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1 **INTRODUCTION**

2 Plaintiffs served Requests for Production (RFPs) Nos. 39-41, requesting adverse
3 event source documents and databases, on April 8, 2014. Defendants responded on May
4 8-9, 2014. Merck served Amended Responses on June 30, 2014. *See Ex. 1* (Amended
5 Merck RFPs); *Ex. 2* (Amylin RFPs); *Ex. 3* (Lilly RFPs); and *Ex. 4* (Novo RFPs). The
6 parties met and conferred in June-July 2014. *See* Certificate of Compliance with LR 26.1.
7 Plaintiffs require this discovery in order to respond to Defendants’ general causation and
8 preemption defenses, and it is typically produced in cases of this type. Plaintiffs now
9 move to compel its production pursuant to Fed. Civ. P. 37(a), and to recover their costs.

10 **I. ADVERSE EVENT REPORTING – AN OVERVIEW**

11 Plaintiffs seek two things in this motion: the underlying documents for each pre-
12 and post-marketing pancreatic cancer adverse event known to each Defendant; and the
13 adverse event databases maintained by each Defendant. The underlying documents are
14 commonly referred to as adverse event “source files,” or source documents, source data,
15 back-up files, or source documentation.¹ Defendants have objected to these requests as
16 irrelevant and unduly burdensome. However, this information is regularly produced in
17 pharmaceutical litigation, and should have been produced here without objection.

18 Against this background, Plaintiffs offer the following overview of adverse event
19 reporting, source files and databases to provide context for the Court.

20 **A. WHAT IS CONTAINED IN A SOURCE FILE?**

21 All source files, whether pre- or post-marketing, typically include the following
22 types of information: the patient’s relevant medical records; internal comments made by
23 the drug manufacturer about the event; emails to and from the patient’s doctors; notes of
24 phone conversations with the patient’s medical providers; notes regarding any expert
25 review; causal assessments made by the manufacturer as to whether the adverse event
26

27 ¹ Formal definitions of “source data” and “source documentation” are also contained in
28 FDA guidance documents. *See, e.g., FDA Guidance for Industry E6 Good Clinical
Practice: Consolidated Guidance, Ex. 5, p. 7.*

1 was related to its drug, and why; and other similar matters. See **Ex. 5** definitions; **Ex. 6**,
2 Declaration of Ramon Rossi Lopez (Lopez Declaration) at ¶ 8.²

3 **B. WHAT ARE PRE-MARKETING ADVERSE EVENT SOURCE FILES?**

4 A *pre-marketing* adverse event occurs before the drug is approved for sale, most
5 often in connection with clinical trials. Source documents for a pre-marketing adverse
6 event may include communications with the trial investigators and others as to the cause
7 of the event. For example, there may be efforts to determine whether a patient’s adverse
8 event was caused by the study drug, an unrelated accident, or something else entirely.
9 Those efforts should be documented in the patient’s source file. **Ex. 6** at ¶ 6.

10 **C. WHAT ARE POST-MARKETING ADVERSE EVENT SOURCE FILES?**

11 *Post-marketing* adverse events occur “in the real world” after a drug is approved
12 and available for sale. Manufacturers typically report these events to the FDA on a
13 “MedWatch” form. See 21 C.F.R. § 314.80. This is a “summary” form that does not
14 include all of the information about an event. The source files for post-marketing adverse
15 events include all of the underlying documents available to the manufacturer when it
16 prepared its MedWatch summary to send to the FDA. **Ex. 6** at ¶ 7.

17 **D. WHY ARE ADVERSE EVENT SOURCE FILES IMPORTANT?**

18 Source files are important for many reasons. They show what actually happened
19 with an adverse event. It is not uncommon for MedWatch summaries to mischaracterize
20 or misstate important aspects of an event. For instance, a manufacturer’s MedWatch
21 summary may say an event was *not* causally related to its drug, when the source
22 documents (e.g., medical records) show the doctors felt the event *was* caused by the drug.
23 The only way to tell if the MedWatch forms given to the FDA accurately characterize an
24 adverse event is to review the source files for that event. **Ex. 6** at ¶¶ 9, 13.

25 _____
26 ² Source files for *litigants* – like Plaintiffs in this MDL – are usually less informative,
27 since they often contain primarily litigation documents (Complaint, etc.). Communication
28 with a patient’s healthcare providers is restricted while a case is in litigation. Such files
may contain a large number of pages, but often little substance. **Ex. 6** at ¶ 21.

