Ⓟ Zyprexa

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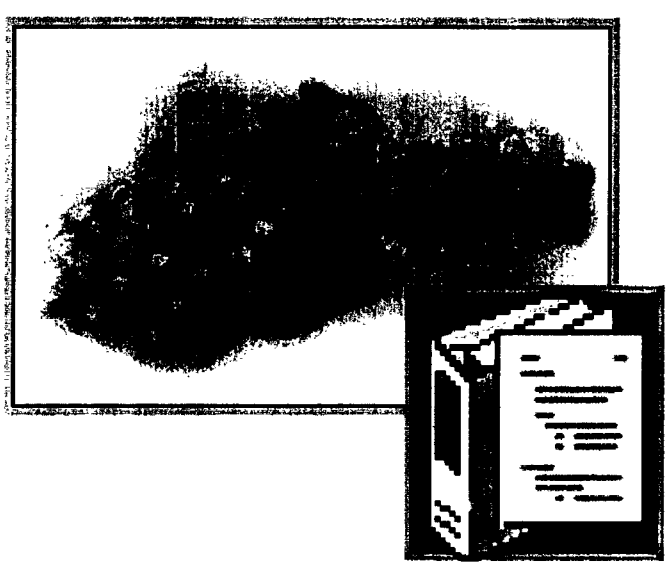
CENSUS OF SPONTANEOUS REPORTS FOR OLANZAPINE DURING THE FIRST TWO YEARS OF MARKETING (9/27/96 TO 9/30/98)



Ken Hornbuckle, DVM, MPH, PhD
Man Fung, M.D., F.A.C.P.

Worldwide Pharmacovigilance and Epidemiology
Eli Lilly and Company

ZY 8032 313

Greg.

This is a report of the first two years of Olanzapine post-marketing safety. I hope you find it interesting and useful.

Thanks!

Edmundo

EXECUTIVE SUMMARY

As of September 30, 1998, the worldwide patient exposure for olanzapine was estimated at 1,773,000 patients. During the first two years of marketing, a total of 7,246 spontaneous reports were received and entered into the Clintrace database. This is equal to an overall reporting rate of 409 reports per 100,000 patients. Of these reports, 1,536 (21%) were serious and 5,710 (79%) were non-serious. Serious is defined by regulatory guidelines to refer to any adverse event which meets any of the following criteria: 1) resulted in death, 2) life-threatening, 3) permanently disabling, 4) required or prolonged inpatient hospitalization, 5) resulted in a congenital anomaly, 6) resulted in cancer, or 8) other reasons serious. The reporting rate of serious and non-serious reports were 87 per 100,000 and 322 per 100,000, respectively.

The purpose of this report is to summarize the safety profile of olanzapine during the first two years of marketing. The report reviews all post-marketing or spontaneous adverse event reports. The safety data are presented in two parts:

1) Part A shows the reporting rates for specific events of interest (i.e., Death, Hematologic, Hepatic, and Hyperglycemia), while adjusting by patient exposure;

2) Part B shows the gross number (i.e., census) of reports received by body systems and events. Please note due to time and resource restraint, the data presented are only raw number and have not been adjusted for patient exposure like Part A.

To obtain the data for this 2-year report, the Clintrace database was searched for spontaneous adverse event reports entered from September 27, 1996 through September 30, 1998. In Part A, reporting rates were computed specially for death, hematologic, hepatic, and hyperglycemia reports. Each of these four categories of events are defined as follow:

1. Death - refers to all reports with death as an outcome.
2. Hematologic - refers to all reports with the following COSTART terms - aplastic anemia, pancytopenia, marrow depression, blood dyscrasia, agranulocytosis, leukopenia, thrombocytopenia, anemia, macrocytic anemia and hypochromic anemia
3. Hepatic - refers to all reports with the following COSTART terms - SGPT increased, SGOT increased, liver function test abnormal, hepatitis, hepatic coma, hepatic failure, liver necrosis, liver damage, liver tenderness, liver fatty deposit and hepatomegaly
4. Hyperglycemia - refers to all reports with the following COSTART terms - hyperglycemia, diabetes mellitus, diabetic acidosis, diabetic coma, ketosis and glucose tolerance decreased

Two types of reporting rates were used in this report for Part A. These were the cumulative and adjusted reporting rates. The cumulative reporting rate was defined as the cumulative number of adverse event reports divided by the cumulative patient exposure estimate. The cumulative reporting rate was computed for each quarter of marketing. For the adjusted reporting rate, the numerator was the number of adverse event reports received in each quarter of marketing. The

denominator was the difference between 1) the estimated patient exposure in a particular quarter and 2) the estimated patient exposure in the previous quarter.

For the reporting rate, the mean and 95% confidence intervals were computed. The lower confidence limit was referred to as LCL, while the upper confidence limit was UCL.

Part B shows the number of adverse event reports by body systems and major adverse events. Many of these groupings were defined by a selected number of COSART terms. An important feature of these groupings is the unduplicated number of reports. Since many patients experience multiple adverse events, the unduplicated number of reports only counts a patient once in a particular grouping. This reflects the approximate number of cases in a particular body system or event condition.

Overall, as can be seen from the data presented, the trends of adverse safety events received are quite stable and in fact are on a downward course for several of the specific events of interest. A careful review of these data over the past 2 years does not show any unusual trend or clinically significant increase in frequency of events reported. Thus, the data presented within this report are consistent with prior cumulative data and the safety profile of olanzapine continues to be reassuring.

PART A - REPORTING RATES

Table A. Cumulative Number of Reports and Cumulative Reporting Rate for Specific Adverse Event Reports, Olanzapine, Spontaneous Reports

Quarter**	1. Mortality		2. Hematologic		3. Hepatic		4. Hyperglycemia		Cumulative Worldwide Patient Exposure (Estimated)
	Number of Reports	Reporting Rate*	Number of Reports	Reporting Rate*	Number of Reports	Reporting Rate*	Number of Reports	Reporting Rate*	
Q1	11	9.7	22	19.5	19	16.8	6	5.3	113,000
Q2	46	16.4	67	23.9	58	20.7	28	10.0	280,000
Q3	77	16.2	109	23.0	106	22.4	49	10.3	474,000
Q4	109	15.8	143	20.8	156	22.7	78	11.3	688,000
Q5	138	14.8	174	18.6	194	20.8	113	12.1	933,000
Q6	180	15.1	209	17.5	240	20.1	138	11.6	1,194,000
Q7	221	15.0	237	16.1	281	19.1	172	11.7	1,472,000
Q8	253	14.3	279	15.7	322	18.2	194	10.9	1,773,000
Mean (sd)	---	14.7 (2.1)	---	19.4 (3.0)	---	20.1 (2.0)	---	10.4 (2.2)	---

