticals, LLC

5 **WILLIAMS & CONNOLLY LLP**
6 Douglas R. Marvin (SBN 933671)
M. Elaine Horn (SBN 460132)
7 Ana C. Reyes (SBN 477354)
8 725 Twelfth Street, N.W.
Washington, D.C. 20005
9 Telephone: (202) 434-5000
*Attorneys for Merck Sharp
& Dohme Corp.*

DLA PIPER LLP (US)
Loren H. Brown (SBN 2533529)
Heidi Levine (SBN 2822740)
Raymond M. Williams (SBN
164068)
1251 Avenue of the Americas,
27th Floor
New York, NY 10020
Telephone: (212) 335-4500

Attorneys for Novo Nordisk Inc.

PEPPER HAMILTON LLP
Nina M. Gussack (SBN 31054)
Kenneth J. King (SBN 1885961)
3000 Two Logan Square East
Eighteenth and Arch Streets
Philadelphia, PA 19103
Telephone: (215) 981-4000

*Attorneys for Eli Lilly and
Company*

11
12
13 **UNITED STATES DISTRICT COURT**
14 **SOUTHERN DISTRICT OF CALIFORNIA**

15
16 **IN RE INCRETIN-BASED**
17 **THERAPIES PRODUCTS**
18 **LIABILITY LITIGATION**

19 *As to All Related and Member Cases*

Case No. 13md2452-AJB (MDD)

MDL 2452

**DEFENDANTS' OPPOSITION
TO MOTION TO COMPEL
FURTHER RESPONSES TO
PLAINTIFFS' SET II WRITTEN
DISCOVERY AGAINST ALL
DEFENDANTS**

Date: October 2, 2014

Time: 10 a.m. (telephonic)

Magistrate: Hon. Mitchell D. Dembin

Judge: Hon. Anthony J. Battaglia

INTRODUCTION

1
2 Preemption discovery, the Court emphasized in its August 14, 2014 order,
3 “should be focused on the FDA’s intent” and “includes communications between
4 the FDA and drug manufacturers at issue and what the FDA had or did not have
5 before it on the use of incretin-mimetic therapies and the causal association with
6 cancer.” Order Following August 14, 2014 Case Management Conference (Doc.
7 No. 567) (“8/14/2014 Order”) at 2. General causation discovery, the Court
8 reiterated, should focus on “the causal link in dispute in this case” – that is, whether
9 “the pharmaceuticals at issue cause pancreatic cancer.” *Id.* (quoting March 25,
10 2014 Order (Doc. No. 377)). The discovery Plaintiffs move to compel does not
11 come within the scope of permissible discovery as defined by the Court. Rather, it
12 sweeps in a wide array of other issues, including: drugs not at issue in this litigation
13 (RFA Nos. 5-9; Rog. No. 3-5; RFP No. 4-5); side effects and conditions other than
14 pancreatic cancer (RFA Nos. 1-11, 30-33, 36-37; Rog. Nos. 2-6; RFP Nos. 4-5, 7-
15 8); communications with regulatory agencies other than the FDA (RFA Nos. 32-37;
16 Rog. No. 6); actions by governmental entities other than the FDA (Rog. Nos. 7-9);
17 and Defendants’ internal communications (RFP No. 10).

18 Plaintiffs maintain that they need this discovery to investigate whether the
19 FDA would approve a pancreatic cancer warning for the drugs at issue here. Pls.’
20 Mem. at 7. But Plaintiffs admit that the regulatory standard governing when the
21 FDA may approve a warning is a *legal* question for which fact discovery is
22 inapplicable. Pls.’ Mem. at 4-5. Moreover, the way in which the FDA would apply
23 its labeling standards to this set of facts will not be illuminated by Defendants’
24 opinions about the evidence related to warnings about other drugs, the actions of
25 foreign regulators, or claims about misconduct unrelated to the drugs and
26 conditions at issue, as this information is irrelevant to preemption. While Plaintiffs
27 claim that their purported “preemption discovery” is necessary to determine how
28 FDA applies its standards, they need look no further than the FDA’s own

1 pronouncement in the *New England Journal of Medicine* article published earlier
2 this year that the available scientific data is inconsistent with a causal association
3 between pancreatic cancer and incretin-based drugs and that the current knowledge
4 is adequately reflected in the drugs' labeling. Amy G. Egan, *et al.*, *Pancreatic*
5 *Safety of Incretin-Based Drugs—FDA and EMA Assessment*, 370 N. Eng. J. Med.
6 794, 796 (Feb. 27, 2014).