1 Source files also show whether pancreatic cancers were properly reported to the
2 FDA. There are reasons to believe such cancers were not correctly reported, and were
3 underreported. *See, e.g.*, Plaintiff’s Opposition to Defendants’ Preemption Motion (Dkt.
4 No. 443), pp. 20-22, and Part II(E)(2)(a), *infra*. These questions can only be answered by
5 reviewing the source documents for each pancreatic cancer adverse event. **Ex. 6** at ¶ 9.

6 Source files can also show whether “safety signals” have been generated. FDA
7 guidance notes that even one “well-documented” adverse event can be a safety signal.
8 *See Ex. 7* at p. 4. Source files can provide the detailed documentation for those signals.
9 **Ex. 6** at ¶ 9.³ Signal detection leads directly to the assessment of *causal association*.⁴

10 Finally, source documents are also necessarily part of Defendants’ preemption
11 defense. To establish that defense, Defendants must prove by “clear evidence” that the
12 FDA would reject any CBE that fully explained the basis for the proposed warning. *See*
13 *Wyeth v. Levine*, 555 U.S. 555, 571 (2009). Such explanation must include a complete
14 and accurate description of the adverse event data.⁵

15 **E. WHAT ARE ADVERSE EVENT DATABASES?**

16 A manufacturer’s adverse event databases typically serve as repositories for most
17 or all of the source files associated with its drugs. Storing the information electronically
18 in a database makes it readily accessible and easy to search, sort and analyze.
19 Manufacturers use these databases to track the rates of adverse events reported over time,

21 ³ The FDA has already recognized a “signal” for pancreatic cancer with the incretins and,
22 as of its last public statement, it continues to investigate that “signal.” *See Ex. 8*,
23 *Pancreatic Safety of Incretin-Based Drugs – FDA and EMA Assessment*, Vol. 370, New
24 England Journal of Medicine, pp. 794-797, February 2014. Since events appear to have
25 been underreported, the “signal” may be far stronger than the FDA has reason to suspect.

26 ⁴ *See, e.g., Ex. 9* at p. 1: Pfizer’s *What is a Safety Signal?* This document quotes an
27 industry-recognized signal definition by the Council for International Organizations of
28 Medical Sciences (CIOMS), as “information that arises from one or multiple sources ...
which suggests a new, **potentially causal association**[.]” (emphasis added).

⁵ *See, e.g., Glynn v. Merck (In re Fosamax Prod. Liab. Litig.)*, 951 F. Supp. 2d 695, 704-
05 (D.N.J. 2013) (preemption analysis includes whether “Defendant failed to provide all
the information it had on femur fractures [the adverse event at issue] to the FDA”).

1 determine trends in the reporting of adverse events, perform causality assessments, and
2 undertake other analyses relevant to the events. **Ex. 6** at ¶ 10.

3 **F. WHY ARE ADVERSE EVENT DATABASES IMPORTANT?**

4 Adverse event databases are extremely important because they contain Defendants’
5 store of knowledge about their adverse events, and are used to perform tracking, trending,
6 causality assessments and other statistical analyses. These databases, and the important
7 analyses they facilitate, are the primary pharmacovigilance tools used by Defendants to
8 evaluate and explain adverse events. Defendants’ experts can be expected to opine on the
9 contents of the databases and how they work, and to duplicate the analyses done by
10 Defendants. Plaintiffs would be at a huge disadvantage if their experts could not perform
11 (and challenge) the analyses done by the defense. It would be fundamentally unfair to
12 allow Defendants to fight this “information battle” fully armed, while giving Plaintiffs
13 only a fraction of the readily available data used by Defendants. **Ex. 6** at ¶¶ 11, 19.

14 **G. ARE SOURCE FILES AND DATABASES NORMALLY PRODUCED?**

15 Adverse event source files and databases are normally produced for all adverse
16 events at issue in this type of complex pharmaceutical litigation, regardless of where each
17 event arose.⁶ Plaintiffs cannot properly challenge Defendants’ characterizations of this
18 crucial data without the source documents and databases.⁷ **Ex. 6** at ¶¶ 12, 15-19.

