Table 7.1.2.1.1
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Trials in Adult Type 1 Diabetics
Sorting by Patient
Treatment = Inhaled Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Patient ID	Age (yrs)	Gender	Dose[1] (mg)	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
102E	5002	0003	27	F	27	1275	Metab	Diabetic ketoacidosis		
102E	5002	0084	52	F	8	474	Repro/ Uro	Bilateral torsion of hydrosalpinges, pelvic adhesions, cystic masses of ovaries and fallopian tubes		
102E	5005	0044	34	F	9	1093	GI	Food poisoning	Mentioned in narrative for decline in FEV1, FVC, DLco	
102E	5005	0108	45	M	20	1845	Cardiac	Triple vessel coronary artery disease		
						1854	Cardiac	Congestive heart failure		
						1910	Nervous	Transient ischemic episode		
102E	5006	0053	47	F	7	823	Repro/ Uro	Excessive intermittent menstruation		
102E	5007	0068	40	M	18	1414	General	Noncardiac chest pain		
102E	5007	0070	56	M	10	557	GI	Cholelithiasis, cholecystitis	Mentioned in narrative for pneumonia	
102E	5007	0106	57	M	23	1073	Cardiac	Acute myocardial infarction	Ischemic heart disease	y (death)
102E	5008	0066	57	M	11	2073	Cardiac	Coronary artery blockage		
102E	5011	0077	35	F	5	1378	Accid/ Inj	Automobile accident	same	y (death)
102E	5012	0035	34	M	7	57	Musculoskel	Back pain		
102E	5013	0013	25	M	10	345	Accid/Inj	Laceration thumb		
102E	5013	1008	44	M	9	196	Metab	Diabetic ketoacidosis		
106	5008	6168	55	F	19	6	Uro	Worsening stress incontinence		
106	5030	6881	36	M	27	99	Metab	Hyperglycemia, inadvertent overdose of inhaled insulin, hypoglycemia, convulsions, unconsciousness		
106	5030	6883	53	F	31	7	Metab	Hypoglycemia, unconscious, hypothermia	same	
106	5044	6275	23	M	18	136 (12)	Metab	Diabetic ketoacidosis		
106	5060	6966	36	M	39	33	Metab	Hypoglycemic coma		y
107	5029	7597	53	M	10	141	Eye	Left eye hemorrhage		
107	5052	7181	53	M	13	23	Metab	Severe hypoglycemic event, motor vehicle accident	same	
107	5063	7419	34	M	27	67	GI	Chronic gastritis		
107	5127	7221	30	F	6	18	Metab	Hypoglycemia, grand mal seizure	same	
111[6]	5005	7683	36	F	8	536	Accid/ Injur	Dog bite hand, cellulitis	Not mentioned in narrative for discontinuation due to frequent hypoglycemia	

Table 7.1.2.1.1
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Trials in Adult Type 1 Diabetics
Sorting by Patient
Treatment = Inhaled Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Patient ID	Age (yrs)	Gender	Dose[1] (mg)	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
						789	Metab	Not in applicant's SAE table	Increasingly frequent hypoglycemia (from narrative)	y
111	5005	7686	54	M	4	313	GI	Abdominal pain		
111	5008	6669	50	F	9	689 (11)	Metab	Hypoglycemia	Also MVA (11 d after last inh ins)	
111	5010	7615	41	F	15	252	Infec	Appendicitis		
111	5010	8105	50	F	24	288	Vasc	Carotid stenosis		
					20	245	Cardiac	Worsening coronary artery disease		
111	5013	6604	46	F	8	190	Neoplasms	Breast cancer		
111	5016	6929	26	M	20	316	Musculoskel	Torn ligament left shoulder	Mentioned in narrative for decline in DLco	
111	5025	6590	24	F	12	493	Metab	Ketoacidosis		
111	5025	6592	44	M	24	509	Metab	Hypoglycemia	also convulsions	
					31	558	Metab	Hypoglycemia, seizure	same	
111	5025	6593	45	M	21	850 (183)	Cardiac	Heart attack		
111	5029	7597	55	M	22	804	GI	Cholecystitis		
111	5029	7599	58	F	3	863	Musculoskel	Torn rotator cuff	Mentioned in narrative for change in HRCT	
					4	224	Proc Comp	Postoperative surgical site hematoma	Mentioned in narrative for change in HRCT	
					3	741	Musculoskel	Adhesive capsulitis shoulder	Mentioned in narrative for change in HRCT	
111	5029	7602	34	M	18	366	Infec	Appendicitis		
111	5030	6883	56	F	14	862 (unk)	Infec	Worsening sinusitis	Mentioned in narrative for high ins Ab	
					14	862 (51)	Heme	Anemia	Mentioned in narrative for high ins Ab	
					12	111	Metab	Hypoglycemic event, unresponsiveness	same	
					17	92	Metab	Hypoglycemia, altered level of consciousness	same	
111	5036	7117	36	M	9	45 (11)	Accid/ Injur	Accidental fall, epidural hematoma, right-sided hemiparesis	Not mentioned in narrative for hypoglycemia	
111	5041	7153	67	M	36	916	Cardiac	Worsening of angina		
111	5042	6713	42	M	9	118	Accid/ injur	Accidental fall, broken leg	same; also had fractured sternum	

Table 7.1.2.1.1
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Trials in Adult Type 1 Diabetics
Sorting by Patient
Treatment = Inhaled Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Patient ID	Age (yrs)	Gender	Dose[1] (mg)	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
									in MVA on day 66	
111	5045	6229	53	M	36	547	Cardiac	Coronary artery disease	Mentioned in narrative for decline in FEV1	
111	5047	6555	40	F	17	652	Infec	Influenza	Mentioned in narrative for high ins Ab	
111	5049	6245	33	M	13	64	Neuro	Seizures		
111	5049	6767	46	M	13	591	Infec	Osteomyelitis, chronic left foot ulcer		
111	5049	6770	54	F	14	329	Cardiac	Myocardial infarction	same	y (death)
111	5049	6772	32	F	3	679	Repro/ Uro	Worsening menorrhagia		
111	5025	5682	62	M	24	734 (168)	Neuro	Delirium of unknown etiology		
					18	492	Metab	Severe hypoglycemia		
111	5052	7180	34	M	7	103	Metab	Hypoglycemia, incoherent speech	same	
111	5053	6782	35	M	18	168	GI	Nausea, vomiting		
					18	168	Metab	Dehydration		
111	5053	6783	54	M	20	576	Cardiac	Angina pectoris		
					11	392	Musculoskel	Left shoulder pain		
111	5055	6622	57	M	21	77 (85)	Metab	Severe hypoglycemic event, unconsciousness	Not mentioned in narrative for decline in FEV1 and DLco	
111	5056	7714	51	M	5	710	Cardiac	Worsening unstable angina	Mentioned in narrative for hi ins Ab	
111	5059	6681	37	F	12	452	GI	Exacerbation cholelithiasis		
111	5060	6960	37	M	18	5	Neuro	Convulsions		
111	5061	7793	44	F	12	727	Metab	Hypoglycemia	Hypoglycemia, unconsciousness	y (10 days later)
111	5061	7794	30	F	16	146	Accid/ Injur	Left wrist fracture, accidental fall	Mentioned in narrative for hypoglycemia	
					26	303	Metab	Hypoglycemia, unconsciousness, incontinence	same	
					27	314	Metab	Hypoglycemia	same	
111	5061	7797	46	M	15	480	Metab	Hypoglycemic event, unconsciousness	same	
111	5066	7741	41	F	30	323	Metab	Hypoglycemic seizure	same	
111	5066	7745	29	M	13	190	Metab	Hypoglycemia, seizure	same	
111	5070	6896	30	F	42	137	Metab	Hypoglycemia	Hypoglycemia, unresponsiveness	

Table 7.1.2.1.1
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Trials in Adult Type 1 Diabetics
Sorting by Patient
Treatment = Inhaled Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Patient ID	Age (yrs)	Gender	Dose[1] (mg)	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
111	5070	6898	42	F	5	304	Metab	Hypoglycemia, seizure	same	
111	5072	6819	38	F	12	642	Infec	Spontaneous bacteremic illness		
111	5075	7328	35	M	16	279	Infec	Right ear infection	Ear infection not mentioned in narrative for decline in FEV1	
111	5076	7227	42	M	9	489	Metab	Diabetic ketoacidosis		
111	5076	7230	47	F	9	121	Accid/ Injur	Accidental fracture right ulna		
					5	194	Infec	Breast abscess		
111	5081	6446	18	F	12	230	Metab	Hypoglycemic episode	same	
111	5098	7071	19	F	7	870	Infec	Gastroenteritis	Mentioned in narrative for decline in DLco	
111	5127	7221	31	F	12	486	Metab	Hypoglycemia, seizure	same	
					12	522	Metab	Hypoglycemia, seizure	same	
					12	527	Metab	Hypoglycemia, seizure	same	
					18	615	Metab	Recurrent hypoglycemia, recurrent seizure	same	
					15	632	Metab	Recurrent hypoglycemia, recurrent seizure	same	y
111	5127	7224	60	M	15	667	Metab	Hypoglycemic event	Hypoglycemia, unconsciousness	
A2171022	1001	0003	23	F	8	241	Metab	Diabetic ketoacidosis		
A2171022	1001	0007	39	M	5	54	Eye	Worsening macular degenerative disease left eye		
A2171022	1001	0009	37	M	11	197	Metab	Hypoglycemic reaction, unconsciousness	same	y
A2171022	1006	0302	37	M	10	31	Metab	Hypoglycemia	Hypoglycemia, motorcycle accident, clavicular rhegma	
					10	192	Metab	Hypoglycemia	same	
A2171022	1006	0319	34	M	13	347	Cardiac	Angina		
A2171022	1007	0361	19	F	9	504	Infec	Pyelonephritis		
A2171022	1007	0364	22	F	8	307	Repro/ Uro	Renal colic		
A2171022	1010	0537	48	M	21	315	GI	Gastroenteritis	same	
						215	Metab	Hypoglycemia		
A2171022	1015	0837	37	M	8	83	Metab	Hypoglycemia, loss of consciousness	same	
A2171022	1016	0891	51	M	10	227	Cardiac	Myocardial infarction		y (death)
A2171022	1017	0949	29	M	7	409	Metab	Diabetic ketoacidosis	Not mentioned in narrative for decline in DLco and	