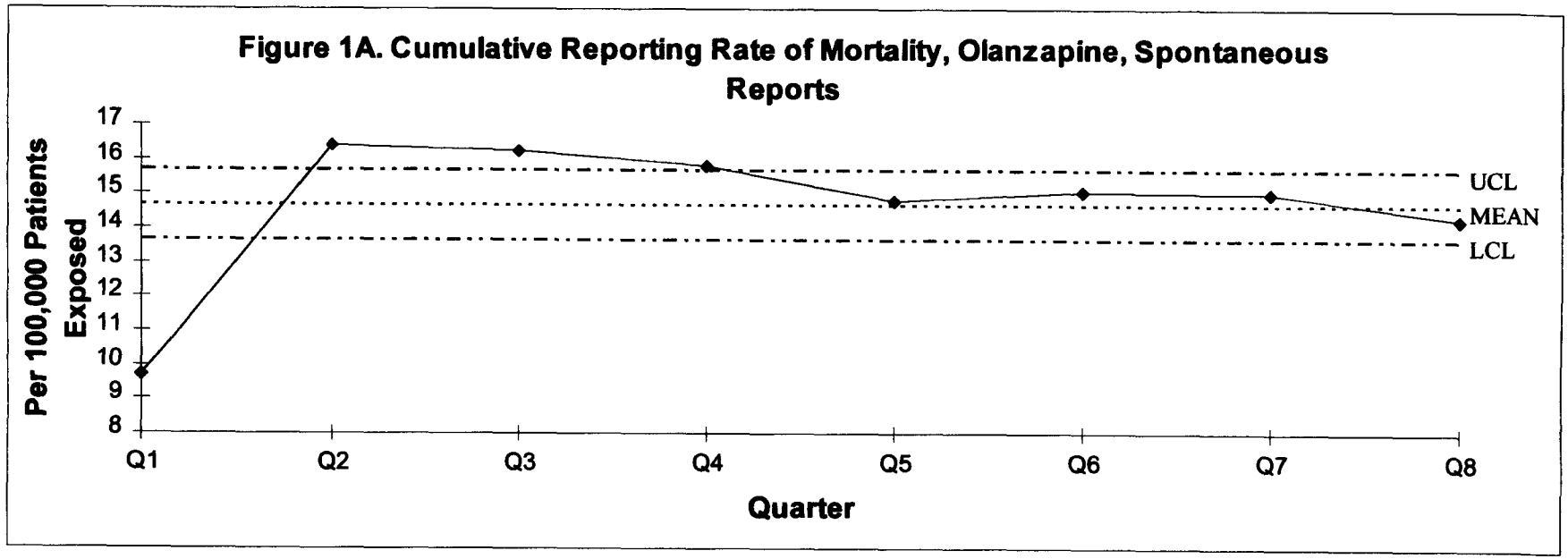
* Cumulative reporting rate per 100,000 patients exposed

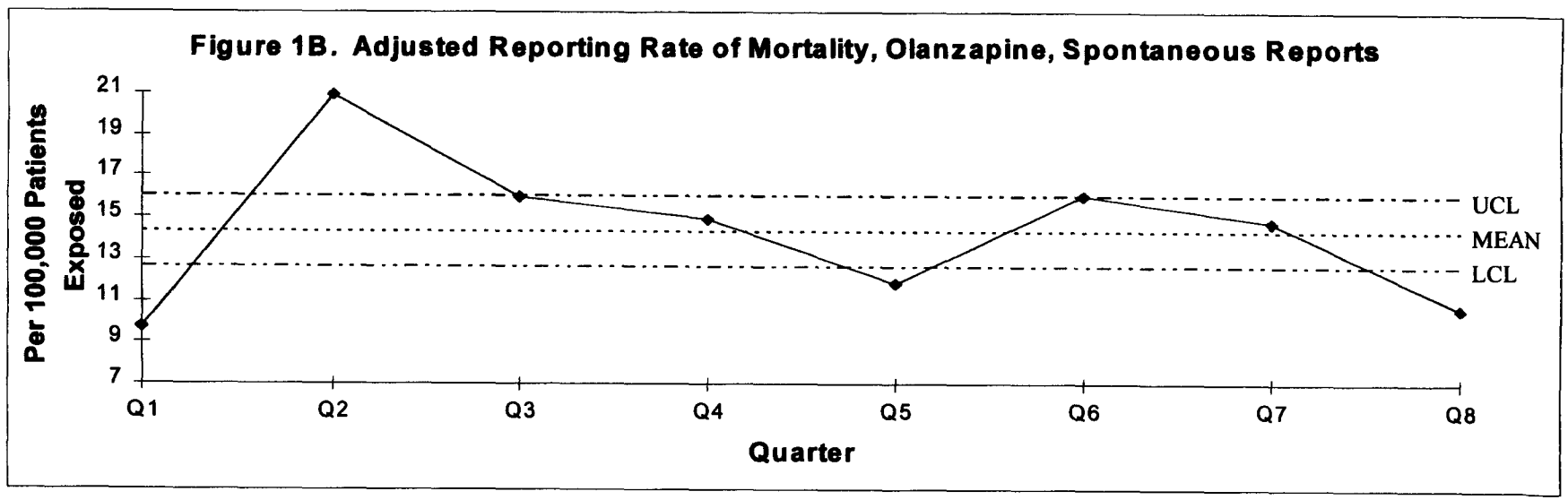
Table B. Number of Reports and Adjusted Reporting Rate for Specific Adverse Event Reports, Olanzapine, Spontaneous Reports

Quarter**	1. Mortality		2. Hematologic		3. Hepatic		4. Hyperglycemia		Adjusted Worldwide Patient Exposure (Estimated)
	Number of Reports	Reporting Rate*	Number of Reports	Reporting Rate*	Number of Reports	Reporting Rate*	Number of Reports	Reporting Rate*	
Q1	11	9.7	22	19.5	19	16.8	6	5.3	113,000
Q2	35	21.0	45	26.9	39	23.4	22	13.2	167,000
Q3	31	16.0	42	21.6	48	24.7	21	10.8	194,000
Q4	32	15.0	34	15.9	50	23.4	29	13.6	214,000
Q5	29	11.8	31	12.7	38	15.5	35	14.3	245,000
Q6	42	16.1	35	13.4	46	17.6	25	9.6	261,000
Q7	41	14.7	28	10.1	41	14.7	34	12.2	278,000
Q8	32	10.6	42	14.0	41	13.6	22	7.3	301,000
Mean (sd)	---	14.4 (3.6)	---	16.8 (5.6)	---	18.7 (4.4)	---	10.7 (3.2)	---

* Adjusted reporting rate per 100,000 patients exposed

MORTALITY





HEMATOLOGIC

Figure 2A. Cumulative Reporting Rate of Hematologic, Olanzapine, Spontaneous Reports