7 Plaintiffs also repeat their complaint that Defendants have referred them to
8 their custodial and other productions, rather than interview employees. But the
9 Court has already ruled that Rule 26 does not require the procedures Plaintiffs
10 demand. Sept. 10, 2014 Hearing Trans. at 27. For these reasons and the reasons set
11 forth below, Plaintiffs' motion should be denied.

12 **I. THE COURT SHOULD DENY THE MOTION AS TO REQUESTS**
13 **PURPORTEDLY RELATED TO THE “REASONABLE EVIDENCE**
14 **OF A CAUSAL ASSOCIATION” STANDARD.**

15 Plaintiffs attempt to justify an array of discovery requests as necessary to
16 provide the Court with a “*factual* basis on which to speculate about what the FDA
17 might have done with a hypothetical warning.” Pls.' Mem. at 7 (emphasis in
18 original). However, Plaintiffs' requests do not seek data about a possible causal
19 association between pancreatic cancer and the drugs at issue, or about the FDA's
20 own evaluation of such data, or even about what data was available to the FDA.
21 Instead, Plaintiffs claim to seek “the facts underlying Defendants' unprecedented
22 arguments” (Pls.' Mem. at 5) that FDA approval of a prescription drug warning
23 requires “reasonable evidence of a causal association” between the drug and the
24 risk, as stated in 21 C.F.R. section 201.57(c)(6)(i). Plaintiffs admit, however, that
25 the regulatory standard for approval of prescription drugs warnings is a *legal*
26 question, not a factual question requiring discovery. *See* Pls.' Mem. at 4-5. As to
27 that legal question, the law is clear that the FDA may not approve a label change in
28

1 the absence of “reasonable evidence of a causal association.”¹

2 Plaintiffs nevertheless insist that “as a *factual* matter, and as *law applies to*
3 *fact*, the ‘reasonable evidence’ standard is free-form and fact-intensive.” Pls.’
4 Mem. at 5 (emphasis in original). Even if this argument were a line of valid
5 inquiry, the discovery sought by Plaintiffs does not address the relevant issues.

6 Plaintiffs’ motion states that they seek to compel two categories of
7 information related to the “reasonable evidence” standard: “information about
8 whether and how the adverse effects warned about for the drugs in this litigation
9 meet the ‘reasonable evidence’ standard,” and “examples, if any exist, of the FDA
10 actually interpreting the ‘reasonable evidence’ standard this way and preventing a
11 manufacturer from adding a warning to a medication.” Pls.’ Mem. at 5. In fact,
12 many of the discovery requests listed in Plaintiffs’ motion fit neither of these
13 categories.² And if Plaintiffs actually wanted information about the scientific

14 ¹ See, e.g., *Dobbs v. Wyeth Pharm.*, 797 F. Supp. 2d 1264, 1272 (W.D. Okla. 2011)
15 (“[T]he FDA requires that a drug warning be based on ‘reasonable evidence of a
16 causal association’ between the use of the drug and the hazard identified in the
17 warning.” (citing 21 C.F.R. § 201.57(c)(6)(i))); *Wells v. Allergan, Inc.*, 2013 U.S.
18 Dist. LEXIS 13191, *19-20 (W.D. Okla. Jan. 31, 2013) (same); *Mason v.*
19 *Smithkline Beecham Corp.*, 596 F.3d 387, 392 (7th Cir. 2010) (“It is technically a
violation of federal law to propose a [Changes Being Effected warning] that is not
based on reasonable evidence.” (citing 18 U.S.C. § 1001)).

20 ² Plaintiffs’ Requests for Admission range well beyond the drugs at issue. Requests
21 for Admission Nos. 5-8 ask whether Defendants believe there is “reasonable
22 evidence of a causal association” for “every serious side effect identified in the
23 Medication Guide” and “every medical condition identified in the Highlights,
24 Warnings and Precautions, Adverse Reactions, Nonclinical Toxicology, Clinical
25 Studies, Patient Counseling Information, and Medication Guide” **for every branded**
26 **prescription drug sold by Defendants**. These requests are not only irrelevant, but
27 would require Defendants to review the scientific evidence related to hundreds of
28 drugs, potentially covering many years. See also, e.g., Rog. No. 4 (requesting
information about any instance in which the FDA required a warning for a “serious
side effect” in a Medication Guide for any of Defendants’ drugs when the defendant
did not believe there was reasonable evidence of a causal association between the
drug and the risk).