Table 7.1.2.1.1
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Trials in Adult Type 1 Diabetics
Sorting by Patient
Treatment = Inhaled Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Patient ID	Age (yrs)	Gender	Dose[1] (mg)	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
									discontinuation from study due to cough	
A2171022	1019	0068	34	F	6	31	Metab	Hypoglycemia, loss of consciousness		
A2171022	1020	1131	35	F	6	1	General	Chest pain		
A2171022	1025	1424	32	M	12	244	Metab	Hypoglycemia, seizure	same	
A2171022	1026	1485	47	F	8	531	Accid/ injur	Trimalleolar fracture right ankle		
A2171022	1026	1489	22	F	20	482	Metab	Hypoglycemia	Hypoglycemia, motor vehicle accident	
A2171022	1029	1661	35	M	12	89	Metab	Hypoglycemia	same	
A2171022	1030	1722	56	F	12	440	Cardiac	Recurrence of paroxysmal supraventricular tachycardia		
A2171022	1031	1785	20	F	12	170	Infec	Kidney infection		
A2171022	1031	1188	62	M	14	125	Infec	Abdominal cellulitis at surgical site		
							Procedural complications (Proc comp)	Ventral and umbilical herniae		
A2171022	1031	1788	62	M	15	316	Infec	Right rotator cuff wound infection, worsening chronic shoulder pain		
					15	570	General	Chest pain		
A2171022	1033	1899	62	M	12	474	Accid/ Injur	Dislocated right trimalleolar ankle fracture		
A2171022	1037	2136	51	F	8	15	Metab	Hypoglycemia, loss of consciousness	same	
A2171022	1037	2140	52	M	6	300	Accid/ injur	Motorcycle accident, multiple lacerations		
A2171022	1039	2253	22	F	7	284	Repro/ Uro	Preterm labor	same	
						284	Metab	Ketoacidosis	same	
A2171022	1050	3914	46	M	12	3	Metab	Hypoglycemia	same	
					21	162	Metab	Hypoglycemic event	same	
					21	165	Metab	Hypoglycemic event	same	
A2171022	5074	3082	51	M	21	4	Metab	Hypoglycemia	same	
A2171022	5096	3140	43	F	2	167	GI	Gallbladder lithiasis		
A2171022	5098	3258	47	F	7	105	Neoplasm	Carcinoma left breast	Lobular breast carcinoma in situ	

Table 7.1.2.1.1
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Trials in Adult Type 1 Diabetics
Sorting by Patient
Treatment = Inhaled Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Patient ID	Age (yrs)	Gender	Dose[1] (mg)	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
A2171022	5147	3376	45	F	15	89	Metab	Recurrent hypoglycemic episodes		
A2171022	5152	3622	48	F	13	54	Cardiac	Myocardial infarction	same	y (death)
A2171022	5155	3735	41	F	5	Not reported (NR)	Eye	Cataract left eye		
					7	331	Repro/ Uro	Spontaneous abortion		
A2171026	1001	0017	50	F	6	10	Metab	Hypoglycemia	same	
A2171026	1001	0005	33	M	14	10	Metab	Hypoglycemia		
					9	58	Metab	Hypoglycemia		

Includes Studies 1001, 1002, 1005, 1007, 1009, 1017, 1022, 1026, 1027, 1028, 1029, 102E, 103, 1030, 1036, 104, 104E, 106, 107, 108, 109, 110, 111
1 Dose at time of adverse event
2 Duration of exposure in days at time of event. If event occurred after discontinuation, the number of days after discontinuation is included in parentheses
3 Applicant's assigned term
4 Term used by investigator or patient; nb- applicant provided SAE narratives only for pulmonary SAEs and SAEs that led to death or discontinuation
5 If patient withdrew due to this adverse event, noted with a "y"
6 For Study 111, an extension of several clinical trials, it was not clear from the applicant's Table 6.3.1.1 whether a patient had Type 1 or Type 2 diabetes. Readers who wish to examine the source Table 6.3.1.1 can tell what type of diabetes the patient had by looking at the 5th number of the patient's identification number in the applicant's Table 6.3.1.1. If this number was a zero, 1 or 8, the patient had Type 2 diabetes. If it was any other number, the patient had Type 1 diabetes (telephone communications with Mr. Brian Green, Pfizer Regulatory Affairs, 31 Mar 05 and 6 Apr 05)
Source: Applicant's Table 6.3.1.1, Section 2.7.4, pgs 1903-2296.

Table 7.1.2.1.2
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 1 Diabetics
Sorting by Patient
Treatment = SQ Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Pt ID	Age	Gender	Dose[1] (U/day)	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
106	5014	6805	56	M	Regular 8	14	Musculoskel	Herniated disc		
106	5019	6141	53	M	Regular 41	7	Skin	Heel infection		
106	5025	6592	42	M	Regular 59	51	Metab	Severe hypoglycemia, convulsions, confusion, expressive aphasia	same	

Table 7.1.2.1.2
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 1 Diabetics
Sorting by Patient
Treatment = SQ Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Pt ID	Age	Gender	Dose[1] (U/day)	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
106	5030	6882	43	M	Regular 25	488	Metab	Hypoglycemia, altered mental status	same	
106	5040	6572	63	F	Regular 7	122	Neuro	Syncope	same	
						122	Cardiac	Sinus arrhythmia, sinus tachycardia	same	DCed from inh ins in Study 111 extension, for recurrent severe hypoglycemia
106	5049	6767	43	M	Regular 22	65	Musculoskel	Fracture foot, sprain ankle		
106	5049	6771	41	F	Regular 21	40	Cardiac	Unstable angina		
					Regular 15	131	Neuro	Seizure		
106	5051	6869	54	M	Regular 6	77	Musculoskel	Increased back pain, bulging spinal discs		
106	5065	6947	22	F	Regular 27	17	Metab	Hypoglycemia, seizure, intentional overdose of study drug	Also tongue-biting with airway obstruction	
					Regular dose unknown	147	GI	Gastroenteritis		
						147	Metab	Ketoacidosis		
107	5027	7735	35	M	Regular 18	45	Metab	Hypoglycemia, loss of consciousness, bicycle accident, facial and knee lacerations, short term memory loss, decreased ability to concentrate	same	
107	5061	7797	45	M	Regular 21	40	Metab	Severe hypoglycemic event, memory loss		
107	5095	7488	18	F	Regular 31	46	GI	Gastrointestinal illness, vomiting		
107	5103	7240	24	F	Regular 24	133	General	Chest pain		
A2171022	1008	0438	47	M	Lispro 19	209	Metab	Hypoglycemia, seizure	same	
					Lispro 17	600	Infec	Chronic meningitis	Not mentioned in narrative for hypoglycemia	
A2171022	1008	0447	29	F	Regular 12	478	Repro/ Uro	Premature labor (after drug exposure to fetus)		
A2171022	1012	0654	64	F	Lispro 27	491	Cardiac	Coronary artery disease		
A2171022	1013	0713	47	F	Lispro 39	306	Skin	Diabetic ulcer toe		
A2171022	1016	0897	55	M	Aspart 18	385	Cardiac	Coronary artery disease		
A2171022	1021	1185	42	F	Aspart 35	184	Neoplasm	Bilateral breast cancer	same	

Table 7.1.2.1.2
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 1 Diabetics
Sorting by Patient
Treatment = SQ Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Pt ID	Age	Gender	Dose[1] (U/day)	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
A2171022	1021	1187	36	F	Lispro 39	355	Psych	Worsening of depression		
					Lispro 51	604	Psych	Worsening of depression		
					Lispro 48	701	Psych	Recurrent depression, suicidal ideation		
A2171022	1021	1190	51	M	Aspart 25	49	GI	Recurrent peptic ulcer		
					Aspart 34	351	Skin	Cellulitis right leg		
A2171022	1023	1306	20	F	Aspart 38	Not reported	Repro/ Uro	Pregnancy		y
					Aspart 52	677	Metab	Severe hypoglycemic event, diabetic seizure		
A2171022	1024	1371	56	F	Aspart 60	244	Metab	Hypoglycemia, acute change in mental status	same	
A2171022	1025	1426	31	F	Regular 42	176	Metab	Hypoglycemia, loss of consciousness		
A2171022	1028	1605	38	F	Lispro 21	348	Neoplasm	Uterine leiomyoma		
A2171022	1029	1665	49	M	Lispro 9	117	Metab	Hypoglycemia, loss of consciousness	same	
					Lispro 14	273	Psych	Exacerbation of depression	Mentioned in narrative for hypoglycemia	
					Lispro 17	330	Psych	Worsening of depression	Mentioned in narrative for hypoglycemia	
A2171022	1036	2075	36	M	Aspart 32	551	Metab	Hypoglycemia, loss of consciousness	same	
A2171022	1037	2135	29	M	Lispro 23	32	Metab	Hypoglycemia	Hypoglycemia, fall	
					Lispro 15	532	Metab	Hypoglycemia	same	
A2171022	1037	2138	48	F	Lispro 16	105	Metab	Hypoglycemic reaction, syncope	same	
A2171022	1037	2145	53	M	Lispro 25	183	Infec	Appendicitis		
A2171022	1038	2192	49	M	Lispro 32	502	Metab	Hypoglycemia, seizure	same	
					Lispro 31	704	Metab	Hypoglycemic event, loss of consciousness	same	
					Lispro 32	727	Metab	Hypoglycemia, loss of consciousness	same	
A2171022	1038	2193	50	M	Lispro 30	374	Metab	Hyperglycemia		
					Lispro 30	390	General	Diaphoresis with mild exertion		
A2171022	1039	2254	29	F	Lispro 6	444	Eye	Retinal detachment		
A2171022	1043	2489	58	M	Lispro 22	16	Neoplasm	Malignant pancreatic tumor	same	y
A2171022	1049	2843	41	F	Lispro 7	189	Metab	Hypoglycemia	same	
A2171022	1049	2847	37	M	Lispro 36	189	Metab	Hypoglycemia, seizure	same	
A2171022	1050	3913	37	M	Lispro 27	354	Metab	Hypoglycemic event, seizure	same	
A2171022	1050	3915	23	F	Regular 30	218	Metab	Hypoglycemic event	same	

