Joseph Glenmullen M.D.
Addendum to Cymbalta Withdrawal
General Causation Report
May 11, 2015

In addition to the documents identified in my general causation report, I have reviewed and will be prepared to testify about the documents listed in the attached index, which support the opinions set forth in my general causation expert report, i.e.:

- Cymbalta causes a high frequency of withdrawal reactions, which can be severe and long-lasting;
- Lilly's failure to use a withdrawal symptom checklist resulted in lower reported rates of withdrawal;
- The rate of withdrawal is, accordingly, likely much higher than those found in studies that recorded discontinuation adverse events;
- Cymbalta is one of the worst offenders when it comes to antidepressant withdrawal;
- The Cymbalta label is inadequate in light of the Cymbalta clinical trials where discontinuation adverse events were recorded;
- One of the biological mechanisms that causes withdrawal is down-regulation, which explains, in part, some of the long-lasting adverse reactions;
- Withdrawal is an important factor in conducting a risk benefit analysis related to antidepressants;
- Lilly promoted its antidepressant Prozac as causing less withdrawal reactions than other antidepressants because of its comparatively long half-life;
- In addition, in clinical trials comparing duloxetine and venlafaxine, the overall withdrawal rates were not statistically significantly different;
- The Cymbalta label omitted data concerning tapering off of Cymbalta obtained from Lilly's clinical trials.

Joseph Glenmullen, M.D.

CYMBALTA DOCUMENTS INDEX

1.	HMAQ (MDD), protocol, design, DEAE/DESS data
2.	HMAT (MDD), study overview, DEAE/DESS data
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4.	HMAV (DPNP), protocol, design, DEAE/DESS data
5.	HMAY (MDD), protocol, DEAE/DESS data
6.	HMBC (MDD), protocol, DEAE/DESS data
7.	HMBH (MDD), study overview, DEAE/DESS data
8.	HMBR (GAD), draft protocol, overview and DEAE/DESS data a) CYM-01813090 (12/17/2009 Perahia email)
9.	HMBU & HMCQ Combo DESS Data (MDD), DEAE/DESS data
10.	HMBU (MDD), protocol, DEAE/DESS data a) CYM-01780901 (10/23/02 Brannan email)
11.	HMBV (MDD), protocol, DEAE/DESS data
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15.	HMCV (MDD), protocol, DEAE/DESS data
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18.	HMDT (GAD), study overview, DEAE/DESS data
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20.	HMDV (GAD), protocol, DEAE/DESS data
21.	HMEN (Lower Back Pain), protocol, DEAE/DESS data
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25.	HMGC (Lower Back Pain), protocol, DEAE/DESS data
26.	SBBR (SUI), study overview, DEAE/DESS data
27.	SBBT (SUI), study overview, DEAE/DESS data
28.	SBBU (SUI), study overview, DEAE/DESS data
29.	Clinical Trials Chart – Attachment A – Interrogatory 21 and RFP 61 a) Lilly response to Interrogatory 21 b) Lilly response to Request for Production 61 c) Herrera/Hexum – Lilly responses to Request for Production 126, 100, 139 d) Herrera/Hexum – Lilly response to Interrogatory 11
30.	CYM-02783656-CYM 02783709 5/3/02 Duloxetine CELE© for Depression U.S. Launch: Psych's and PCP's
31.	CYM-02783967-02783995 7/2002 Cymbalta Discrete Choice Model Summary
32.	CYM-02783884-02783953 7/8/02 Duloxetine/Cymbalta Discrete Choice Study
33.	CYM-02786215-02786331 8/2/02 Eli Lilly & Co. Cymbalta US Strategic Pricing Study