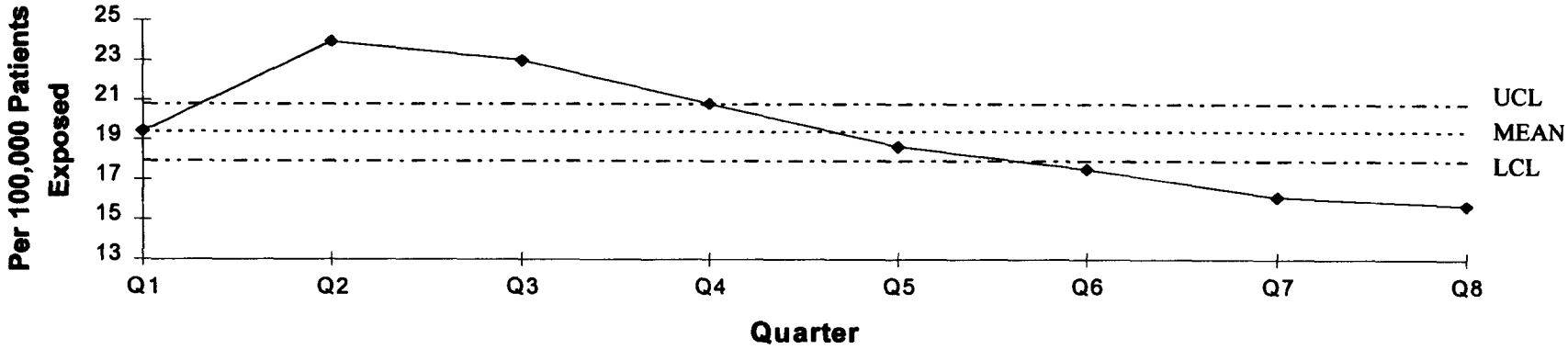
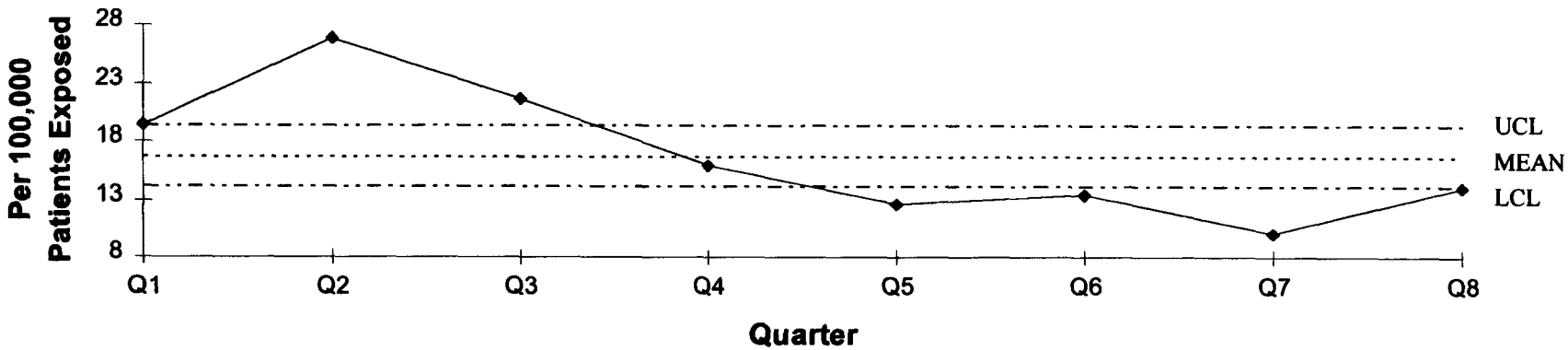
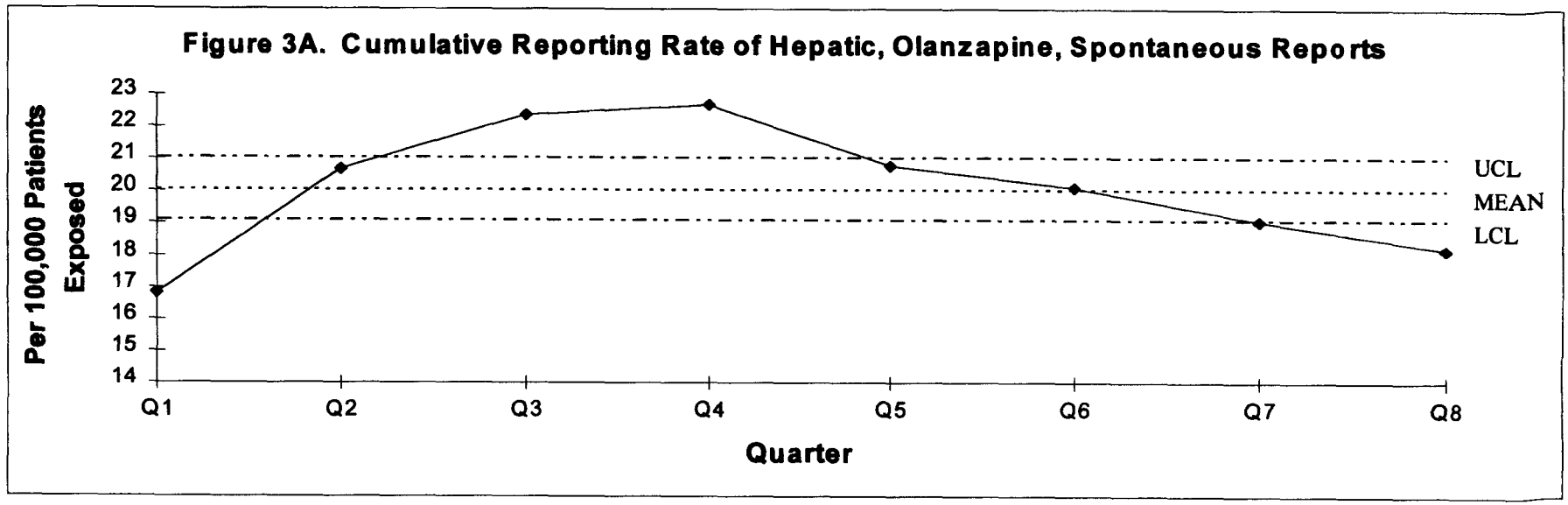
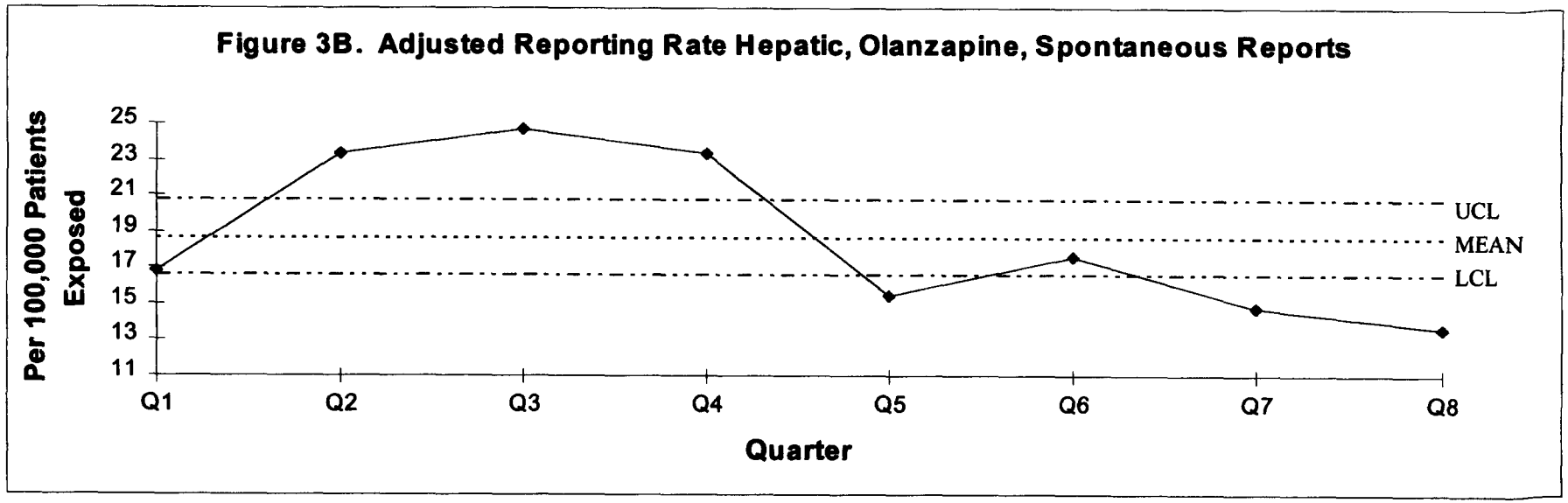