19 **II. ARGUMENT**

20 The adverse event discovery sought here is relevant to both general causation and
21 preemption; its production is common in litigation of this type; and producing it will not
22 unduly burden the Defendants. Plaintiffs will first address those matters and then discuss
23 specific information and examples as to each Defendant.

24
25 ⁶ This subject is discussed in Part II(C), *infra*, where many examples of similar cases are
26 listed to show: (a) how common the production of this documentation has become; and
27 (b) how obstructive the Defendants’ position is in the instant case.

28 ⁷ Plaintiffs’ discovery requests also cover pancreatitis, a known risk factor for pancreatic
cancer, but Plaintiffs have limited their request for source files to pancreatic cancers and
other similar classifications (pancreatic neoplasm, tumor, etc.). *See Ex. 6*, ¶ 12.

1 **A. ADVERSE EVENT SOURCE DOCUMENTATION IS RELEVANT**
2 **TO GENERAL CAUSATION**

3 The most pervasive theme in Defendants’ withholding of their adverse event
4 source files and databases has been that adverse events are “irrelevant” to general
5 causation, such that no discovery of them should be allowed.⁸ That argument ignores: (1)
6 this Court’s oral directives and written Orders; (2) sworn testimony from Defendants’
7 own witnesses; (3) FDA guidance; (4) scientific literature; and (5) the substantial weight
8 of other legal authority. Each will be addressed in turn.

9 **1. The Court’s Oral Directives and Written Orders**

10 **Oral – 2/18/14:** The alleged lack of pancreatic cancer signals from Defendants’
11 clinical trials was discussed in open court on February 18, 2014, in the context of general
12 causation. Plaintiffs were concerned that Defendants had improperly excluded cancers
13 from their clinical trials, skewing results and hiding safety signals. After being apprised
14 of this concern, the Court specifically addressed the “**completeness of the clinical and**
15 **other scientific data**” as including “**signal detection related communications or**
16 **documents[.]**” *See Ex. 10*, Transcript of Proceeding, Feb. 18, 2014 (discussion generally
17 at pp. 14-15, 20-22; quoted passages at p. 22) (emphasis added).

18 Adverse event source files and databases are the very building blocks of signal
19 detection, and the FDA has taken great pains to ensure that drug manufacturers
20 vigorously monitor their products to promptly detect and analyze safety signals. *See, e.g.*,
21 21 C.F.R. § 314.80; **Ex. 7** (FDA pharmacovigilance guidance); **Ex. 9** (“What is a Safety
22 Signal?”). Defendants’ fundamental thesis is that the Court must have meant something
23 else when discussing “signal detection.” Plaintiffs submit that this argument renders the
24 Court’s statement meaningless.

25 _____
26 ⁸ *See, e.g.*, **Ex. 1**, Merck RFP No. 39 (“Merck objects to producing source files as ...
27 irrelevant”); **Ex. 2**, Amylin RFP No. 39 (“Adverse event reports are ... of little or no
28 value in this litigation”); **Ex. 3**, Lilly RFP No. 39 (referring Plaintiffs to Amylin for
further production because Lilly’s “collaboration agreement with Amylin ... terminated
in 2011”); **Ex. 4**, Novo RFP No. 39 (“source files for adverse events [are not] relevant”).

1 **Written – 2/18/14:** The Court released its written Order on February 18, 2014,
2 defining general causation discovery as having “**some tendency in logic** to prove or
3 disprove whether Defendants’ [drugs] cause pancreatic cancer.” (Dkt. No. 325 at ¶ 1).

4 Defendants now argue that their source files and databases have “**no tendency in**
5 **logic**” to prove or disprove causation. The FDA would be disappointed to hear that. The
6 entire premise of its pharmacovigilance regulations is that “postmarketing safety data
7 collection and risk assessment based on observational data are *critical* for evaluating and
8 characterizing a product’s risk profile[.]” **Ex. 7**, p. 3 (emphasis added). It is precisely
9 *because* adverse event reports so often give accurate early warning signals on causation
10 that they are so closely monitored. Adverse events alone may not always be sufficient to
11 prove causation, but to say they have *no tendency to prove it* is absurd.⁹

12 **Written – 6/5/14:** The Court’s June 5, 2014 Order on Defendants’ preemption
13 motion (Dkt. No. 472) quoted Plaintiffs’ motion papers, noting that “**source documents**
14 **for adverse event reports**” fall within the “**universe of [relevant] documents and**
15 **information.**” The Court then stated that “Plaintiffs have also alleged instances of under-
16 reporting or misreporting by Defendants to the FDA. Such serious allegations require
17 substantial evidence to support, and **Plaintiffs must have a full opportunity to discover**
18 **it, if indeed it exists.**” *Id.* at p. 5 (emphasis added).