1 evidence supporting warnings on the drugs at issue, they could examine the
2 IND/NDAs, study data, and adverse event reports already produced by Defendants.

3 Nor do the requests genuinely seek information about FDA policies and
4 practices. For instance, Plaintiffs ask if Defendants “believe” that “reasonable
5 evidence of a causal association” exists for every medical condition mentioned in
6 the labels of every branded drug they market. (RFA Nos. 5-8.) They argue that
7 “[i]f . . . the FDA has *ever* allowed a warning despite the absence of ‘reasonable
8 evidence,’ then Defendants’ entire argument . . . has been proven meritless.” Pls.’
9 Mem. at 7 (emphasis in original). Plaintiffs’ argument misses the mark. That a
10 defendant might dispute the scientific basis for a single FDA-approved drug
11 warning scarcely *proves* that the FDA does not apply the regulatory standard based
12 on its independent assessment. Scientists routinely disagree. And because the
13 appropriate analysis for each drug and each medical condition is particularized,
14 whether or not the FDA has ever rejected any warning for incretin-based drugs
15 about any condition *other* than pancreatic cancer, much less a warning for an
16 unrelated drug, is not probative of whether the FDA would approve a proposed
17 pancreatic cancer warning here, where the FDA has plainly stated there is no
18 reasonable evidence of a causal association and has further stated that the current
19 labeling (with no mention of pancreatic cancer) is adequate. *See Mason*, 596 F.3d
20 at 395 (declining to give weight in a preemption analysis to the history of Prozac in
21 a preemption case involving Paxil’s warnings because the two antidepressants “are
22 different drugs made by different manufacturers”). Plaintiffs’ discovery will not
23 clarify FDA policy, as they maintain, but draw Defendants into a distracting
24 “gotcha” game based on irrelevancies.

25 Plaintiffs specifically complain that Defendants did not admit or deny
26 whether reasonable evidence exists to support the current pancreatitis warnings on
27 their drugs. Pls.’ Mem. at 6. Here, again, Plaintiffs plainly hope to leverage
28 Defendants’ views about one risk into a prediction of how the FDA would respond

1 to a warning about a different condition. Although the FDA also addressed the
2 scientific data related to pancreatitis and incretin mimetic drugs in its *New England*
3 *Journal* article, the regulatory issues surrounding pancreatitis and pancreatic cancer
4 warnings for these drugs are distinct, as are the data related to these conditions.
5 Whether the FDA would approve a proposed warning when it has expressly
6 concluded that the current data is inconsistent with the existence of a causal
7 association cannot properly be conflated with the question of whether it would call
8 for the withdrawal of an existing warning.

9 Finally, Plaintiffs' motion seeks to compel responses to Request for
10 Production No. 6, concerning communications from the FDA demonstrating that it
11 believes there is no reasonable evidence of a causal association between pancreatic
12 cancer and the drugs at issue. Plaintiffs have articulated no reason why the
13 responses already provided by each defendant are inadequate. Thus the motion as
14 to this request should be denied. *See Hupp v. San Diego County*, 2014 WL
15 1404510, *2 (S.D. Cal. April 10, 2014) (“[T]he moving party...carries the burden
16 of informing the court of ... why the responses are deficient”).

17 **II. THE COURT SHOULD DENY THE MOTION AS TO**
18 **INTERROGATORIES ABOUT FRAUD AND QUI TAM ACTIONS,**
19 **GOVERNMENTAL INVESTIGATIONS AND CORPORATE**
20 **INTEGRITY AGREEMENTS.**

21 Plaintiffs' interrogatories about governmental investigations, Qui Tam and
22 Whistleblower actions, and Corporate Integrity Agreements (Rogs. 7-9) plainly
23 seek to impugn Defendants on the basis of unrelated alleged misconduct irrelevant
24 to either preemption or general causation. The discovery sought by these
25 interrogatories is inadmissible information about alleged “prior bad acts,” which
26 cannot be used to show that any Defendant acted in conformity with the earlier acts
27 or allegations. Fed. R. Evid. 404(b).