34.	CYM-02784114-02784271 8/17/04 Cymbalta Patient Segmentation Study
35.	CYM-02785859-02785913 Executive Summary
36.	CYM-02212693-698 8/17/11 Zhang email re FDA request
37.	CYM-01868698 Cymbalta Supportive Optional Document to the Duloxetine Core Data Sheet Pre-Read Based on Clinical Trial Data in the Adult Population Data from April 2010 through October 2011
38.	CYM-02806828-829 5/5/08 Detke email re Withdrawal scale for Duloxetine
39.	CYM-01873412-413 6/25/08 Perahia email re 20 mg rationale
40.	CYM-02784272-02784352 1/5/06 Cymbalta Data Impact Test with PCP's
41.	CYM-01797201-017972049 10 November 2006 Summary of the Minutes of the Cymbalta National Advisory Board
42.	CYM-01862937-01862975 6/7/07 Duloxetine Clinical Answers
43.	CYM-01876671-676 1/31/08 Crucitti email re EU GAD regulatory question
44.	CYM-02053036 3/8/07 FDA memorandum to Tom Laughren re DMETS Medication Error Postmarketing Safety Review
45.	CYM-01932483-486 AMDP-5
46.	CYM-00145366-367 HMBU TEAE by AMDP
47.	CYM-00149293-294 HMCQ TEAE by AMDP
48.	CYM-00149596-602 HMCQ & HMCQ TEAE by AMDP
49.	CYM-01955578-590 Duloxetine Discontinuation Symptoms
50.	CYM-01780878-881 2/16/12 Chang email re Duloxetine AE report
51.	CYM-01780901-905 10/23/2002 Brannan email re HMBU: Taper period
52.	CYM-02363882-885 9/17/06 Stephens email re Follow-up on the PLR meeting – tapering
53.	CYM-01780840-843 8/28/08 Crucitti email re abrupt vs taper discontinuation-treated patients and attachments
54.	CYM-01816937-938

	10/2/06 Perahia email re inner tension, a Cymbalta AE?
55.	CYM-00062115-136 WebMD website
56.	CYM-01866789-828 The Market and Competition for Cymbalta
57.	CYM-01725885-991 Cymbalta US, BC III, September 16th, 2008
58.	CYM-01725351-413 Cymbalta 2010 Lilly USA, LLC Brand Council III September 2, 2009
59.	Declaration of Sarah L. Helgeson and Exhibits 1-11 to declaration (Medical Information Letters)
60.	3/19/2015 letter from Lilly's counsel to R. Brent Wisner
61.	Fava, "Prospective Studies of Adverse Events Related to Antidepressant Discontinuation," J. Clin Psych 2006;67 (suppl 4)
62.	Allgulandar, "Pharmacotherapy of generalized anxiety disorder: results of duloxetine treatment from a pooled analysis of three clinical trials," Current Medical Research and Opinions, Vol. 23, No. 6, 2007, 1245-1252
63.	Boulenger, "Efficacy and safety of vortioxetine (Lu AA21004), 15 and 20 mg/day: a randomized double-blind, placebo controlled, duloxetine-referenced study in the acute treatment of adult patients with major depressive disorder," Intl Clin Psychopharm, 2014, Vol 29 No. 3
64.	Newman, "A Black-Box Warning for Antidepressants in Children?" NEJM, October 14, 2004, 1595-1598
65.	Spielmans, "A Case Study of Salami Slicing: Pooled Analyses of Duloxetine for Depression," Psychotherapy and Psychosomatics, 2010; 79:97-106
66.	Spielmans, "Duloxetine Does Not Relive Painful Symptoms in Depression: A Meta-Analysis," Psychotherapy and Psychosomatics, 2008;77:12-16
67.	Turner, "Selective Publication of Antidepressant Trials and its Influence on Apparent Efficacy," NEJM, January 16, 2008, 358;3, 252-260
68.	Hyman, "Initiation and Adaptation: A Paradigm for Understanding Psychotropic Drug Action," Am J Psych 153:2, February 1996
69.	Blier, "Physiologic Mechanisms Underlying the Antidepressant Discontinuation Syndrome," J Clin Psych 2006; 67 (suppl 4)
70.	Richelson, "Pharmacology of Antidepressants," Mayo Clin Proc. 2001;76:511-527
71.	Maund et al. "Benefits and harms in clinical trials of duloxetine for treatment of major depressive disorder: comparison of clinical study reports, trial registries, and publications," BMJ, 2014 Jun 4;348:g3510.