19 To date, Defendants have interpreted “full opportunity” as “no opportunity.” This
20 is causing unnecessary delay, and constantly erodes the parties’ ability to meet the
21 aggressive schedule Defendants themselves proposed. The Court has consistently found
22 this information relevant, and it is. Defendants should now be compelled to produce it.

23 **2. Sworn Testimony from Defendants’ Own Witnesses**

24 Merck witness Linda Hostelley testified during her 30(b)(6) deposition that Merck
25 uses its post-marketing adverse event reports “**in aggregate**” to make “**causality**
26

27 ⁹ To be sure, it is also well recognized that adverse event reports alone “may often be
28 sufficient to assign causality.” **Ex. 11: Postmarketing Surveillance and Adverse Drug**
Reactions: Current Perspectives and Future Needs. JAMA, March 3, 1999; 281:9.

1 **assessments.”** See **Ex. 12** at 60:22-63:17 (“the causality assessments ... are done in
2 aggregate form in the post-marketing arena”). This sworn testimony is flatly inconsistent
3 with Defendants’ assertions that adverse event reports are “irrelevant” to causation.

4 **3. FDA Guidance**

5 FDA guidance provides that even *one* well-documented adverse event can be
6 viewed as a safety signal. See Part I(D), *supra*. Access to source files is very important
7 here because “the quality of the reports is critical for appropriate evaluation of the
8 relationship between the product and adverse events.” **Ex. 7** at p. 4. Again, the Court and
9 the FDA recognize the relevance of safety signal documents. They should be produced.

10 **4. Scientific Literature**

11 Respected scientific journals also readily connect adverse events to causation. For
12 example, the prestigious Journal of the American Medical Association notes that post-
13 marketing surveillance “can be effective in revealing unusual or rare adverse events that
14 occur with the use of medications, **and such reports may often be sufficient to assign**
15 **causality.”** **Ex. 11** (emphasis added). Again, production is warranted.

16 **5. Other Legal Authority**

17 Adverse events are also relevant to general causation when used to support expert
18 opinions under *Daubert*. Such reports are “frequently utilized by experts in rendering
19 scientific opinions and, under *Daubert*, should be considered by the court in assessing the
20 reliability of those opinions.” *In re Phenylpropanolamine (PPA) Products Liab. Litig.*,
21 289 F. Supp. 2d 1230, 1242 (W.D. Wash. 2003), citing *Kennedy v. Collagen Corp.*, 161
22 F.3d 1226, 1228-31 (9th Cir. 1998)(abuse of discretion to exclude expert testimony based
23 in part on review of adverse reaction case reports). See also *McClellan v. I-Flow Corp.*,
24 710 F. Supp. 2d 1092 (D. Ore. 2010), which allowed general causation testimony based
25 in part on a case series study. The court first correctly noted that “while epidemiological
26 evidence is significant and can be helpful, it is not necessary to establish general
27 causation.” *Id.* at 1109. It then permitted expert testimony based in part on the case series,
28 because such data is not “unreliable as a source of expert testimony.” *Id.* at 1113.

1 The vast majority of adverse event reports related to any drug are reported by its
2 manufacturer. The MedWatch summaries manufacturers prepare and submit to the FDA
3 are known to be fraught with error. *See* Part I(D), *supra*. Plaintiffs’ experts require the
4 underlying source files so they have *accurate* information to support their opinions.