28 To the extent Plaintiffs purport to seek information showing that Defendants
misled or defrauded the FDA about the specific drugs at issue in this litigation, the

1 information is still inadmissible under *Buckman Co. v. Plaintiffs' Legal Committee*,
2 531 U.S. 341 (2001). *Buckman* held that, due to the FDA's exclusive enforcement
3 power, the Food, Drug and Cosmetic Act, 21 U.S.C. § 301, *et seq.*, impliedly
4 preempts state law claims alleging that a pharmaceutical company defrauded the
5 FDA. 531 U.S. at 350, 353. Likewise, evidence and argument offered to show that
6 a manufacturer misled the FDA must be excluded. *See In re Fosamax*, 2014 U.S.
7 Dist. LEXIS 42253, 58 (D.N.J. Mar. 26, 2014) (citing *Buckman* in rejecting
8 plaintiff's argument that summary judgment based on preemption could be defeated
9 by evidence purporting to show pharmaceutical manufacturer withheld information
10 from the FDA); *In re Baycol Prods. Litig.*, 532 F. Supp. 2d 1029, 1053 (D. Minn.
11 2007) (excluding testimony that defendant concealed information from the FDA);
12 *Bouchard v. Am. Home Prods. Corp.*, 213 F. Supp. 2d 802, 812 (N.D. Ohio)
13 (same). Because the information Plaintiffs seek is inadmissible and not calculated
14 to lead to admissible evidence, the motion to compel should be denied.

15 **III. THE COURT SHOULD DENY THE MOTION AS TO REQUEST FOR**
16 **PRODUCTION NO. 10.**

17 Plaintiffs fail to show either that Request for Production No. 10 is “relevant
18 and necessary” discovery, as required by the Court’s August 14, 2014 Order Setting
19 Discovery Dispute Protocol (Doc. No. 568 at 3), or that Defendants have not
20 adequately responded to the Request. The request seeks documents in which an
21 employee or “consultant” of a Defendant recommends a “reference” to pancreatic
22 cancer in the Prescribing Information or Medication Guide of Byetta®, Januvia®,
23 Janumet® or Victoza®. To the extent this Request seeks recommendations
24 communicated to the FDA, Defendants produced to Plaintiffs the entire IND/NDA
25 files for their drugs, including all correspondence with the FDA, before this
26 discovery was propounded. There is nothing further to compel.

27 Plaintiffs do not even attempt to explain why they believe any other
28 recommendations “relate to both preemption and general causation,” as they assert

1 in their motion. Pls.’ Mem. at 4. For this reason alone, the motion should be
2 denied. *See Hupp*, 2014 WL 1404510, at *2 (“[T]he moving party...carries the
3 burden of informing the court of ... the relevance of the requested information to
4 the prosecution of his action.”). “Recommendations” are not “actual scientific
5 evidence” about whether the drugs at issue cause pancreatic cancer – and thus are
6 not general causation discovery as the Court defined it on March 25, 2014 and
7 reaffirmed on August 14, 2014. 8/14/2014 Order at 2 (quoting March 25, 2014
8 Order (Doc. No. 377)). Nor do recommendations never communicated to the FDA
9 indicate what the agency “would or would not have done with regards to a proposed
10 labeling change.” 8/14/2014 Order at 2. Thus the Request is likewise improper as
11 preemption discovery.

12 Despite failing to offer any rationale for the request, Plaintiffs complain that
13 Amylin’s response is “insufficient” because it refers Plaintiffs to its custodial
14 productions, which Plaintiffs characterize as an admission Amylin “has *not*
15 performed a Rule 26 investigation.” Pls.’ Mem. at 8 (emphasis in original). On the
16 contrary, Amylin’s (and the other Defendants’) responses comply with the custodial
17 approach to discovery agreed upon by the parties and ordered by the Court. *See*
18 Apr. 21, 2014 Procedures for Production of Electronically Stored Information (Doc.
19 Nos. 414, 415) at 6. As the Court is aware, Defendants have produced custodial
20 files from over 40 custodians in their toxicology, safety, medical, clinical and
21 regulatory departments, culled using very broad search terms defined by Plaintiffs.
22 Defendants properly responded that documents responsive to Request No. 10, if
23 they exist, may be found in these files.³

24 The cases cited by Plaintiffs do not support their claim that Defendants have
25

26 ³ This Court has previously rejected similar complaints from Plaintiffs regarding the
27 scope of employee interviews and references to custodial productions. “They’ve
28 certified they’ve made reasonable inquiry. That is what Rule 26(g) requires, and
they appear to have met that.” Sept. 10, 2014 Hearing Trans. at 27.