Figure 2B. Adjusted Reporting Rate of Hematologic, Olanzapine, Spontaneous Reports



HEPATIC





HYPERGLYCEMIA

Figure 4A. Cumulative Reporting Rate of Hyperglycemia, Olanzapine, Spontaneous Reports

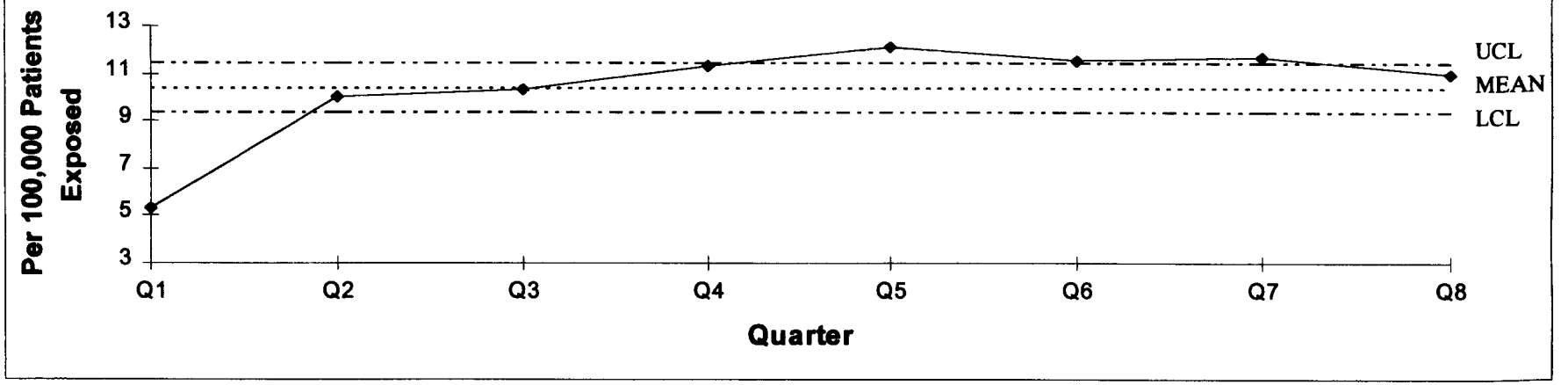
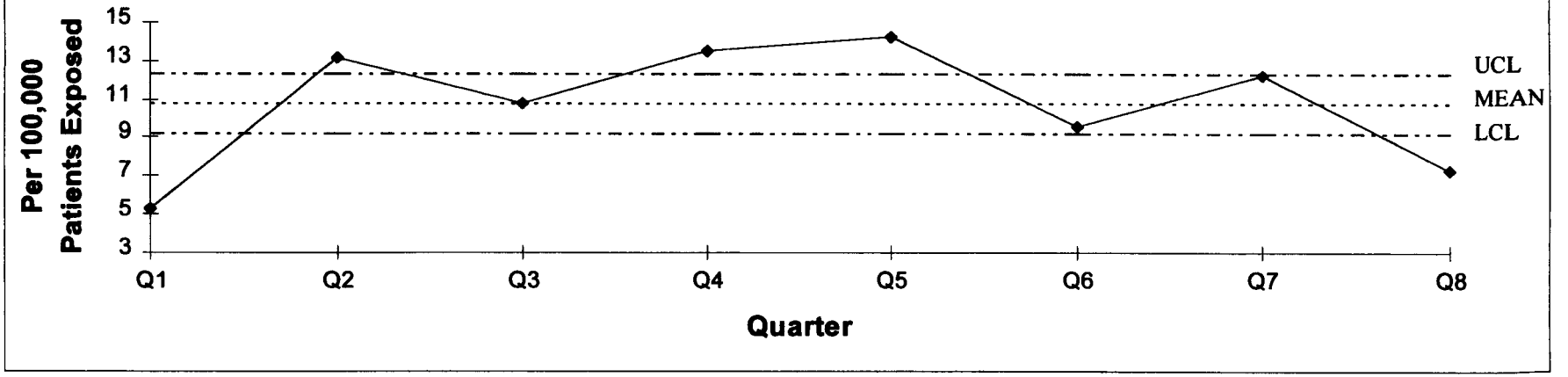


Figure 4B. Adjusted Reporting Rate of Hyperglycemia, Olanzapine, Spontaneous Reports



PART B. NUMBER OF REPORTS

CENSUS OF ADVERSE EVENTS FROM CLINTRACE DATABASE, OLANZAPINE, SPONTANEOUS REPORTS

EVENT	Q1-2*	Q3-4*	Q5-6*	Q7-8*	TOTAL
CARDIOVASCULAR					
I. Conduction					
Atrial Fibrillation	3	4	2	2	11
Atrial Flutter	0	1	0	0	1
Supraventricular Tachycardia	0	3	2	2	7
Unduplicated Reports	**3**	**8**	**4**	**4**	**19**
AV Block	1	0	1	0	2
AV Block 2nd Degree	1	0	0	0	1
Bundle Branch Block	1	2	2	2	7
Heart Block	0	1	0	0	1
Bradycardia	8	8	6	6	28
Sinus Bradycardia	0	1	0	1	2
Unduplicated Reports	**11**	**12**	**9**	**8**	**40**
Ventricular Fibrillation	1	0	0	1	2
Ventricular Tachycardia	1	1	1	0	3
Ventricular Extrasystole	1	2	1	0	4
Extrasystoles	0	1	1	0	2
Heart Arrest	8	6	7	8	29
QT Interval Prolonged	1	5	0	3	9
Unduplicated Reports	**11**	**14**	**10**	**10**	**45**
Arrhythmia	6	4	6	6	22
Extrasystoles	0	1	1	0	2
Palpitation	4	5	2	8	19
EKG Abnormal	5	5	10	8	28
Unduplicated Reports	**15**	**15**	**18**	**22**	**70**

* Q1-2 represents 9/27/96 - 3/31/97; Q3-4 represents 4/1/97 - 9/30/97
Q5-6 represents 10/1/97 - 3/31/98; Q7-8 represents 4/1/98 - 9/30/98