5 **B. ADVERSE EVENT SOURCE DOCUMENTATION IS RELEVANT**
6 **TO PREEMPTION**

7 Defendants’ preemption motion was based on an FDA article addressing a “safety
8 signal” arising from “post-marketing reports of ... pancreatic cancer[.]” **Ex. 8**. The FDA
9 continues to investigate that signal, but it did not review the source files. As part of any
10 preemption defense, Defendants must prove they gave the FDA *all* of their material
11 information on the link between their drugs and pancreatic cancer.¹⁰ Plaintiffs reasonably
12 believe, based on past experience (*see* **Ex. 6** at ¶¶ 13-14) and specific problems already
13 found in Defendants’ MedWatch summaries (*see* Part II(E)(2)(a), *infra*), that the source
14 files contain highly material information. They need to review and analyze those files.
15 The requested discovery is therefore also directly relevant to the preemption defense.¹¹

16 The landscape has also changed since the preemption motion was filed. [REDACTED]
17 [REDACTED]
18 [REDACTED]
19 [REDACTED]
20 [REDACTED]
21 [REDACTED]

22 Defendants have objected to providing
23 discovery from outside the United States, but science knows no boundaries. Plaintiffs
24 need to review the source files and databases for adverse events relied upon by Health

25 ¹⁰ *See, e.g., Glynn v. Merck (In re Fosamax Prod. Liab. Litig.)*, *supra* n. 5.

26 ¹¹ *See also* Plaintiffs’ Opposition to Defendants’ Preemption Motion (Dkt. No. 443), pp.
27 20-22, discussing safety signals apparently generated but overlooked for Byetta. Plaintiffs
28 understood the Court’s Order of June 5, 2014 (Dkt. No. 472) to require full discovery on
that matter, and Defendants should now provide it. *See* Part II(A)(1), *supra*.

¹² [REDACTED]
[REDACTED]

1 Canada for the same reason they need to review that information for events relied on by
2 the FDA: the source files contain *safety signal and causation information withheld by*
3 *Defendants from the FDA*. Such information goes to the heart of preemption analysis.¹³

4 **C. ADVERSE EVENT SOURCE DOCUMENTATION IS COMMONLY**
5 **PRODUCED IN CASES OF THIS TYPE**

6 Defendants have forced Plaintiffs to file this motion to obtain discovery commonly
7 provided in litigation of this type.¹⁴ Production of these files is typical; deciding *Daubert*
8 or impossibility preemption motions *without* them would be unprecedented.

9 **D. IT IS NOT UNDULY BURDENSOME FOR DEFENDANTS TO**
10 **PRODUCE ADVERSE EVENT SOURCE DOCUMENTATION**

11 Defendants’ “undue burden” objections are groundless. Manufacturers are required
12 to maintain source files. *See* 21 C.F.R. § 314.80(j). Inspections are conducted to ensure
13 compliance with those regulations. *See Ex. 20*, p.3, sec. 5.¹⁵ This documentation is
14 always at the ready – the only “extra” expense is that of redacting patient and provider
15 identifying information. That process is essentially the same as for review and redaction
16 of all the other documents involved in Defendants’ productions. At most, it is a “burden”
17 akin to the other burdens of litigation, but there is nothing “undue” about it.

18
19 ¹³ A Motion to Compel is being prepared on foreign discovery. That motion has taken on
20 added significance, since it now appears that material aspects of the general causation
21 science around the Defendants’ drugs are being developed outside the United States.

22 ¹⁴ *See, e.g., Ex. 6* (Lopez Declaration: production of *adverse event databases and source*
23 *files in a dozen or more well-known drug and device cases*, at ¶¶ 2, 4, 12 and 15-19); **Ex. 16**
24 (Chantix Discovery Plan: production of *adverse event database*, at p. 7); **Ex. 17**
25 (Fosamax correspondence: Merck’s production of “*source materials underlying adverse*
26 *event reports*” at p. 4); **Ex. 18** (Pradaxa Amended CMO No. 17: production of worldwide
27 *adverse events database* at pp. 2-3); and **Ex. 19** (*Zyprexa correspondence obtained from*
28 *source files produced in the litigation*, as discussed in Lopez Declaration at ¶ 14).

¹⁵ **Ex. 20** is an FDA letter to Pfizer regarding adverse event documentation. It illustrates
Plaintiffs’ point about the *inaccuracy* of the summaries manufacturers prepare for the
FDA (*see* Part I(D), *supra*). As stated in section 5: “*reports were either misclassified or*
downgraded in severity to non-serious without a reasonable justification.” (Emphasis
added.) Hence the importance of reviewing the actual source documents.