Table 7.1.2.1.2
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 1 Diabetics
Sorting by Patient
Treatment = SQ Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Pt ID	Age	Gender	Dose[1] (U/day)	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
A2171022	5060	2904	41	M	Lispro 5	8	Metab	Hypoglycemic, loss of consciousness	same	
A2171022	5060	2907	45	F	Aspart 54	374	Psych	Major depression		
A2171022	5074	3081	27	F	Lispro 29	171	Infec	Appendicitis		
A2171022	5090	3210	36	F	Lispro 8	457	Neoplasm	Worsening of colonic polyposis		
A2171022	5138	3316	29	M	Lispro 8, Regular 12	8	Metab	Hypoglycemia	same	
A2171022	5138	3319	39	F	Lispro 59	38	Metab	Hypoglycemic episode, loss of consciousness	same	
					Lispro 45	668	Metab	Hypoglycemic episode	same	
A2171022	5147	3375	42	M	Lispro 21	122	Metab	Hypoglycemic reaction, unconsciousness	same	
A2171022	5147	3380	35	M	Lispro 22	313	Infec	Influenza		
A2171022	5152	3620	52	M	Lispro 24	677	Metab	Hypoglycemia, loss of consciousness	same	
A2171022	5154	3680	36	M	Lispro 60	42	Metab	Hypoglycemic event		
A2171028	1042	4077	38	F	Lispro 31	108	Resp	Exacerbation of asthma	same	
A2171030	1004	0099	64	F	Aspart 20	315	GI	Bowel obstruction, Crohn's disease	same	y
						315	Cardiac	Non-ST segment (sic) myocardial infarction	same	

Includes Studies 1001, 1002, 1005, 1007, 1009, 1017, 1022, 1026, 1027, 1028, 1029, 102E, 103, 1030, 1036, 104, 104E, 106, 107, 108, 109, 110, 111
1 Dose at time of adverse event
2 Duration of exposure in days at time of event. If event occurred after discontinuation, the number of days after discontinuation is inciuded in parentheses
3 Applicant's assigned term
4 Term used by investigator or patient; nb- applicant provided SAE narratives only for pulmonary SAEs and SAEs that led to death or discontinuation
5 If patient withdrew due to this adverse event, noted with a "y"
Source: Applicant's Table 6.3.1.1, Section 2.7.4, pgs 1903-2296

Table 7.1.2.1.3
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
Treatment = Inhaled Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Patient ID	Age (yrs)	Gender	Dose[1]	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	W/D?[5]
103	5002	0095	43	F	18	67	Musculoskel	Surgical removal of spinal rods and screws		
103	5014	0022	64	M	18	84	Nervous	Cerebral vascular accident	same	y
						84	Cardiac	Bradycardia, premature ventricular contractions	same	
103E	5002	0003	53	M	18	298	Vasc	Femoral artery blood clot		
103E	5002	0010	42	M	21	1022	Cardiac	Coronary artery disease	same	y
103E	5002	0089	62	M	1	1741	Vasc	Cerebrovascular accident	same	y
103E	5002	0089	61	M	6	1403	Cardiac	Chest pain		
					1	1707	Vasc	Intracranial bleeding		
103E	5002	0092	58	F	20	344	Cardiac	Congestive heart failure	Mentioned in narrative for decline in FEV1 and DLco, and renal insuff	
					18	1580	Renal	Not in listing	End-stage renal disease	y
					18	998	Heme	Exacerbation of chronic anemia	Mentioned in narrative for decline in FEV1 and DLco, and renal insuff	
					24	1227	Resp	Bronchitis	Mentioned in narrative for decline in FEV1 and DLco, and renal insuff	
					24	1227	Cardiac	Congestive heart failure	Mentioned in narrative for decline in FEV1 and DLco, and renal insuff	
103E	5002	0094	50	F	12	716	GI	Gangrenous cholecystitis		
103E	5005	0063	59	F	6	172	Resp	Pneumonia	same	
					6	172	Accid/ Inj	Syncope	Syncope while driving, MVA	
103E	5005	0069	60	M	3	397 (16)	Cardiac	Pericardial effusion	same	
					3	397 (42)	Infec	HIV+, Hep B	same	y
					3	397 (16)	Resp	Bilateral pleural effusions	same	
103E	5006	0047	45	F	18	38	Metab	Hypokalemia	Not mentioned in narrative for decline in DLco	
103E	5006	0048	60	M	21	469	Musculoskel	Hip replacement surgery	Not mentioned in death narrative	
					27	934	Cardiac	Acute myocardial infarction	Mentioned in death narrative	
103E	5008	0041	65	F	12	501	Cardiac	Coronary artery disease		
					12	700	Cardiac	Worsening coronary artery disease		
					19	804	Cardiac	Chest pain		
					10	1063	Cardiac	Unstable angina		
103E	5010	0071	64	M	13	1082	Cardiac	Acute myocardial infarction		
103E	5013	0012	48	M	18	40 (14)	GI	Gastroenteritis	Not mentioned in narrative for d/c due	

Table 7.1.2.1.3
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
Treatment = Inhaled Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Patient ID	Age (yrs)	Gender	Dose[1]	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	W/D?[5]
									to decline in DLco	
103E	5013	0013	54	F	9	2	Cardiac	Chest pain	Not mentioned in narrative for d/c due to restrictive ventilatory defect and decline in DLco	
103E	5014	0023	66	M	18	666	Vasc	Transient ischemic attack		
103E	5014	0024	55	M	24	796	Skin	Toe ulcer		
					30	1659	Infec	Infection of surgical amputation site second toe		
103E	5014	0030	59	M	6	2027	Cardiac	Restenosis stent	Mentioned in narrative for shortness of breath	
					33	2094	Cardiac	Chest pain	Mentioned in narrative for shortness of breath	
					33	2094	Resp	Shortness of breath	same	
					24	502	Resp	Shortness of breath	same	
					24	502	Cardiac	Coronary artery disease	Mentioned in narrative for shortness of breath	
					24	1332	Cardiac	Worsening coronary artery disease	Mentioned in narrative for shortness of breath	
104E	5002	0073	46	F	13	458	Repro/ Uro	Uterine fibroids		
104E	5005	0068	65	F	4	297	Cardiac	Coronary artery disease	Mentioned in narrative for declines in FVC, FEV1, and DLco	
					4	351	Cardiac	Worsening coronary artery disease	Mentioned in narrative for declines in FVC, FEV1, and DLco	
					4	660	Musculoskel	Distal radial fracture	Not mentioned in narrative for declines in FVC, FEV1, and DLco	
					10	808	Cardiac	Coronary artery disease	Mentioned in narrative for declines in FVC, FEV1, and DLco	
104E	5005	0071	56	F	5	106	Neoplasms	Breast adenocarcinoma		
104E	5006	0018	64	M	9	829	Cardiac	Myocardial infarction		
104E	5006	0019	63	M	4	863	Cardiac	Myocardial infarction		
104E	5010	0058	55	M	7	1249	Resp	Acute inhalation injury due to sulfuric acid		
104E	5010	0061	57	M	24	586	Musculoskel	Laminectomy		
104E	5011	0034	69	M	24	1748	GI	Elevated liver enzymes, jaundice		
					12	430	Cardiac	Ischemic heart disease, aortic stenosis		

Table 7.1.2.1.3
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
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Cutoff Date = 1 Sep 04

Trial	Center	Patient ID	Age (yrs)	Gender	Dose[1]	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	W/D?[5]
					8	479	GI	Multiple duodenal ulcers, upper GI bleed		
					14	570	GI	Diverticulosis		
					3	701	GI	Diverticulitis		
					3	739	Repro/ Uro	Benign prostatic hypertroph		
104E	5011	0040	63	M	9	1881	Cardiac	Chest pain		
104E	5014	0049	62	M	21	1122	Cardiac	Coronary artery disease		
					18	1227	Cardiac	Acute congestive heart fail		
104E	5016	0002	47	F	36	874	Repro/ Uro	Worsening ovarian cyst		
104E	5016	0004	54	M	24	248	GI	Colonic impaction		
104E	5016	0005	65	M	24	952	Cardiac	Acute myocardial infarction	same	y (death)
104E	5016	0006	65	M	4	1216	Neuro	Paraplegia	same	y
104E	5016	0007	63	M	13	1772	Cardiac	Cardiopulmonary arrest	same	y (death)
104E	5016	0010	52	M	30	1243	Cardiac	Coronary occlusion		
108	5010	8003	75	M	9	116	Neoplasm	Esophageal cancer, progression of cancer, liver metastases, gastrointestinal bleeding	same	y (death)
108	5020	8087	58	M	21	172	Skin	Foot ulceration, foot cellulitis		
108	5024	8493	68	F	13	171	Skin	Diabetic bullosis	Mentioned in narrative for decline in DLco	
108	5026	8345	55	M	18	21	Cardiac	Worsening coronary artery disease	Mentioned in narrative for decline in FEV1 and DLco; underwent CABG same day	
108	5024	8133	65	M	30	65	Repro/ Uro	Impotence		
108	5043	8113	49	M	35	144	Musculoskel	Pinched back nerve, left hip pain, capsulitis left shoulder	Capsulitis mentioned in narrative for decline in PFTs	
						144	Infec	Urinary tract infection	Not mentioned in narrative for decline in PFTs	
108	5048	8119	48	M	24	65	GI	Esophageal bleed	same	y (death)
108	5051	8555	56	F	19	70	Cardiac	Unstable angina		
108	5055	8537	63	M	45	44	Cardiac	Worsening coronary artery disease	Mentioned in narrative for later DC due to pulmonary edema	
108	5060	8092	49	M	20	143	GI	Pancreatitis		