CENSUS OF ADVERSE EVENTS FROM CLINTRACE DATABASE, OLANZAPINE, SPONTANEOUS REPORTS

EVENT	Q1-2*	Q3-4*	Q5-6*	Q7-8*	TOTAL
CARDIOVASCULAR (Continue)					
II. Coronary Disease					
Myocardial Infarction	4	4	5	4	17
Myocardial Ischemia	0	0	0	1	1
Cardiovascular Disorder	4	1	6	3	14
Coronary Artery Disorder	2	3	1	2	8
Arterial Thrombosis	0	0	0	0	0
Arteriosclerosis	1	2	2	2	7
Coronary Occlusion	0	1	0	0	1
Chest Pain Substernal	0	0	0	1	1
Unduplicated Reports	**10**	**10**	**13**	**12**	**45**
III. Hypotension					
Syncope	11	26	16	19	72
Dizziness	36	40	38	35	149
Shock	1	3	2	6	12
Vasodilatation	4	4	10	6	24
Hypotension	22	31	29	20	102
Postural Hypotension	14	14	6	9	43
Unduplicated Reports	**76**	**102**	**89**	**86**	**353**
IV. Others					
Cor Pulmonale	0	1	1	0	2
Pericardial Effusion	0	0	1	1	2
Pericarditis	0	0	0	1	1
Myocarditis	0	0	1	1	2
Pulmonary Hypertension	0	1	0	1	2
Cardiomegaly	0	1	0	1	2
Cardiomyopathy	0	1	1	1	3
Cardiovascular Disorder	4	1	6	3	14
Congestive Heart Failure	1	3	2	4	10
Heart Failure	2	4	3	3	12
Unduplicated Reports	**7**	**11**	**14**	**15**	**47**

* Q1-2 represents 9/27/96 - 3/31/97; Q3-4 represents 4/1/97 - 9/30/97
Q5-6 represents 10/1/97 - 3/31/98; Q7-8 represents 4/1/98 - 9/30/98

CENSUS OF ADVERSE EVENTS FROM CLINTRACE DATABASE, OLANZAPINE, SPONTANEOUS REPORTS

EVENT	Q1-2*	Q3-4*	Q5-6*	Q7-8*	TOTAL
DERMATOLOGIC					
I. Hair					
Alopecia	9	25	28	22	84
Hair Disorder	2	0	1	1	4
Hirsutism	1	1	1	2	5
Unduplicated Reports	**11**	**26**	**29**	**24**	**90**
II. Skin					
Rash	67	73	58	53	251
Petechial Rash	0	2	0	0	2
Maculopapular Rash	4	5	7	8	24
Vesiculobullous Rash	2	10	6	2	20
Photosensitivity Reaction	2	3	4	7	16
Urticaria	5	6	9	12	32
Exfoliative Dermatitis	0	1	3	1	5
Toxic Epidermal Necrolysis	0	0	0	0	0
Unduplicated Reports	**75**	**97**	**77**	**80**	**329**

* Q1-2 represents 9/27/96 - 3/31/97; Q3-4 represents 4/1/97 - 9/30/97
Q5-6 represents 10/1/97 - 3/31/98; Q7-8 represents 4/1/98 - 9/30/98

CENSUS OF ADVERSE EVENTS FROM CLINTRACE DATABASE, OLANZAPINE, SPONTANEOUS REPORTS

EVENT	Q1-2*	Q3-4*	Q5-6*	Q7-8*	TOTAL
DIGESTIVE / GASTOINTESTINAL					
I. Liver					
A. Hepatocellular					
SGPT Increased	31	44	20	25	120
SGOT Increased	27	36	19	13	95
Liver Funtion Tests Abnormal	20	53	55	48	176
Hepatitis	2	5	6	6	19
Hepatic Coma	0	0	0	1	1
Hepatic Failure	1	2	2	3	8
Liver Necrosis	0	0	0	0	0
Liver Damage	1	0	2	0	3
Liver Tenderness	0	1	0	0	1
Liver Fatty Deposit	0	0	2	2	4
Hepatomegaly	0	1	1	1	3
Unduplicated Reports	**58**	**98**	**84**	**82**	**322**
B. Cholestatic					
GGT Increased	13	20	11	12	56
Cholestatic Jaundice	0	0	2	0	2
Jaundice	2	7	7	13	29
Bilirubinemia	7	9	11	6	33
Bilirubinuria	0	0	1	0	1
Alkaline Phosphatase Increased	2	12	11	10	35
Unduplicated Reports	**22**	**33**	**35**	**31**	**121**
C. Miscellaneous					
Non-specific LDH increase	**1**	**5**	**6**	**2**	**14**
II. Pancreas					
Pancreatitis	2	4	3	2	11
Hemorrhagic Pancreatitis	0	0	2	0	2
Necrotizing Pancreatitis	0	0	0	0	0
Amylase Increased	3	2	3	0	8
Pancreas Disorder	1	0	1	0	2
Unduplicated Reports	**4**	**5**	**8**	**2**	**19**

* Q1-2 represents 9/27/96 - 3/31/97; Q3-4 represents 4/1/97 - 9/30/97
Q5-6 represents 10/1/97 - 3/31/98; Q7-8 represents 4/1/98 - 9/30/98

CENSUS OF ADVERSE EVENTS FROM CLINTRACE DATABASE, OLANZAPINE, SPONTANEOUS REPORTS

EVENT	Q1-2*	Q3-4*	Q5-6*	Q7-8*	TOTAL
ENDOCRINE					
I. Blood Sugar Elevation					
Hyperglycemia	27	42	40	48	157
Diabetes Mellitus	1	9	24	10	44
Diabetic Acidosis	1	8	6	9	24
Diabetic Coma	1	1	0	0	2
Ketosis	2	2	2	2	8
Glucose Tolerance Decreased	0	0	1	0	1
Unduplicated Reports	**28**	**50**	**60**	**56**	**194**
II. Hypoglycemia	**1**	**5**	**4**	**4**	**14**

* Q1-2 represents 9/27/96 - 3/31/97; Q3-4 represents 4/1/97 - 9/30/97
Q5-6 represents 10/1/97 - 3/31/98; Q7-8 represents 4/1/98 - 9/30/98

CENSUS OF ADVERSE EVENTS FROM CLINTRACE DATABASE, OLANZAPINE, SPONTANEOUS REPORTS

EVENT	Q1-2*	Q3-4*	Q5-6*	Q7-8*	TOTAL
HEMATOLOGIC (General)					
I. Reduction					
Aplastic Anemia	2	0	1	1	4
Pancytopenia	4	1	1	2	8
Marrow Depression	2	0	1	1	4
Blood Dyscrasia	0	0	1	1	2
Agranulocytosis	2	1	2	0	5
Leukopenia	48	55	45	44	192
Thrombocytopenia	19	21	13	16	69
Anemia	4	4	7	8	23
Macrocytic Anemia	0	1	0	0	1
Hypochromic Anemia	0	1	1	0	2
Unduplicated Reports	**67**	**76**	**66**	**70**	**279**
II. Other					
WBC Abnormal	2	0	2	1	5
Abnormal Platelets	0	0	0	1	1
Erythrocytes Abnormal	1	2	0	3	6
Polycythemia	1	2	0	0	3
Thrombocythemia	2	0	2	3	7
Eosinophilia	6	7	7	5	25
Granulocytosis	0	0	0	1	1
Lymphocytosis	1	1	1	0	3
Monocytosis	0	2	0	0	2
Leukocytosis	8	14	15	17	54
Unduplicated Reports	**20**	**24**	**27**	**26**	**97**