1 The undue burden argument also fails because pancreatic cancer is very rare. The
2 FDA adverse event database shows approximately 203 pancreatic cancer adverse events
3 for Merck through Q1 2013; 335 for Amylin; and 206 for Novo (as of October 2013).¹⁶
4 By comparison, source files produced in similar cases often reach the thousands. *See*,
5 *e.g.*, **Ex. 6** (Lopez Declaration) at ¶¶ 15, 17 and 20. Defendants have very few files to
6 review and redact. It will take them very little time and effort to produce those files.¹⁷

7 Finally, normal discovery costs are not unduly burdensome. “Part of the cost of
8 doing business in the United States is the responsibility to respond to the orderly demands
9 of litigation.” *New Medium Technologies LLC v. Barco N.V.*, 242 F.R.D. 460, 469 (N.D.
10 Ill. 2007). This is true of any defendant, but these Defendants are also very large
11 companies making – quite literally – *billions* of dollars from the sale of the very drugs
12 involved in this case.¹⁸ They are not entitled to relief.¹⁹

13 **E. DEFENDANTS SHOULD BE COMPELLED TO PRODUCE THEIR**
14 **ADVERSE EVENT SOURCE FILES AND DATABASES**

15 Plaintiffs have laid out their arguments on relevance and burden above, and will
16 not repeat them here. This section will address: (1) the information Defendants have
17 produced; (2) why that information is insufficient; (3) other issues raised by Defendants;
18 and (4) what additional information they should be required to provide.

19
20 ¹⁶ Byetta reporting is entirely covered by Amylin, so there are none for Lilly.

21 ¹⁷ For further perspective, Defendants have now produced over 19 million pages in this
22 MDL, with significant redactions. They know how to review and redact on a large scale,
23 and can easily adapt those skills to a few hundred adverse event files.

24 ¹⁸ For illustrative purposes, *see, e.g.*, **Ex. 21**, an article hailing “Merck & Co.’s Januvia
25 diabetes franchise” as “the most successful prescription drug to be launched since 2006,
26 [generating] global sales of **\$5.7 billion** in 2012.” \$5.7 billion per year equates to over
27 \$15.6 million *per day* – and that is only *one* of the Defendants. Article available at:
28 <http://www.forbes.com/sites/simonking/2013/10/03/the-numbers-behind-the-job-cuts-5-reasons-why-merck-co-was-forced-to-wield-the-axe/>.

¹⁹ *See, e.g.*, **Ex. 22** (Pretrial Order No. 24 in the AMS Pelvic Mesh Litigation), at p. 5
 (“product liability litigation is a modern cost of doing business,” and defendant doing
 “billions of dollars in sales” is not entitled to protection from those costs).

1 **1. What Information have Defendants Provided?**

2 Defendants produced their MedWatch summaries given to the FDA, and limited
3 “extractions” from their safety databases. Plaintiffs understand that each Defendant’s
4 safety database is the primary location of its pancreatic cancer adverse event source files.

5 Defendants did not produce their pancreatic cancer adverse event source files, and
6 did not produce full and functional versions of their safety databases.

7 **2. Why is the Information Provided by Defendants Insufficient?**

8 The information produced to date is insufficient because it does not provide the
9 source files and databases essential to Plaintiffs’ analysis of several important issues.

10 a. Resolving “known problems” with adverse event reports

11 Plaintiffs cannot track down “known problems” with adverse event reports without
12 the source files. [REDACTED]

13 [REDACTED]

14 [REDACTED]

15 [REDACTED]

16 [REDACTED]

17 [REDACTED]. See Ex. 12 (Hostelley Dep.

18 Tr.) at 229:24-231:3; 232:14-25; 238:9-241:9, referring to Ex. 23-24.²⁰ Merck will know

19 _____

20 ²⁰ Plaintiffs are not trying to single out Merck [REDACTED]

21 [REDACTED]:

22 • [REDACTED]

23 [REDACTED]

24 [REDACTED]

25 [REDACTED]

26 [REDACTED]

27 [REDACTED]

28 [REDACTED]

[REDACTED]

1 the “true story” behind these exhibits within minutes of receiving this brief, because its
2 experts can (and will) query Merck’s database when the issue is brought to their
3 attention. Plaintiffs and their experts must be able to do the same. This is important in any
4 pharmaceutical litigation, but extremely important here, since the rarity of pancreatic
5 cancer makes finding (or losing) a cancer event statistically very significant.