Table 7.1.2.1.3
Serious Adverse Event Listing
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Trial	Center	Patient ID	Age (yrs)	Gender	Dose[1]	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	W/D?[5]
108	5060	8097	73	M	29	43	Cardiac	Congestive heart failure	Mentioned in narrative for decline in PFTs and bronchitis	
						43	Resp	Bronchitis	same	
108	5099	8038	39	M	10	54	Skin	Worsening foot ulcers	Mentioned in narrative for abnormal chest X-ray	
108	5138	8144	57	M	10	107	Musculoskel	Hip fracture	Mentioned in narrative for decline in FVC and DLco	
109	5042	0475	56	F	20	16	Cardiac	Acute myocardial infarction, unstable angina	Mentioned in narrative for discontinuation due to cough, and decline in PFTs	
109	5043	0031	65	F	18	75	Resp	Shortness of breath		y
						75	Skin	Ankle edema		
109	5044	0348	46	M	33	34	Cardiac	Chest pain		
109	5051	0737	56	M	27	18	Cardiac	Atypical angina		
109	5053	0354	42	M	33	71	Psych	Situational depression		
					39	83	Skin	Lower extremity cellulitis		
109	5071	0483	66	M	21	12	Metab	Hypoglycemic event		
111[6]	5002	0056	50	M	8	478	Neoplasm	Prostate adenocarcinoma		
111	5002	0447	70	M	13	42	Cardiac	Chest pain, coronary artery disease		
111	5002	8589	50	M	18	421	Cardiac	Myocardial infarction		
111	5005	8067	52	M	12	111	Musculoskel	Cervical bone spur	Event not in narrative for decline in PFTs	
						435	Resp	Not in applicant's Table 6.3.1.1	Bronchitis, 19% decline in total lung capacity, 23% decline in DLco (from narrative)	y
111	5005	8443	61	M	5	600	Vasc	Dry gangrene toe		
					10	715	Infec	Osteomyelitis toe		
111	5007	8044	64	M	8	839	GI	Hiatal hernia, chest pain		
					7	20	Cardiac	Chest pain		
					7	31	Vasc	Bilateral carotid artery stenosis		
					10	233	Vasc	Hypertension		
111	5008	1012	74	F	7	781	Cardiac	Angina attack		
					9	298	Musculoskel	Herniated disc		
111	5010	8105	49	F	21	245	Cardiac	Worsening coronary artery disease		

Table 7.1.2.1.3
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
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Cutoff Date = 1 Sep 04

Trial	Center	Patient ID	Age (yrs)	Gender	Dose[1]	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	W/D?[5]
111	5013	0068	54	F	69	248	Metab	Thyroid nodule	Not mentioned in narrative for decline in FVC	
111	5014	0389	57	M	24	328	Cardiac	Worsening coronary artery disease		
					24	470	Cardiac	Worsening coronary artery disease		
111	5014	0393	57	M	36	217	Cardiac	Worsening coronary artery disease		
					36	668	Musculoskel	Torn rotator cuff		
111	5016	8053	65	M	9	683	Musculoskel	Guillain Barre syndrome	Mentioned in narrative for HRCT and CXR findings	
111	5016	8054	78	F	6	486	GI	Gastroenteritis	Mentioned in narrative for decline in DLco	
111	5016	8065	72	M	16	874	Repro/ Uro	Hematuria		
111	5017	8450	73	M	14	469	Metab	Hypoglycemia, car accident	same	
111	5020	0244	63	F	14	576	General	Chest pain		
111	5022	1389	55	F	12	184	Accid/ Injur	Automobile accident, cervical spinal cord compression		
111	5024	0129	45	M	45	954 (112)	Metab	Obesity	Not mentioned in narrative for atelectasis and pneumonia	
					45	954 (116)	Resp	Atelectasis left lung	same	
					24	420	Cardiac	Chest pain	Mentioned in narrative for atelectasis and pneumonia	
					30	679	Infec	Pneumonia	same	
					30	756	GI	Cholecystitis	Mentioned in narrative for atelectasis and pneumonia	
111	5025	8021	51	M	18	582	Neoplasm	Basal cell carcinoma		
111	5025	8413	53	M	18	686 (43)	Neuro	Hydrocephalus		
					18	686 (133)	Neuro	Chronic bilateral subdural hematoma		
111	5026	0599	55	M	30	285	GI	Upper abdominal pain		
111	5026	0601	60	M	13	391	Cardiac	Coronary artery disease		
111	5028	0694	54	M	14	12	Cardiac	Coronary ischemia, coronary blockage	Mentioned in narrative for discontin due to cough; pt had PTCA	
111	5029	0336	41	M	26	678	Musculoskel	Ruptured disc		
111	5029	0436	67	F	17	747	Metab	Hyponatremia		
						747	General	Chest pain		
111	5029	0437	57	M	20	618	Neuro	Cerebrovascular accident	same	y
111	5029	1495	56	M	3	27	Cardiac	Worsening left chest pain, coronary		

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Trial	Center	Patient ID	Age (yrs)	Gender	Dose[1]	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	W/D?[5]
								artery disease		
111	5029	8371	58	M	28	728 (194)	Cardiac	Myocardial infarction	Not mentioned in narrative for decline in FVC	
					35	615	GI	Duodenal ulcer, esophagitis	Mentioned in narrative for decline in FVC	
111	5029	8421	68	F	19	498	Musculoskel	Worsening osteoarthritis left knee		
					19	634	Heme	Deep vein thrombosis		
					19	730	Musculoskel	Decreased range of motion knee		
111	5030	0616	61	M	31	1001 (71)	Infec	Pneumonia	same	
					30	439	Cardiac	Mitral valve regurgitation, multivessel coronary artery disease	Mentioned in narrative for pneumonia	
					30	498	Cardiac	Atrial fibrillation, atrial flutter	Not mentioned in narrative for pneumonia	
					30	696	Cardiac	Angina	Not mentioned in narrative for pneumonia	
111	5030	0617	58	M	19	447	GI	Pancreatitis, acute cholecystitis		
111	5030	8354	57	M	16	413	Infec	Cellulitis		
111	5030	8356	44	M	10	15	GI	Constipation	Not mentioned in narrative for hypoglycemia and MVA- see event in Study 111	
					10	15	Musculoskel	Mechanical low back pain	Not mentioned in narrative for hypoglycemia and MVA- see event in Study 111	
111	5031	0089	51	M	9	403	Cardiac	Inferior myocardial infarction		
					9	403	Neuro	Left arm paresthesia		
111	5031	0508	56	M	9	686	Repro/ Uro	Kidney stone		
111	5031	0512	43	M	12	143	Musculoskel	Bone spurs back		
111	5034	0366	75	M	12	1011	Cardiac	Worsening ischemic heart disease		
					13	321	Vasc	Right carotid artery occlusion		
111	5034	0368	64	M	51	229	Musculoskel	Spinal stenosis		
111	5034	1006	73	M	13	331	GI	Gastric ulcer, duodenal ulcer		
					13	334	Musculoskel	Exacerbation or arthritis hip		
111	5034	8035	68	M	30	727	Cardiac	Myocardial infarction, coronary artery disease	same	y
111	5034	8462	68	M	12	346	Cardiac	Worsening coronary artery disease		y

Table 7.1.2.1.3
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
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Cutoff Date = 1 Sep 04

Trial	Center	Patient ID	Age (yrs)	Gender	Dose[1]	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	W/D?[5]
111	5040	8445	72	F	12	888	Neoplasm	Renal cell carcinoma		
					9	97	Neoplasm	Papillary thyroid carcinoma		
					9	97	Metab	Primary hyperparathyroidism		
111	5040	8446	75	F	15	583	Neoplasm	Endometrial carcinoma		
					19	552	Musculoskel	Worsening degenerative joint disease		
111	5040	8448	76	M	17	15	Vasc	Carotid stenosis	Mentioned in narrative for decline in DLco	
111	5041	8024	62	M	17	256	Neoplasm	Cancer	Metastatic colon cancer	y
					15	789	Skin	Diabetic foot ulcer		
111	5041	8487	61	M	15	598	Cardiac	Coronary blockage		
					15	221	Skin	Worsening diabetic foot ulcer		
111	5042	0070	52	M	39	364	Vasc	Deep vein thrombosis		
111	5042	0476	58	M	19	718	General	Sarcoidosis	same	y
111	5042	0477	56	F	12	315	General	Chest pain	Mentioned in narrative for decline in DLco	
111	5042	8002	74	M	21	510	Neoplasm	Extranodal lymphoma	same	y
					21	510	Musculoskel	Pathological fracture	same	
111	5042	8479	62	M	8	95	Proc Comp	Postsurgical complication suture rupture	Mentioned in narrative for decline in FEV1	
						95	Cardiac	Inferior wall myocardial infarction	Mentioned in narrative for decline in FEV1	
111	5043	0394	72	M	12	350	Neoplasm	Prostate carcinoma		
111	5043	0395	45	F	6	625 (8)	Psych	Suicidal depression		
					4	249	Psych	Depression		
					4	267	Musculoskel	Disc herniation, worsening lower back pain		
					9	508	Musculoskel	Decreased left shoulder mobility		
111	5043	8113	50	M	36	133	Infec	Abscess of amputation stump	Not mentioned in narrative for decline in PFTs	
					36	266	Cardiac	Acute myocardial infarction	Mentioned in narrative for decline in PFTs	
					41	483	Cardiac	Worsening coronary artery disease	Mentioned in narrative for decline in PFTs	
111	5043	8547	61	M	8	60 (1)	Cardiac	Congestive heart failure, chest pain		y

Table 7.1.2.1.3
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Trial	Center	Patient ID	Age (yrs)	Gender	Dose[1]	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	W/D?[5]
111	5044	8013	73	M	12	669	Poisoning	Hyperammonemia, suspected selenium toxicity, altered mental status, acute renal failure, congestive heart failure	same	y
						669 (4)	Poisoning	Multiorgan failure	same	y (death)
111	5044	8364	53	F	9	26	Repro/ Uro	Kidney stone		
111	5045	1383	47	M	18	463	Cardiac	Congestive heart failure, coronary artery disease, possible pulmonary edema	Mentioned in narrative for incr ins Ab and decline in DLco	y
111	5045	8089	66	M	7	377	Musculoskel	Left shoulder pain, torn rotator cuff		
111	5046	0484	61	M	21	138	Infec	Pneumonia	same; also decline in DLco	
111	5046	8336	76	M	22	920	Cardiac	Acute myocardial infarction, cardiac arrest, worsening coronary artery disease	same; also had decline in DLco	y (death)
111	5048	0041	71	M	16	44	Neoplasm	Encapsulated fibrosarcoma	Not mentioned in narrative for decline in DLco	
					9	122	Cardiac	Unstable angina	Mentioned in narrative for decline in DLco	
111	5040	0042	48	M	40	70	Accid/ Injur	Temporary paralysis lower extremities, motor vehicle accident		
111	5048	0412	63	M	11	97	Cardiac	Coronary artery disease	Mentioned in death narrative	
					6	589	Accid/ Injur	Blunt force trauma to head and face while on coumadin, cerebral hemorrhage	same	y (death)
111	5048	0414	73	M	6	240	Cardiac	Acute myocardial infarction	same	y (death)
111	5048	0496	78	M	18	239	GI	Elevated liver function tests, elevated bilirubin, obstructive biliary tract disease		y
111	5048	8120	54	F	18	581	Cardiac	Congestive heart failure	Mentioned in narrative for decline in DLco	
					18	729 (132)	Resp	Shortness of breath	Mentioned in narrative for decline in DLco	
					16	166	Cardiac	Congestive heart failure	Mentioned in narrative for decline in DLco	
111	5048	8403	76	M	18	685 (85)	Vasc	Transient cerebral ischemia	Not mentioned in narrative for change in end-of-study HRCT	
					13	48	Vasc	Ischemic bowel, thrombosis of mesenteric artery	Not mentioned in narrative for change in end-of-study HRCT	