* Q1-2 represents 9/27/96 - 3/31/97; Q3-4 represents 4/1/97 - 9/30/97
Q5-6 represents 10/1/97 - 3/31/98; Q7-8 represents 4/1/98 - 9/30/98

CENSUS OF ADVERSE EVENTS FROM CLINTRACE DATABASE, OLANZAPINE, SPONTANEOUS REPORTS

EVENT	Q1-2*	Q3-4*	Q5-6*	Q7-8*	TOTAL
HEMATOLOGIC (Coagulation)					
I. Coagulation - Part A					
Coagulation Disorder	0	0	3	0	3
Ecchymosis	1	5	2	4	12
Epistaxis	6	5	6	5	22
Hematemesis	1	3	1	3	8
Hemoptysis	0	0	0	0	0
Hematuria	3	4	7	3	17
Hemorrhage	1	1	0	2	4
Hemorrhagic Cystitis	0	1	0	0	1
Melena	0	0	2	0	2
Prothrombin Increased	1	1	2	0	4
Increased Anticoagulant Effect	1	1	0	0	2
Thromboplastin Increased	0	1	0	1	2
Petechia	1	1	1	0	3
Purpura	0	0	0	1	1
Petechial Rash	0	2	0	0	2
Eye Hemorrhage	0	0	1	1	2
Rectal Hemorrhage	2	3	1	0	6
Vaginal Hemorrhage	0	0	0	0	0
Cerebral Hemorrhage	0	1	0	1	2
Subarachnoid Hemorrhage	1	0	0	0	1
GI Hemorrhage	0	2	0	0	2
Unduplicated Reports	**17**	**27**	**25**	**20**	**89**
II. Coagulation - Part B					
Prothrombin Decreased	0	3	4	4	11
Thrombosis	0	2	1	3	6
Deep Thrombophlebitis	1	5	2	2	10
Pulmonary Embolus	5	5	2	3	15
Thrombophlebitis	0	2	0	4	6
Unduplicated Reports	**6**	**17**	**6**	**14**	**43**

* Q1-2 represents 9/27/96 - 3/31/97; Q3-4 represents 4/1/97 - 9/30/97
Q5-6 represents 10/1/97 - 3/31/98; Q7-8 represents 4/1/98 - 9/30/98

CENSUS OF ADVERSE EVENTS FROM CLINTRACE DATABASE, OLANZAPINE, SPONTANEOUS REPORTS

EVENT	Q1-2*	Q3-4*	Q5-6*	Q7-8*	TOTAL
METABOLIC / NUTRITIONAL					
I. Edema					
Face Edema	42	48	29	27	146
Generalized Edema	3	5	2	10	20
Peripheral Edema	86	140	94	92	412
Edema	24	40	37	30	131
Unduplicated Reports	**137**	**212**	**150**	**147**	**646**
II. Special Edema					
Tongue Edema	6	12	6	4	28
Labial Edema	0	0	1	0	1
Genital Edema	0	0	0	2	2
Retinal Edema	0	0	1	0	1
Unduplicated Reports	**6**	**12**	**8**	**6**	**32**
III. Weight Gain	**94**	**171**	**182**	**203**	**650**
IV. Weight Loss	**7**	**9**	**9**	**11**	**36**
V. Hyponatremia/SIADH					
ADH Inappropriate	1	0	1	2	4
Hyponatremia	1	13	11	13	38
Water Intoxication	2	0	1	3	6
Unduplicated Reports	**3**	**13**	**12**	**14**	**42**
VI. Serum Sodium Elevation					
Hypernatremia	2	3	0	2	7
Dehydration	3	3	1	2	9
Diabetes Insipidus	0	3	0	0	3
Unduplicated Reports	**5**	**6**	**1**	**4**	**16**
VII. Cholesterol and Triglycerides					
Hypercholesteremia	2	4	3	4	13
Hyperlipemia	1	5	5	8	19
Unduplicated Reports	**2**	**8**	**6**	**8**	**24**

* Q1-2 represents 9/27/96 - 3/31/97; Q3-4 represents 4/1/97 - 9/30/97
Q5-6 represents 10/1/97 - 3/31/98; Q7-8 represents 4/1/98 - 9/30/98

CENSUS OF ADVERSE EVENTS FROM CLINTRACE DATABASE, OLANZAPINE, SPONTANEOUS REPORTS

EVENT	Q1-2*	Q3-4*	Q5-6*	Q7-8*	TOTAL
NERVOUS SYSTEM					
I. Cerebral					
Cerebral Hemorrhage	0	1	0	1	2
Cerebrovascular Accident	3	6	0	1	10
Cerebrovascular Disorder	0	0	1	0	1
Cerebral Ischemia	0	0	1	1	2
Intracranial Hypertension	0	0	0	1	1
Subarachnoid Hemorrhage	1	0	0	0	1
Brain Edema	0	2	1	4	7
Papilledema	0	2	1	0	3
Unduplicated Reports	**4**	**11**	**4**	**8**	**27**
CNS Depression	0	1	0	2	3
Coma	8	22	18	26	74
Stupor	10	16	19	10	55
Acute Brain Syndrome	0	0	0	4	4
Delirium	7	10	22	7	46
Encephalitis	1	0	0	0	1
Encephalopathy	1	2	0	1	4
Unduplicated Reports	**26**	**47**	**56**	**45**	**174**
II. Extrapyramidal Symptoms					
A. Dystonia					
Dystonia	23	18	24	9	74
Oculogyric Crisis	5	3	5	6	19
Generalized Spasm	1	1	0	0	2
Opisthotonos	0	0	0	3	3
Torticollis	1	2	0	3	6
Unduplicated Reports	**30**	**23**	**29**	**20**	**102**
B. Parkinsonism					
Extrapyramidal Sydrome	27	55	35	30	147
Akinesia	1	1	0	6	8
Cogwheel Rigidity	6	7	11	8	32
Hypertonia	26	44	55	45	170
Hypokinesia	1	1	4	1	7
Masked Facies	2	0	1	0	3
Unduplicated Reports	**56**	**101**	**89**	**78**	**324**

* Q1-2 represents 9/27/96 - 3/31/97; Q3-4 represents 4/1/97 - 9/30/97
Q5-6 represents 10/1/97 - 3/31/98; Q7-8 represents 4/1/98 - 9/30/98

CENSUS OF ADVERSE EVENTS FROM CLINTRACE DATABASE, OLANZAPINE, SPONTANEOUS REPORTS

EVENT	Q1-2*	Q3-4*	Q5-6*	Q7-8*	TOTAL
II. Extrapyramidal Symptoms (cont.)					
C. Akathisia					
Akathisia	34	35	35	27	131
Hyperkinesia	5	10	11	11	37
Unduplicated Reports	**37**	**43**	**45**	**38**	**163**
D. Tardive Dyskinesia					
Tardive Dyskinesia	8	16	15	15	54
Dyskinesia	10	15	22	13	60
Twitching	14	27	23	24	88
Buccoglossal Syndrome	2	4	6	6	18
Choreoathetosis	2	2	5	1	10
Unduplicated Reports	**34**	**61**	**67**	**58**	**220**
E. Other					
Movement Disorder	19	19	26	23	87
Myoclonus	2	7	5	9	23
Unduplicated Reports	**21**	**25**	**31**	**32**	**109**
III. Seizure					
Abnormal Encephalogram	1	11	2	15	29
Convulsion	33	46	40	34	153
Grand Mal Convulsion	17	12	17	11	57
Unduplicated Reports	**51**	**65**	**57**	**59**	**232**