6 Other “known problems” are discussed in Plaintiffs’ Opposition to the Preemption
7 Motion (Dkt. No. 443) at pp. 20-22. [REDACTED]

8 [REDACTED]
9 [REDACTED]
10 [REDACTED]
11 [REDACTED]²¹ How those matters
12 affected the clinical trial results and the analysis of safety signals is still unknown, and
13 requires discovery of the underlying source files.

14 b. Detecting “unknown problems” with adverse event reports

15 Many MedWatch summaries appear completely normal. That does not mean they
16 are *accurate*. A MedWatch may completely ignore or misstate what actually occurred.²²
17 Plaintiffs have no way of knowing about such problems until they review the source files.

18 c. Database “extractions” are not sufficient

19 The database extractions produced by Defendants do not provide the information
20 Plaintiffs need. Each Defendant’s extraction is somewhat different, but in general terms,
21

22 [REDACTED]
23 [REDACTED]
24 [REDACTED] Without an opportunity to review the source
files, Plaintiffs can neither verify nor challenge causality.

25 ²¹ The Restaino and Moskow declarations and exhibits have been re-filed under seal
because they were removed from the record by the Court’s June 5, 2014 Order (Dkt. No.
26 472, p. 7), and they provide necessary support for this discovery motion. *See Ex. 28-29.*

27 ²² There is a dramatic example of this from the Zyprexa litigation, where the source files
for an otherwise unremarkable adverse event report showed the manufacturer had
28 incorrectly coded a doctor’s letter as reporting only *one* adverse event, when it had
actually reported *eight*. *See Ex. 6* (Lopez Declaration) at ¶ 14, and *Ex. 19*.

1 Plaintiffs cannot tell whether all tables and fields in the database, containing all relevant
2 information for each pancreatic cancer event, are contained in the extraction.

3 Using Merck again as an example, in other cases it has simply deleted the database
4 fields with personal identifiers and produced a non-proprietary form of its native database
5 in a way that made it as functional for Plaintiffs as it was for Merck. For this MDL,
6 Merck instead deleted personal data and then unilaterally chose information to extract in
7 a *non-native format* (Access). Even if Merck said all the pertinent data were there,
8 Plaintiffs would justifiably question whether the extraction would provide their experts
9 with the same sorting, analytical and other capabilities that Merck’s experts will have.

10 This is an easy problem to solve. The courts recognize the importance of providing
11 both sides with the same tools, and have fashioned production Orders to that effect.²³

12 d. Fairness

13 Withholding the source files and databases gives Defendants an enormous
14 advantage they do not deserve. Their failure to produce this highly probative evidence,
15 while seeking a fast track to preemption and *Daubert* motions, indicates they know that
16 their source data does not match the hand-crafted summaries they provided to the FDA.
17 Plaintiffs need the source files and databases to moot the controversy about adverse event
18 reporting: *both sides* will then know who said what; when it was said; what the
19 Defendant did to investigate or follow up on it; and how all of that information was
20 summarized for the FDA. Defendants’ staggering information advantage will be erased.

21 As matters now stand, Defendants are saying “trust me,” and Plaintiffs are forced
22 to take them at their word. That is unfair. Adverse event reporting errors are common in
23 pharmaceutical litigation. *See* Part I(D). Not only is it *unwise* to trust an opponent that
24 has a multi-billion-dollar incentive to shade the data in its favor, it is also *unnecessary*.
25 The source data is readily available and should be produced.

26
27 ²³ *See, e.g., Ex. 18* (Pradaxa Amended CMO No. 17) at pp. 2-3. Plaintiffs have used the
28 Pradaxa Order as the basis for their Proposed Order in this matter, but would agree to
other methods that put Plaintiffs and Defendants on a level playing field.

1 e. Importance

2 The need for adverse event source files and databases is compelling here because
3 pancreatic cancer is very rare. Switching even *one* pre-marketing pancreatic cancer or a
4 few post-marketing cancers from “unrelated” to “related” has a large statistical impact.

5 **3. What Other Issues Have Been Raised by Defendants?**

6 a. Merck’s offer to produce Plaintiffs’ source files

7 Merck offered to produce Plaintiffs’ source files without redacting privacy data, so
8 its costs would be low. Merck also proposed that Plaintiffs would have to pay for any
9 further source files unless they articulated a basis for production that was acceptable to
10 Merck. Merck did not explain what it would consider to be acceptable.