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Trial	Center	Patient ID	Age (yrs)	Gender	Dose[1]	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	W/D?[5]
					13	62	Cardiac	Congestive heart failure, atrial fibrillation	Not mentioned in narrative for change in end-of-study HRCT	
					13	106	Renal	Acute renal insufficiency, hematuria, hyperkalemia	Not mentioned in narrative for change in end-of-study HRCT	
					13	106	Heme	Worsening anemia		
111	5048	8428	57	M	12	222	Cardiac	Angina		
111	5048	8609	69	F	16	588	Infec	Urinary tract infection	Not mentioned in narrative for decline in FEV1 and DLco	
					7	4	Cardiac	Non-Q-wave myocardial infarction	Mentioned in narrative for decline in FEV1 and DLco	
111	5048	8610	54	F	18	675 (169)	Resp	Shortness of breath	same; also decline in DLco	
					24	305	Cardiac	Exertional angina	Not mentioned in narrative for dyspnea and decline in DLco	
111	5049	0119	50	F	10	6	Cardiac	Recurrent chest pain, worsening coronary artery disease		
111	5049	0570	68	F	6	12	Metab	Hyponatremia		
					7	603	Heme	Iron deficiency anemia		
					7	603	Renal	Renal insufficiency		
111	5049	0573	65	M	8	346	Cardiac	Atrial fibrillation		
111	5049	8378	67	M	15	722 (5)	Cardiac	Worsening coronary artery disease	same	y
111	5051	0737	58	M	41	478	Musculoskel	Carpal tunnel syndrome	Mentioned in narrative for decline in DLco	
111	5052	1007	52	M	28	817	Cardiac	Coronary artery disease	Mentioned in narrative for decline in PFTs	
					28	905	GI	Pancreatitis	Mentioned in narrative for decline in PFTs	
111	5053	0010	59	F	19	905 (147)	Neoplasm	Merkel cell carcinoma		
					25	381	Cardiac	Coronary artery disease		
111	5053	0353	65	M	18	84	Resp	Abnormal pulmonary function test	Worsening pulmonary function	y
111	5053	0354	42	M	39	29	Infec	Recurrent right leg cellulitis		
					13	134	Skin	Exacerbation of bilateral foot ulcers		
111	5054	8381	54	M	18	359	Cardiac	Myocardial infarction		
111	5055	0581	70	M	44	717	Cardiac	Exacerbation of congestive heart failure	same	y
111	5055	8537	65	M	54	356	Resp	Pulmonary edema	same; reason for discontinuation changed from original reason of pulm	y

Table 7.1.2.1.3
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
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Trial	Center	Patient ID	Age (yrs)	Gender	Dose[1]	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	W/D?[5]
									edema to nonserious decrease in pulm function	
111	5058	1078	65	M	7	113	Infec	Cellulitis right leg		
111	5060	0664	56	M	19	49	Cardiac	Acute myocardial infarction	same	
					19	98	Cardiac	Acute myocardial infarction	same	y
111	5060	0665	70	M	34	234	Infec	Pneumonia	same	
111	5060	0672	73	M	21	658	Cardiac	Myocardial infarction	same	
					21	658	Neoplasm	Rectal tumor	Malignant rectal tumor	y
					21	663 (29)	Cardiac	Recurrent myocardial infarction	same	
111	5060	8041	68	M	54	218	Musculoskel	Left knee pain	Mentioned in narrative for pneumonia and decline in DLco	
111	5060	8062	55	M	20	79	Proc Comp	Worsening of incisional hernia		
111	5060	8110	53	M	22	562	Cardiac	Unstable angina	same; underwent CABG	y
111	5062	0641	70	M	8	1	Musculoskel	Increased worsening of rotator cuff tendonitis		
111	5062	0642	49	M	41	282 (22)	Cardiac	Coronary artery disease	same	
					41	181	Resp	Worsening pulmonary function tests	same	
111	5069	8393	69	F	13	99	Infec	Infected left knee prosthesis		
					13	99	Proc Comp	Left knee reconstruction		
					16	350	Cardiac	Recurrent atrial fibrillation, congestive heart failure		
111	5070	0721	62	M	5	871	Cardiac	Exacerbation atrial fibrillation	Mentioned in narrative for decline in FEV1	
111	5070	0721	60	M	5	212	Eye	Left eye vitreous hemorrhage		
					5	47	Cardiac	Recurrent atrial fibrillation		
					5	269	Cardiac	Recurrent atrial fibrillation		
					4	363	Cardiac	Recurrent atrial fibrillation		
					5	234	Cardiac	Recurrent atrial fibrillation		
111	5070	8031	48	M	30	829	Resp	Respiratory distress	same	y
					20	279	Infec	Perianal abscess	Not mentioned in narrative for resp distress	
111	5071	0073	69	F	8	561	Neoplasm	Bowel tumor, signet ring cell carcinoma	Mentioned in narrative for decline in TLC	
					8	691	Neoplasm	Anemia, neutropenia, bacterial cellulitis left hand IV site, chemotherapy	Mentioned in narrative for decline in TLC	

Table 7.1.2.1.3
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All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
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Cutoff Date = 1 Sep 04

Trial	Center	Patient ID	Age (yrs)	Gender	Dose[1]	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	W/D?[5]
111	5071	8405	71	M	9	838	Infec	Cellulitis	Not mentioned in narrative for decline in PFTs and pneumonia	
111	5071	8406	74	F	9	669	Vasc	Transient ischemic attack	Mentioned in narrative for decline in DLco	
111	5071	8429	70	M	12	758	Cardiac	Coronary artery stenosis		
111	5072	0504	55	M	30	1072	Neoplasm	Cancer large intestine	Mentioned in narrative for decline in DLco	
111	5072	0507	73	M	5	478	Vasc	Ruptured cerebral hemorrhage, subarachnoid hemorrhage, subdural hematoma	same	y
					5	478 (7)	Vasc	Vasospasm, pulmonary emboli	same	
					5	478 (7)	Infec	Pneumonia	same	
111	5072	8072	49	F	9	72 (11)	Accid/ injur	Accidental fall, contusions		
					9	72 (11)	Vasc	Acute vein thrombophlebitis left leg, left femoral line		
111	5073	0542	65	F	10	512	GI	Cholelithiasis	Mentioned in narrative for decline in DLco	
111	5073	0562	64	F	23	229	Neoplasm	Breast cancer		
111	5073	8039	63	F	17	716	Neuro	Nerve root compression	Not mentioned in narrative for decline in DLco	
111	5073	8571	60	F	18	52	Cardiac	Recurrent sinus tachycardia		
					18	379	GI	Sialolithiasis		
111	5073	8572	61	M	12	159	Cardiac	Non-Q wave myocardial infarction		
					12	178	Cardiac	Acute coronary syndrome		
					12	251	Cardiac	Possible unstable angina		
					13	338	Cardiac	Probable ischemic heart episodes		
					16	477	Musculoskel	Broken leg		
111	5073	8585	72	F	18	775 (74)	Cardiac	Angina attack	Mentioned in narrative for decline in DLco	
					18	350	Cardiac	Unstable angina	Mentioned in narrative for decline in DLco	
111	5074	0110	65	M	13	167	GI	Subacute intestinal obstruction	Mentioned in narrative for bronchitis	
					13	167	Repro/ Uro	Left renal calculus, left hydronephrosis	Mentioned in narrative for bronchitis	
					13	167	Infec	Chronic pyelonephritis	Mentioned in narrative for bronchitis	
					32	353	Infec	Acute bronchitis	same	

Table 7.1.2.1.3
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
Treatment = Inhaled Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Patient ID	Age (yrs)	Gender	Dose[1]	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	W/D?[5]
111	5076	0700	65	M	19	336	Cardiac	Myocardial infarction	same	y
					19	336	Cardiac	Aortic valve stenosis	same	
111	5099	8038	40	M	24	149	Infec	Cellulitis left leg		
111	5112	1465	76	F	7	344	Neoplasm	Hamartoma right upper lobe lung		
111	5113	1013	46	M	24	520	Infec	Pneumonia		
111	5114	1022	71	M	10	662	Neoplasm	Prostate cancer		y
111	5116	1059	60	M	18	516	Neoplasm	Urothelial carcinoma		
111	5123	0796	55	F	11	403	Infec	Facial cellulitis		
111	5127	0161	43	M	18	86	Accid/ Injur	Fracture left wrist, accidental fall	Mentioned in narrative for d/c due to cough	
111	5127	0652	65	F	3	217	Eye	Detached retina right eye		
111	5127	0655	65	M	14	249	Musculoskel	Worsening arthritis		
					11	544	Neuro	Syncope		
111	5127	0656	72	M	12	432	Neoplasm	Squamous cell lung carcinoma	same	y
111	5129	0219	52	M	18	100	GI	Abdominal pain		
111	5131	1074	62	F	36	229	Accid/ Injur	Hemothorax, fall from horse	Mentioned in narrative for decline in FEV1	
111	5134	1051	58	F	9	609 (78)	Resp	Restrictive lung disease	same	
A2171001	0004	0025	63	M	20	307	Cardiac	Acute myocardial infarction, ventricular tachycardia, ventricular fibrillation, congestive heart failure	same	y (death)
						307	Infec	Pneumonia, sepsis	same	
A2171001	0004	3014	56	F	7	275	Neuro	Transient ischemic attack		
					7	328	Cardiac	Chest pain		
A2171001	0005	1029	49	M	18	351	Neoplasm	Vocal cord polyp	same	
A2171001	0005	1030	45	F	45	294 (137)	Resp	Asthma attack	same	
						294 (137)	Cardiac	Chest pain	same	
A2171001	0005	0031	37	F	8	132	Cardiac	Unspecified chest pain		
A2171001	0011	0041	62	F	7	141	GI	Biliary lithiasis		
A2171001	0015	1051	72	F	21	157	Cardiac	Angina pectoris		
A2171001	0018	1058	56	F	16	224	Musculoskel	Rheumatoid arthritis		
A2171001	0035	1076	62	F	17	207	Neoplasm	Basal cell carcinoma of skin		
A2171001	0045	3036	77	F	9	366 (1)	Neuro	Syncope		
						366 (1)	Heme	Anemia		