1 failed to satisfy their discovery obligations. In *3M Innovative Properties Company*
2 *v. Tomar Electronics*, the court found the defendant’s investigation inadequate
3 because the defendants failed to institute a litigation hold, produced the emails of
4 only a single custodian, and apparently did no electronic searches at all. 2006 U.S.
5 Dist. LEXIS 80571, *16-21 (D. Minn. July 21, 2006). Similarly, in *Brown v.*
6 *Tellermate Holdings Ltd.*, defense counsel failed to interview employees and a
7 vendor to learn about access to an electronically-stored database of sales
8 information and consequently misrepresented the availability of data. *See* 2014
9 U.S. Dist. LEXIS 90123, *6-28, 48-51 (S.D. Ohio July 1, 2014). In contrast to the
10 deficient conduct described in those cases, Defendants identified the key employees
11 most likely to have responsive information, conducted a careful search of their files,
12 and produced responsive documents. Nor have Defendants misrepresented the
13 availability of data. Rather, they maintain that the limited custodial production
14 ordered by the Court does not oblige them to interview thousands of employees and
15 search each of their custodial files.

16 **IV. THE COURT SHOULD DENY THE MOTION AS TO REQUESTS**
17 **FOR INFORMATION ABOUT REGULATORY DISCUSSIONS**

18 In compliance with the Court’s August 14, 2014 Order, Defendants have
19 responded fully to Plaintiffs’ discovery to the extent it relates to communications
20 with the FDA about pancreatic cancer and the drugs at issue in this litigation. In
21 contravention of that same order, Plaintiffs seek to compel information about
22 regulatory discussions and actions relating to adverse effects *other than pancreatic*
23 *cancer* (specifically, “all cancers” and pancreatitis) (Rog. No. 6; RFA Nos. 30-33,
24 36-37) and by bodies *other than the FDA* (RFA Nos. 32-37). Plaintiffs claim that
25 the requests “are likely to produce relevant information that will streamline the
26 proceedings.” Pls.’ Mem. at 9. In fact, the opposite is true.

27 Plaintiffs claim, for example, that information about whether Amylin “is in
28 discussions with the FDA about adding a warning for all cancers” would potentially

1 “call into question Defendants’ contentions about the ‘reasonable evidence’
2 standard.” Pls.’ Mem. at 9. Any possible FDA actions or discussions for warnings
3 regarding “all cancers” (or pancreatitis) would not indicate how the FDA would
4 respond to a proposed warning for *pancreatic* cancer, a pathology distinct from a
5 catchall reference to “all cancers” or pancreatitis. The requested information is
6 therefore irrelevant to the preemption inquiry.

7 Information about labeling discussions with foreign regulatory bodies is even
8 less relevant to preemption.⁴ As courts have repeatedly acknowledged,
9 pharmaceutical regulators outside the United States act in accordance with their
10 own priorities and labeling requirements, tailored to populations and medical
11 practices distinct from those in the United States. *See. e.g., Meridia Prods. Liab.*
12 *Litig. v. Abbott Labs.*, 447 F.3d 861, 867 (6th Cir. 2006) (“American regulators
13 have different priorities and deal with often more diverse populations than their
14 European counterparts.”); *In re: Seroquel Prods. Liab. Litig.*, 601 F. Supp. 2d
15 1313, 1318 (M.D. Fl. 2009) (affirming exclusion of evidence about foreign
16 regulatory action because its meaning can’t be understood without knowledge of
17 the regulatory context); *Doe v. Hyland Therapeutics Div.*, 807 F. Supp. 1117, 1129
18 (S.D.N.Y. 1992) (“The forum whose market consumes the product must make its
19 own determination as to the levels of safety and care required.”); *Harrison v. Wyeth*
20 *Labs.*, 510 F. Supp. 1, 4-5 (E.D. Pa. 1980) (each country makes its own
21 determination about the need for drug warnings, given its unique needs and
22 standards of safety), *aff’d* , 676 F.2d 685 (3d Cir. 1982). Thus labeling decisions or
23 discussions by foreign regulators cannot be used as a proxy for ascertaining how the
24 FDA would treat a proposed pancreatic cancer warning – especially when the FDA

25
26 _____
27 ⁴ Defendants discuss the irrelevance to the preemption inquiry of communications
28 with foreign regulatory agencies at more length in Defendants’ Opposition to
Motion to Compel Against All Defendants for their Communications With or
Related to Foreign Regulatory Agencies (Doc. No. 675) at 6-8.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28

By: /s/ Heidi Levine
Heidi Levine

Attorney for Novo Nordisk Inc.
E-mail: heidi.levine@dlapiper.com

By: /s/ Kenneth J. King
Kenneth J. King

Attorney for Eli Lilly and Company
Email: kingk@pepperlaw.com