* Q1-2 represents 9/27/96 - 3/31/97; Q3-4 represents 4/1/97 - 9/30/97
Q5-6 represents 10/1/97 - 3/31/98; Q7-8 represents 4/1/98 - 9/30/98

CENSUS OF ADVERSE EVENTS FROM CLINTRACE DATABASE, OLANZAPINE, SPONTANEOUS REPORTS

EVENT	Q1-2*	Q3-4*	Q5-6*	Q7-8*	TOTAL
RESPIRATORY					
Apnea	7	10	17	3	37
Dyspnea	33	34	31	44	142
Hypoxia	0	2	1	1	4
Cyanosis	0	2	1	1	4
Hypoventilation	1	6	3	2	12
Interstitial Pneumonia	1	0	1	0	2
Eosinophilic Pneumonia	0	0	0	1	1
Lung Fibrosis	0	0	1	1	2
Lung Edema	4	2	6	1	13
Pleural Effusion	1	1	1	2	5
Pneumonia	4	12	11	8	35
Respiratory Acidosis	0	2	0	1	3
Respiratory Disorder	5	6	3	10	24
Unduplicated Reports	**52**	**71**	**65**	**65**	**253**
RENAL					
Acute Kidney Failure	1	2	2	2	7
Kidney Failure	4	2	1	4	11
BUN Increased	4	1	2	2	9
Creatinine Increased	4	6	7	0	17
Anuria	0	0	2	2	4
Oliguria	0	1	0	2	3
Nephrosis	0	1	1	1	3
Nephritis	1	0	0	0	1
Kidney Cortex Necrosis	0	1	0	0	1
Kidney Function Abnormal	3	2	5	0	10
Kidney Tubular Necrosis	0	1	0	0	1
Unduplicated Reports	**13**	**14**	**17**	**13**	**57**
Urinary Urgency	0	3	2	1	6
Urinary Frequency	2	10	6	3	21
Urinary Incontinence	10	29	26	20	85
Unduplicated Reports	**12**	**38**	**32**	**24**	**106**
Urinary Retention	7	8	7	17	39
Urination Impaired	3	3	0	2	8
Unduplicated Reports	**10**	**11**	**7**	**19**	**47**

* Q1-2 represents 9/27/96 - 3/31/97; Q3-4 represents 4/1/97 - 9/30/97
Q5-6 represents 10/1/97 - 3/31/98; Q7-8 represents 4/1/98 - 9/30/98

CENSUS OF ADVERSE EVENTS FROM CLINTRACE DATABASE, OLANZAPINE, SPONTANEOUS REPORTS

EVENT	Q1-2*	Q3-4*	Q5-6*	Q7-8*	TOTAL
SPECIAL SENSES					
I. Eye					
Blindness	0	0	0	0	0
Cataract NOS	1	1	1	0	3
Cataract Specified	0	0	2	1	3
Unduplicated Reports	**1**	**1**	**3**	**1**	**6**
II. Deafness					
Deafness	**2**	**3**	**1**	**2**	**8**

* Q1-2 represents 9/27/96 - 3/31/97; Q3-4 represents 4/1/97 - 9/30/97
Q5-6 represents 10/1/97 - 3/31/98; Q7-8 represents 4/1/98 - 9/30/98

CENSUS OF ADVERSE EVENTS FROM CLINTRACE DATABASE, OLANZAPINE, SPONTANEOUS REPORTS

EVENT	Q1-2*	Q3-4*	Q5-6*	Q7-8*	TOTAL
SEXUAL DYSFUNCTION					
I. Sexual Function Abnormal					
Priapism	4	8	6	8	26
Abnormal Ejaculation	0	1	5	5	11
Impotence	9	7	8	7	31
Libido Decreased	2	4	5	4	15
Libido Increased	6	3	4	3	16
Anorgasmia	0	1	1	2	4
Penis Disorder	0	2	0	0	2
Enlarged Clitoris	0	1	0	0	1
Unduplicated Reports	**20**	**24**	**28**	**26**	**98**
II. Menstrual					
Amenorrhea	1	11	21	19	52
Menorrhagia	4	3	3	3	13
Dysmenorrhea	0	0	1	0	1
Metrorrhagia	0	3	7	3	13
Menstrual Disorder	6	4	6	3	19
Unduplicated Reports	**11**	**20**	**36**	**28**	**95**
III. Breast					
Prolactin Increased	5	6	12	12	35
Breast Pain	3	4	4	10	21
Breast Enlargement	0	2	5	3	10
Gynecomastia	3	3	3	18	27
Male Lactation	0	0	3	2	5
Female Lactation	7	15	17	18	57
Unduplicated Reports	**12**	**27**	**37**	**53**	**129**
MISCELLANEOUS					
I. Anaphylaxis					
Allergic Reaction	9	4	9	5	27
Anaphylactoid Reaction	2	0	0	0	2
Angioedema	0	3	3	3	9
Laryngismus	1	1	1	4	7
Larynx Edema	0	0	0	1	1
Urticaria	5	6	9	12	32
Unduplicated Reports	**16**	**14**	**20**	**23**	**73**

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Q5-6 represents 10/1/97 - 3/31/98; Q7-8 represents 4/1/98 - 9/30/98

CENSUS OF ADVERSE EVENTS FROM CLINTRACE DATABASE, OLANZAPINE, SPONTANEOUS REPORTS

EVENT	Q1-2*	Q3-4*	Q5-6*	Q7-8*	TOTAL
MISCELLANEOUS (Continue)					
II. Death					
Death (Mapped to death)	9	9	10	15	43
Sudden Death	3	4	1	3	11
All Others	34	50	60	55	199
Unduplicated Reports	**46**	**63**	**71**	**73**	**253**
III. Drug Interaction					
Drug Interaction	19	27	22	25	93
Drug Level Increased	3	12	6	3	24
Drug Level Decreased	5	5	9	1	20
Unduplicated Reports	**27**	**43**	**34**	**28**	**132**
IV. Neuroleptic Malignant Syndrome					
NMS	19	27	39	26	111
Myopathy	2	6	7	1	16
Creatine Phosphokinase Elevation	25	58	47	32	162
Unduplicated Reports	**36**	**71**	**64**	**41**	**212**
V. Overdose					
Accidental Overdose	9	2	6	1	18
Intentional Overdose	48	111	101	86	346
Overdose	45	19	40	40	144
Unduplicated Reports	**102**	**132**	**147**	**126**	**507**
VI. Suicide Attempt					
Suicide Attempt	20	28	51	45	144
Intentional Overdose	48	111	101	86	346
Overdose	45	19	40	40	144
Unduplicated Reports	**104**	**145**	**160**	**149**	**558**

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Q5-6 represents 10/1/97 - 3/31/98; Q7-8 represents 4/1/98 - 9/30/98