Table 7.1.2.1.3
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
Treatment = Inhaled Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Patient ID	Age (yrs)	Gender	Dose[1]	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	W/D?[5]
A2171001	0046	3370	57	M	12	298	GI	Inguinal hernia		
A2171001	0056	0124	63	M	14	371	GI	Hernia inguinalis		
A2171001	0059	0135	62	M	3	175 (14)	Neoplasm	Urticaria	same	y
						175 (14)	Neoplasm	Urothelium carcinoma	no narrative	
A2171001	0060	1138	58	M	12	64	Cardiac	Abnormal treadmill test		
A2171001	0079	0178	63	F	13	470	Neoplasm	Colon carcinoma	no narrative	
A2171001	0090	1198	67	F	8	84	Vasc	Hypotension		
A2171001	0090	0198	64	F	9	330	Neoplasm	Gastric cancer	no narrative	
A2171001	0093	1209	64	M	9	109	Cardiac	Left anterior descending artery stenosis	same	
A2171001	0096	0219	76	M	7	154	Accid/ Injur	Motor vehicle accident, concussion, forehead wound		
A2171001	0110	1243	56	M	23	186	Accid/ Injur	Fractured right heel		
A2171001	0134	1373	66	M	4	13	Cardiac	Myocardial infarction, acute cardiac failure	same	y
A2171001	0138	0278	70	F	5	379	Musculoskel	Coxarthrosis		
A2171001	0140	0303	58	F	15	228	Vasc	Segmental stenosis of left internal carotid		
A2171001	0141	3051	50	M	13	734	Cardiac	Myocardial infarction		
A2171001	0143	3084	63	F	36	532	Accid/ Injury	Fracture right arm		
A2171001	0145	1305	57	F	39	770	Cardiac	Acute myocardial infarction		
A2171001	0145	0305	52	M	32	240	Infec	Acute appendicitis, gangrene appendix		
A2171002	0002	7337	69	M	9	673	Accid/ Injur	Fall	Fall, head trauma, loss of consciousness	y
A2171002	0004	5025	53	M	9	3	Infec	Herpes zoster		
						3	Musculoskel	Ruptured disc		
A2171002	0005	6031	47	F	20	559	Vasc	Arterial hypertension		
A2171002	0005	6032	42	M	3	177	Cardiac	Palpitations		
A2171002	0037	6061	65	M	9	431	Cardiac	Acute myocardial infarction		
A2171002	0037	6062	55	M	15	396	Cardiac	Unstable angina	same	
					15	180	Infec	Bronchopneumonia	same; also decline in FEV1	
A2171002	0043	6002	53	F	4	44	Repro/ Uro	Disturbance of micturition		
A2171002	0043	6003	62	M	24	435	Eye	Cataract		
A2171002	0047	7051	59	M	12	44	GI	Elevated gamma glutamyl transferase		
A2171002	0049	7354	58	F	9	522	Metab	Hypothyroidism		

Table 7.1.2.1.3
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
Treatment = Inhaled Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Patient ID	Age (yrs)	Gender	Dose[1]	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	W/D?[5]
A2171002	0054	5106	69	M	7	582	Vasc	Hypertensive crisis		
A2171002	0056	1002	56	M	9	440	GI	Acute incarceration inguinal hernia		
A2171002	0067	5125	67	M	18	864	Repro/ Uro	Nephritic colic		
A2171002	0074	5149	62	M	11	338	Neuro	Facial paralysis		
A2171002	0074	6149	53	M	7	563	Repro/ Uro	Renal colic		
A2171002	0085	5171	68	M	10	242	Cardiac	Recurrent tachyarrhythmia	Tachycardia mentioned in narrative for decline in FEV1 and FVC	
					12	175	Cardiac	Cardiac insufficiency, worsening of coronary artery disease	Cardiomegaly mentioned in narrative for decline in FEV1 and FVC	
A2171002	0089	5183	70	M	9	253	Musculoskel	Thoracalgia		
A2171002	0108	5285	64	M	12	455	Neuro	Transient ischemic attack		
A2171002	0119	5234	50	M	12	209	Musculoskel	Calf pain		
A2171002	0119	5236	67	M	11	666	Neoplasm	Metastatic bronchial carcinoma	same	y
A2171002	0131	5262	54	F	14	289	Infec	Pneumonia	same	
A2171002	0133	6266	64	M	12	228	Resp	Pneumothorax	Event not mentioned in bronchial carcinoma narrative	
					11	676	Neoplasm	Metastatic bronchial carcinoma	same	
A2171002	0131	5262	54	F	14	289	Infec	Pneumonia		
A2171002	0141	7398	64	M	16	481	Musculoskel	Bunion		
A2171002	0141	7429	62	M	21	267	Vasc	Arterial hypertensive crisis, epistaxis	Hypertensive crisis not mentioned in narrative for decreased FEV1	
A2171002	0141	8038	75	F	9	671	Neoplasm	Duodenal carcinoma		
A2171002	0141	8060	70	F	12	638	Neoplasm	Chronic myelogenous leukemia		
						726	Neoplasm	Blast cell crisis		y
A2171002	0141	8376	46	F	11	15	Metab	Cushing Syndrome suspect		
A2171002	0142	7373	64	M	8	448	Vasc	Cerebellar ischemic vascular accident	Mentioned in narrative for decline in DLco	
A2171002	0142	8044	63	M	3	600	GI	Inguinal hernia		
A2171002	0142	8380	70	M	12	25	GI	Acute biliary pancreatitis	same	
A2171002	0143	8030	56	M	9	191	Cardiac	Coronary artery disease	Event not mentioned in narrative for decline in DLco; arterial thrombosis mentioned for Study Days 204-209	y
A2171007	5141	0006	29	F	3	1 (5)	Repro/ Uro	Prolapsed umbilical cord- baby, pregnant pregestational diabetic	same	y
						1 (28)	Neuro	Sagittal sinus thrombosis		

Table 7.1.2.1.3
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
Treatment = Inhaled Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Patient ID	Age (yrs)	Gender	Dose[1]	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	W/D?[5]
A2171017	1002	1008	66	M	45	124	General	Atypical chest pain		
A2171017	1003	1001	61	M	57	199	Accid/ Injur	Fall		
A2171017	1022	1003	51	F	10	289	Repro/ Uro	Unable to void		
							Metab	Worsening panniculus		
A2171017	1028	1005	34	M	32	235	Infec	Pneumonia		
A2171017	1030	1001	55	F	22	107	General	Weakness		
					27	174	Musculoskel	Musculoskel chest pain		
A2171017	1031	1009	70	M	18	28	Cardiac	Congestive heart failure, pulmonary edema		y
A2171017	1040	0181	59	F	21	143	Neuro	Stroke		
A2171017	1062	1004	64	F	34	64	Skin	Left leg cellulitis		
A2171017	1062	1007	49	M	32	51	Cardiac	Increased heart rate		
					57	115	Cardiac	Coronary artery disease		
A2171017	1075	0391	55	F	36	30	GI	Nausea, vomiting		
						30	Neuro	Dizziness		
A2171027	1016	0648	49	M	3	90	Cardiac	Myocardial infarction	Myocardial infarction after hypoglycemic episode	y (death)
A2171027	5148	1329	43	M	13	6	Metab	Hypoglycemic episode, loss of consciousness	same	
A2171029	1006	1607	53	F	4	671	Vasc	Exacerbation of worsening hypertension		
A2171029	1010	0374	60	F	15	114	Cardiac	Atypical chest pain, coronary artery disease		
					12	174	Psych	Exacerbation bipolar disorder		
A2171029	1017	0541	63	M	14	211	Neuro	Neuritis		
A2171029	1019	1730	62	M	21	95	GI	Obstructed bile duct		
A2171029	1021	0607	58	M	8	271	Infec	Appendicitis		
A2171029	1025	1904	60	M	16	523	Cardiac	Multivessel coronary artery disease		
						528	GI	Partial small bowel obstruction		
A2171029	1025	1913	65	F	11	258	Resp	Asthma exacerbation	same	y
A2171029	1026	0659	61	M	22	226	Neoplasm	Colon carcinoma with metastases to kidney, liver, pancreas, lung	same	y (death)
A2171029	1038	0847	63	M	12	339	Accid/ injur	Torn tendon right knee, accidental [illegible]		
A2171029	1041	0897	57	M	18	432	Renal	Acute renal failure, hyperkalemia		
A2171029	1043	2257	46	F	19	533	GI	Acute cholecystitis, abdominal pa[illegible]		