11 From Plaintiffs’ perspective this was not a meaningful offer. First, the Plaintiffs’
12 source files can be expected to contain largely litigation documents because a defendant’s
13 communications with a plaintiff’s doctors are restricted in litigation. *See* n. 2, *supra* p. 2.
14 Second, obtaining only a subset of Merck’s source files is of little value because Merck
15 performs adverse event causality assessments *only in the aggregate*. *See Ex. 12*
16 (Hostelley Dep. Tr.) at 55:5-58:8; 61:4-17. Plaintiffs need *all* of Merck’s source files in
17 order to verify *any* of its causality assessments. Third, Merck’s relevance and undue
18 burden objections appeared meritless, such that Plaintiffs were being asked to pay for
19 something they were clearly entitled to, and that Merck was clearly obligated to pay for.²⁴

20 b. Merck’s proposed charges for producing source files

21 Merck had estimated the value of its attorney time for producing adverse event
22 source files at “between \$280,000 and \$400,000.”²⁵ At that time, Merck was estimating

23
24 ²⁴ Defendant Novo recently joined in Merck’s proposal to produce only the Plaintiffs’
25 adverse event source files, and require Plaintiffs to pay for the rest. *See Ex. 30* (email of
26 July 30, 1014 from Novo attorney Heidi Levine to Plaintiffs’ attorney Mike Johnson).

27 ²⁵ This estimate was prepared in March, when Merck and Plaintiffs were exchanging
28 drafts of a motion on this subject. *See Ex. 31* (Declaration of Erica Smith-Klocek, Esq.).
The motion was tabled after Defendants successfully moved to have Plaintiffs re-issue
“general causation” discovery. Given the vital role that adverse event discovery now
plays in this litigation, the motion has been expanded to cover all Defendants.

1 costs for pancreatitis as well as pancreatic cancer, which greatly inflated the estimate. To
2 the extent that Merck continues to rely on that estimate, it is inappropriate.

3 **4. What Should Defendants be Compelled to Provide?**

4 Defendants should be compelled to produce their safety databases as requested in
5 RFP No. 39, so Plaintiffs' experts have access to their contents and capabilities. As noted
6 above, the Pradaxa litigation serves as an example of how this can be done. *See Ex. 18*
7 (Pradaxa Amended CMO No. 17) at pp. 2-3. Defendants should also be compelled to
8 provide their adverse event source documentation as requested in RFP Nos. 40-41, to the
9 extent that documentation is not included in their databases.²⁶

10 **III. SANCTIONS**

11 This is not a battle Plaintiffs should have had to fight. Defendants argued for an
12 expedited schedule while withholding crucial evidence regularly produced in cases of this
13 type. Withholding production has made it inordinately difficult, if not impossible, for
14 Plaintiffs to work within the aggressive schedule Defendants requested. They should not
15 be allowed to profit by intentionally delaying discovery until Plaintiffs have no time left
16 to use it. Plaintiffs request an award of their fees and costs incurred in having to bring this
17 motion, pursuant to Fed. R. Civ. P. 26(g)(1)(B), 37(a)(3)(B)(iv) and 37(a)(4).

18 **IV. CONCLUSION**

19 Plaintiffs respectfully request that Defendants be compelled to produce their
20 adverse event safety databases as requested in RFP No. 39, in such a way that Plaintiffs
21 have access to the contents and capabilities of those databases on equal footing with
22 Defendants. To the extent that any of their adverse event source documentation is not
23 included in their safety databases, Defendants should also be compelled to produce that
24 documentation as requested in RFP Nos. 40-41.

25
26
27 ²⁶ Defendants Amylin and Lilly have been grouped together for purposes of this motion
28 because Lilly has transitioned its Byetta activities to Amylin, with "minor exceptions not
material here." *See Ex. 3*, Lilly RFP Nos. 39-41; and *Ex. 2*, Amylin RFP Nos. 39-41.
Plaintiffs do not care who provides the Byetta discovery, as long as they obtain it.

1 DATED: August 12, 2014

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CERTIFICATE OF SERVICE

I hereby certify that on August 12, 2014, I caused the above document to be filed via the CM/ECF system for the Southern District of California, and the CM/ECF system served the same upon all registered users at their registered email addresses.

s/Michael K. Johnson

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