CENSUS OF ADVERSE EVENTS FROM CLINTRACE DATABASE, OLANZAPINE, SPONTANEOUS REPORTS

EVENT	Q1-2*	Q3-4*	Q5-6*	Q7-8*	TOTAL
MISCELLANEOUS (Continue)					
VII. External Aggression					
Intentional Injury	1	4	2	6	13
Antisocial Reaction	0	0	0	1	1
Hostility	39	36	37	39	151
Personality Disorder	25	28	24	27	104
Unduplicated Reports	**59**	**64**	**60**	**67**	**250**
VIII. Immune Complex Deposition					
Reaction	9	4	9	5	27
Allergic Reaction	0	1	1	0	2
Vasculitis	0	1	0	0	1
Hemolysis	0	1	1	1	3
Hemolytic Anemia	0	1	1	0	2
Thrombocytopenic Purpura	0	0	1	1	2
Sedimentation Rate Increased	14	13	10	14	51
Arthralgia	0	2	1	2	5
Arthritis	0	0	1	3	4
LE Syndrome	2	6	7	1	16
Myopathy	0	0	1	0	1
Myositis	1	2	2	1	6
Neuropathy	0	1	0	0	1
Polyneuritis	1	0	1	0	2
Interstitial Pneumonia	0	0	0	1	1
Eosinophilic Pneumonia	0	0	1	1	2
Lung Fibrosis	0	1	2	0	3
Urticaria	5	6	9	12	32
Petechial Rash	0	2	0	0	2
Maculopapular Rash	4	5	7	8	24
Vesiculobullous Rash	2	10	6	2	20
Erythema Multiforme	0	0	1	3	4
Nephritis	1	0	0	0	1
Nephrosis	0	1	1	1	3
Unduplicated Reports	**38**	**54**	**57**	**53**	**202**
IX. Lack of Drug Effect	**49**	**75**	**72**	**47**	**243**

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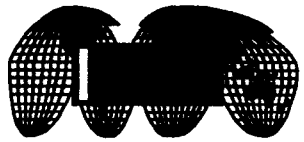

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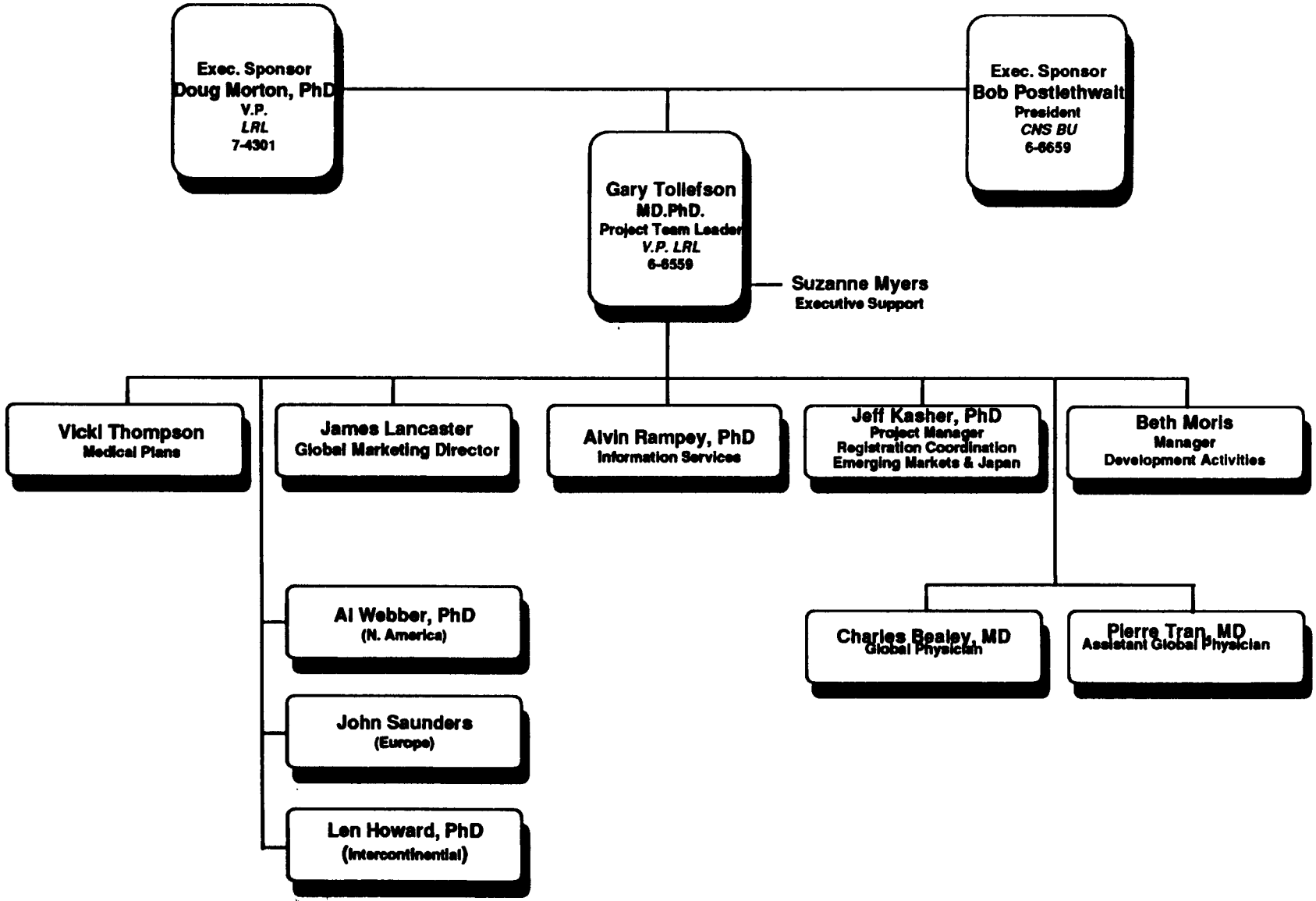

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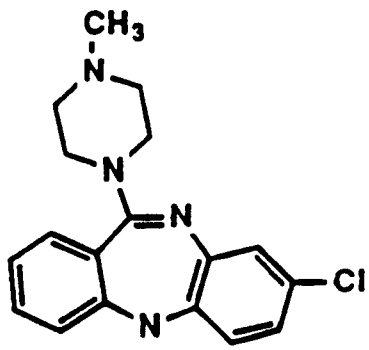

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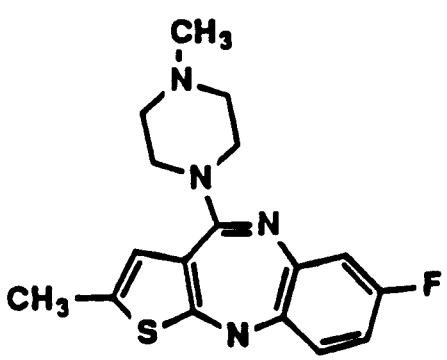

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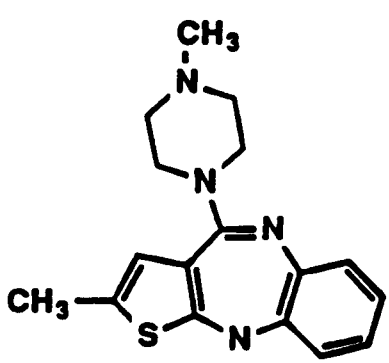

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