Table 7.1.2.1.3
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
Treatment = Inhaled Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Patient ID	Age (yrs)	Gender	Dose[1]	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	W/D?[5]
A2171029	1043	2260	57	M	14	123	Infec	Cellulitis	Mentioned in narrative for incr ins Ab	
A2171029	1044	0958	74	M	20	460	Cardiac	Non-Q wave myocardial infarction		
					20	550	General	Noncardiac chest pain		
					19	709	Vasc	Orthostatic hypotension		
A2171029	1044	0960	53	F	16	583	Musculoskel	Lumbar spondyloradiculopathy		
A2171029	1045	2319	68	M	4	21	Resp	Bronchospasm NOS, hypersensitivity NOS	Acute bronchospasm, "questionable" allergic reaction to inhaled insulin	y
A2171029	1048	2495	51	M	18	364	Neoplasm	Prostate cancer		
A2171029	1049	2554	52	F	9	11	Infec	Right tonsil abscess		
A2171029	1057	4388	63	F	9	184	Proc comp	Posthysterectomy adhesions	Mentioned in narrative for bronchitis	
					15	476	Proc Comp	Posthysterectomy adhesions		
					12	218	Resp	Acute bronchitis	same	
A2171029	1059	2607	45	M	13	224	Metab	Hypoglycemic episode, seizure	same	
						138	Allerg	Allergic reaction to fexofenadine	Not mentioned in narrative for hypoglycemic episode	
A2171029	1069	1258	45	M	19	525	Infec	Infected fire ant bite		
A2171029	1069	1261	67	M	18	148	Infec	Diverticulitis		
A2171029	1069	1266	55	M	30	417	Neuro	Transient ischemic attack		
A2171029	1069	1280	52	M	30	180	Neuro	Migraine		
A2171029	1073	3086	66	M	7	514	Cardiac	Recurrent arrhythmia		
A2171029	1075	1371	53	M	20	65	Infec	Bacterial osteomyelitis right foot		
A2171029	1075	1373	70	M	9	394	Neuro	Transient global amnesia		y
A2171029	1075	1375	48	F	9	299	Neuro	Left Bell's palsy		
A2171029	1078	1490	58	M	12	16	Cardiac	Coronary artery blockage		
A2171029	1079	3260	69	M	15	225	Infec	Osteomyelitis, worsened back pain		y
A2171029	1081	3381	62	M	18	431	Infec	Urinary tract infection		
A2171029	1081	3384	38	M	18	556	Musculoskel	Muscle pain in back	Not mentioned in narrative for hypoglycemia and seizure	
A2171029	1081	3387	45	M	17	359	Resp	Bronchitis	same	
A2171029	1081	3390	58	F	15	333	Cardiac	Myocardial infarction		
A2171029	1083	3442	56	F	8	156	Cardiac	Myocardial infarction, hypotensive episode		
A2171029	1084	3497	48	M	18	279	Infec	Bilateral lower extremity cellulitis		
A2171029	1085	3552	51	M	11	45	Resp	Respiratory failure	same	y
A2171029	1085	3554	73	M	27	59	Neoplasm	Prostate cancer	same	y

Table 7.1.2.1.3
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
Treatment = Inhaled Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Patient ID	Age (yrs)	Gender	Dose[1]	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	W/D?[5]
A2171029	1088	3616	76	M	17	517	GI	Gastrointestinal bleed, epigastric pain		y
						517	Metab	Hyperglycemia		
A2171029	1093	3854	64	F	10	14	Metab	Hypoglycemia, unconsciousness	same	
					10	21	Metab	Hypoglycemia, unconsciousness	same	
A2171029	1093	3857	62	M	5	316	Metab	Hypoglycemia, loss of consciousness	same; also fall with front teeth injury	
					5	336	Metab	Recurrent hypoglycemia	same	
A2171029	1096	4030	63	M	6	596	Cardiac	Worsening bradycardia		
A2171029	1100	3323	58	M	9	410	GI	Esophageal spasm		
A2171029	1101	4271	60	M	6	168	Cardiac	Congestive heart failure		y
A2171029	1113	5158	68	F	Dose unk	406	Resp	New onset asthma, cough	same	y
A2171029	1115	5408	56	F	8	141	Cardiac	Myocardial infarction		
A2171029	1119	5633	59	F	7	39	Cardiac	Unstable angina		y
A2171029	1119	5661	57	F	7	103	Neoplasm	Cystic nephroma		
A2171030	1015	1393	72	M	12	9	Metab	Ketoacidosis	same	
					12	35	Infec	Pneumonia	same	
A2171030	1018	1691	63	M	24	69	Resp	Recurrence of exacerbation of COPD	same	y
A2171030	1026	2489	68	F	12	191	Resp	COPD exacerbation		
A2171030	1043	4174	64	M	8	85	Accid/ Injur	Accidental fall		
A2171030	1049	5069	75	M	25	26	Accid/ Injur	Fall down stairs, right wrist fracture, fractured ribs		
A2171036	5005	1002	70	M	9	73	GI	Constipation		
						73	Repro/ Uro	Dysuria		
A2171036	5005	1006	70	M	9	97	Cardiac	Myocardial infarction	same	y (death)
A2171036	5007	1006	65	M	8	131	Cardiac	Exacerbation of coronary artery disease		
A2171036	5008	1003	57	M	9	72	Musculoskel	Worsening osteoarthritis knee		
					11	228	Cardiac	Exacerbation coronary artery disease		
A2171036	5010	1004	Unk	M	7	229	Metab	Multinodular goiter		
A2171036	5010	0071	67	M	25	22	Neoplasm	B-cell lymphoma		
A2171036	5011	1004	48	F	18	398	Cardiac	Myocardial infarction	same	y (death)
A2171036	5011	1006	69	M	19	111	Repro/ Uro	Worsening erectile dysfunction		
A2171036	5013	1001	70	F	15	49	Infec	Pyelonephritis		
A2171036	5014	1002	65	M	18	457	Cardiac	Cardiac pacemaker insertion		

Table 7.1.2.1.3
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
Treatment = Inhaled Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Patient ID	Age (yrs)	Gender	Dose[1]	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	W/D?[5]
A2171036	5014	1006	54	M	7	391	Cardiac	Angina, coronary artery disease		

Includes Studies 1001, 1002, 1005, 1007, 1009, 1017, 1022, 1026, 1027, 1028, 1029, 102E, 103, 1030, 1036, 104, 104E, 106, 107, 108, 109, 110, 111
1 Dose at time of adverse event
2 Duration of exposure in days at time of event. If event occurred after discontinuation, the number of days after discontinuation is included in parentheses
3 Applicant's assigned term
4 Term used by investigator or patient; nb- applicant provided SAE narratives only for pulmonary SAEs and SAEs that led to death or discontinuation
5 If patient withdrew due to this adverse event, noted with a "y"
6 For Study 111, an extension of several clinical trials, it was not clear from the applicant's Table 6.3.1.1 whether a patient had Type 1 or Type 2 diabetes. Readers who wish to examine the source Table 6.3.1.1 can tell what type of diabetes the patient had by looking at the 5th number of the patient's identification number in the applicant's Table 6.3.1.1. If this number was a zero, 1 or 8, the patient had Type 2 diabetes. If it was any other number, the patient had Type 1 diabetes (telephone communications with Mr. Brian Green, Pfizer Regulatory Affairs, 31 Mar 05 and 6 Apr 05)
Source: Applicant's Table 6.3.1.1, Section 2.7.4, pgs 1903-2296

Table 7.1.2.1.4
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
Treatment = SQ Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Pt ID	Age	Gender	Dose[1] (Units), Type SQ Insulin	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
103E	5011	0080	59	F	Isophane 48	413	GI	Cholelithiasis	Mentioned in narrative for pneumonia	
						413	Resp	Pneumonia	same	
						609	GI	Incisional ventral hernia	Mentioned in narrative for pneumonia	
103E	5013	0210	57	F	Isophane 56	54	GI	Fecal impaction		
						54	Urinary	Urinary retention		
108	5007	8056	76	F	Isophane 47, Regular 21	85	Cardiac	Myocardial infarction, coronary artery disease	Mentioned in narrative for abnl end-of-study CXR	
108	5024	8566	60	F	Isophane 104, Regular 47	168	Musculoskel	Back pain		
108	5030	8356	43	M	Isophane 49, Regular 30	46	Metab	Hypoglycemia, possible accidental drug overdose, unconsciousness,	same	

Table 7.1.2.1.4
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
Treatment = SQ Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Pt ID	Age	Gender	Dose[1] (Units), Type SQ Insulin	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
								motor vehicle accident		
108	5037	8465	60	M	Isophane 12, Regular 29	85	Cardiac	Cardiac ischemia	same	y
108	5041	8506	69	M	Isophane 29, Regular 8	73	Accid/ Injur	Motor vehicle accident, broken pelvis, fractured rib	same	y
108	5042	8475	41	M	Isophane 70, Regular 54	63	Infec	Pneumonia, respiratory distress	same	
						63	GI	Ulcerative esophagitis, gastritis, duodenal ulcer	Mentioned in narrative for pneumonia	
						63	Cardiac	Paroxysmal atrial fibrillation	Not mentioned in narrative for pneumonia	
						63	Heme	Idiopathic anemia	Mentioned in narrative for pneumonia	
108	5048	8428	56	M	Isophane 50, Regular 32	42	Cardiac	Coronary artery block		
108	5049	8378	65	M	Isophane 75, Regular 25	184	Neuro	Stroke		
108	5051	8556	66	F	Isophane 64, Regular 23	140	Neoplasm	Ovarian cancer		
108	5060	8041	67	M	Isophane 54, Regular 24	142	Cardiac	Unstable angina		
						142	Infec	Bilateral pneumonia		
108	5073	8572	60	M	Isophane 100, Regular 37	128	Cardiac	Non-Q wave myocardial infarction		
108	5027	8514	41	F	Isophane 25, Regular 7	89	Skin	Cellulitis		
A2171001	0112	3366	78	F	Isophane 14, Mixtard 52, Metformin 2000, Glibenclamide 7.5	582	Musculoskel	Polymyalgia rheumatica		
					Isophane 64, Mixtard 52, Metformin 2000, Glibenclamide 7.5	596	Metab	Hypoglycemia, syncope		
						596	Musculoskel	Exacerbation of polymyalgia rheumatica		
					Isophane 64, Mixtard 60, Metformin 2000, Glibenclamide 7.5	751	Metab	Hyperglycemia		
A2171027	1002	0050	50	M	Isophane 20, Lispro 3	106	GI	Small bowel obstruction		
						126	GI	Recurrent small bowel obstruction		
						136	GI	Recurrent small bowel obstruction		
A2171027	1008	0351	54	M	Glargine 18, Regular 23	19	Metab	Hypoglycemic episode, loss of consciousness	same	
A2171027	1010	0398	32	M	Glargine 50, Regular 33	56	Accid/ injur	Bone fracture accidental	Fracture of left knee	y
A2171027	1010	0401	39	F	Isophane 48, Regular 23	84	Metab	Hypoglycemia	same	
A2171027	1015	0601	48	M	Isophane 14, Lispro 21	38	Cardiac	Heart attack		

Table 7.1.2.1.4
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
Treatment = SQ Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Pt ID	Age	Gender	Dose[1] (Units), Type SQ Insulin	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
A2171027	1016	0643	30	M	Glargine 32, Lispro 30	25	Metab	Hypoglycemia, loss of consciousness	Hypoglycemia, loss of consciousness, car accident	
A2171027	1019	0790	27	F	Isophane 40, Lispro 18	139	Metab	Hypoglycemia	same	
A2171027	1027	1583	50	M	Isophane 64, Lispro 30	188	Cardiac	Myocardial infarction		
A2171027	5138	1232	61	M	Isophane 16, Lispro 25	30	Metab	Hypoglycemia	same	
					Isophane 16, Lispro 24	135	Metab	Hypoglycemic, coma	Hypoglycemia, not arousable	
A2171028	1051	1280	73	M	Isophane 28, Regular 44	277	Musculoskel	Lumbar vertebrae canal stenosis		
A2171029	1005	0181	65	M	Glargine 20, Lispro 16	Not reported (NR)	Musculoskel	Paracentral disc protrusion		
						170	Cardiac	Atrial fibrillation		
						172	Cardiac	Atrial fibrillation recurrence		
A2171029	1005	0189	53	F	Glargine 40, Aspart 50	328	Neoplasm	Carcinoid tumor stomach		
A2171029	1006	1608	56	M	Glargine 30, Lispro 34	548	Neuro	Cerebrovascular accident		
A2171029	1007	0242	42	M	Glargine 40, Aspart 40	498	Neuro	Transient ischemic attack		
A2171029	1014	1667	58	M	Glargine 75, Lispro 41	227	Cardiac	Coronary artery disease	Not mentioned in narrative for dyspnea and declines in FEV1, DLco, FVC, TLC	
						227	Resp	Shortness of breath	Dyspnea	
A2171029	1017	0542	67	M	Glargine 14, Lispro 10	4	Infec	Left foot cellulitis, left heel ulceration	same	
					Glargine 20, Lispro 20	150	Metab	Hypoglycemic episode, loss of consciousness	same	
						149	Infec	Osteomyelitis left 3rd toe	same	
A2171029	1019	1727	59	F	Isophane 30, Lispro 12	734	GI	Pancreatitis	same	
A2171029	1020	1788	46	M	Glargine 45, Regular (dose unk)	512	Vasc	Deep vein thrombosis		
A2171029	1022	1847	66	M	Glargine 10, Lispro 19	121	Metab	Hypoglycemic event, unconsciousness	same	
A2171029	1025	1909	57	F	Glargine 35, Aspart 60	59	Metab	Hypoglycemia, panic attack	same	
					Glargine 30, Aspart 45	231	Psych	Bipolar affective disorder aggravated	same	
					Glargine 35, Aspart 63	290	Psych	Bipolar affective disorder aggravated	same	
					Glargine 39, Aspart 86	399	Psych	Relapse of depression	same	
					Glargine 37, Aspart 54	476	Psych	Relapse of depression	same	

Table 7.1.2.1.4
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
Treatment = SQ Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Pt ID	Age	Gender	Dose[1] (Units), Type SQ Insulin	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
A2171029	1033	2144	61	M	Glargine 30, Aspart 27	326	Infec	Pneumonia	same	
A2171029	1039	3022	65	M	Isophane 90, Regular 60	187	Neoplasm	Prostate adenocarcinoma	same	y
A2171029	1044	0959	71	F	Isophane 65, Lispro 15	109	GI	Stomach pain	same	
					Isophane 62, Lispro 14	131	Metab	Hypoglycemic episode	same	
A2171029	1044	0961	51	M	Isophane 108, Regular 72	239	Metab	Hypoglycemia, acute cataplexy, loss of consciousness	same	
A2171029	1044	0965	65	M	Isophane 70, Regular (dose unk)	617	General	Chest pain		
A2171029	1048	2494	77	F	Glargine 24, Lispro 5	77	Accid/ Injur	Fractured right hip	Not mentioned in narrative for colon cancer	
					Glargine 25, Lispro 15	300	Neoplasm	Colon cancer	same	
					Glargine 15, Lispro 10	380	GI	Vomiting and diarrhea during chemotherapy, weakness	Not mentioned in narrative for colon cancer	
A2171029	1049	2560	58	M	Isophane 60, Regular 20	163	Infect	Cellulitis foot		
						179	Infect	Infected plantar ulcer		
A2171029	1059	2608	37	M	Mixtard (dose unk)	488	Accid/ injur	Motorcycle accident, multiple rib fractures, bilateral pneumothorax	same	
A2171029	1059	2615	44	M	Glargine 41, Lispro 50	207	GI	Partial small bowel obstruction		
					Glargine 40, Lispro 40	365	GI	Obstructed organoaxial volvulus of stomach, recurrent incarcerated incisional hernia, vomiting		
						366	Metab	Hyperglycemia		
A2171029	1064	1080	73	M	Mixtard 59	165	Musculoskel	Progressive left knee pain, osteoarthritis		
A2171029	1065	2794	48	M	Glargine 50, Lispro 23	179	Metab	Hypoglycemia, unconsciousness, seizure	Hypoglycemia, unconsciousness, seizure, tongue laceration	
A2171029	1069	1283	63	F	Isophane 28, Aspart 50	234	Cardiac	Angina pectoris		
A2171029	1074	3142	52	F	Glargine 65, Lispro 30	132	Cardiac	Aortic insufficiency, congestive heart failure, shortness of breath	same	
A2171029	1077	1432	53	F	Glargine 28, Lispro 21	394	Infec	Gastrointestinal infection, vomiting		
A2171029	1078	1491	67	M	Glargine 62, Regular 44	590	Cardiac	Coronary occlusion	Mentioned in narrative for respiratory failure	
							Resp	Hypoxemia	Respiratory failure	
							Renal	Acute renal failure	Mentioned in narrative for respiratory failure	

Table 7.1.2.1.4
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
Treatment = SQ Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Pt ID	Age	Gender	Dose[1] (Units), Type SQ Insulin	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
A2171029	1081	3380	55	F	Glargine 35, Regular 33	79	Metab	Hypoglycemia, loss of consciousness	same	
					Glargine 35, Regular 33	47	Resp	Bronchitis, acute chest pain	Chest pain mentioned in narrative for hypoglycemia	
					Glargine 48, Regular 13	182	Metab	Hypoglycemic episode	Hypoglycemia, jerking movements, unawareness of surroundings	
A2171029	1088	3613	72	M	Mixtard 48	253	Metab	Hypoglycemia	same	
					Mixtard 48	275	Metab	Hypoglycemia	Hypoglycemia, unconsciousness	
A2171029	1088	3619	69	M	Isophane 12, Regular 25, Lispro 29	575	General	Pain exacerbated		
						575	Neuro	Confusion		
A2171029	1096	4027	61	M	Isophane 27, Regular 35	452	Metab	Hypoglycemia	same	
					Isophane 29, Regular 42	489	Metab	Hypoglycemia	same	
A2171029	1101	4269	49	F	Isophane 46, Lispro 25	189	Neoplasm	Ovarian cancer metastatic		y
A2171029	1110	4977	43	F	Glargine 88, Lispro 45	126	Musculoskel	Multiple sclerosis		
A2171029	1115	5392	55	M	Glargine 70, Regular 18	9	Cardiac	Worsening coronary artery disease		
A2171029	1115	5400	48	F	Isophane 48, Regular 36	464	Psych	Bipolar disorder		
A2171029	1115	5405	56	M	Lispro 31	350	Cardiac	Atrial fibrillation		
A2171029	1118	5583	73	M	Isophane 98, Lispro 37	288	GI	Recurrent inguinal hernia		
						294	Proc Comp	Surgical wound infection		
A2171029	1118	5589	59	F	Isophane 30, Aspart 15	299	Musculoskel	Noncardiac chest muscle pain		
A2171029	1119	5652	76	F	Isophane 68, Regular 18	464	GI	Worsening cholelithiasis		
A2171030	1015	1394	77	M	Mixtard 126	6	Metab	Hypoglycemia, loss of consciousness, hypothermia	same	
						7	GI	Projectile vomiting, nausea		
A2171030	1017	1593	64	M	Isophane 42, Regular 9	329	Repro/ Uro	Bladder neck obstruction		
A2171030	1021	1989	72	M	Isophane 8, Regular 19, Lispro 9	152	GI	Inguinal hernia		
A2171030	1032	3085	64	M	Isophane 49, Regular 19, Metformin 1000, Glipizide 10	93	Cardiac	Myocardial infarction (pt also included in oral agents table)	same	y (death)
A2171030	1043	4176	69	F	Isophane 72, Aspart 54	819	Vasc	Uncontrolled hypertension		
A2171030	1056	5767	75	M	Isophane 57, Regular 60	NR	Cardiac	Myocardial infarction		
A2171030	1078	7941	57	M	Glargine 42, Lispro 48	350	General	Drug maladministration inadvertently used wrong insulin vial		

Table 7.1.2.1.4
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
Treatment = SQ Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Pt ID	Age	Gender	Dose[1] (Units), Type SQ Insulin	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
A2171030	1078	7944	55	M	Glargine 88, Lispro 66	1221	Cardiac	Exacerbation of coronary artery disease		

Includes Studies 1001, 1002, 1005, 1007, 1009, 1017, 1022, 1026, 1027, 1028, 1029, 102E, 103, 1030, 1036, 104, 104E, 106, 107, 108, 109, 110, 111
1 Dose at time of adverse event
2 Duration of exposure in days at time of event. If event occurred after discontinuation, the number of days after discontinuation is included in parentheses
3 Applicant's assigned term
4 Term used by investigator or patient; nb- applicant provided SAE narratives only for pulmonary SAEs and SAEs that led to death or discontinuation
5 If patient withdrew due to this adverse event, noted with a "y"
Source: Applicant's Table 6.3.1.1, Section 2.7.4, pgs 1903-2296

Table 7.1.2.1.5
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
Treatment = Oral Agent(s)
Cutoff Date = 1 Sep 04

Trial	Center	Pt ID	Age (yrs)	Gender	Agent/Dose[1] (mg/day)	Time (days)[2]	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
104	5002	0041	42	F	Metformin 1500, Glipizide 10	44	Infec	Boil of labia majora		
104E	5007	0032	60	M	Glipizide 10	55	Neoplasms	Adenocarcinoma prostate	same	y
109	5042	0477	55	F	Pioglitazone 45, Glibenclamide 10	83	Psych	Anxiety	Not mentioned in narrative for decline in DLco with inhaled insulin	
110	5103	1428	63	M	Rosiglitazone 8	37	GI	Gastric ulcer, duodenal ulcer		
110	5123	1069	49	M	Rosiglitazone 8	2	GI	Cholelithiasis		
A2171001	0005	1032	58	M	Metformin 500, Glibenclamide 10	13	Resp	Breathing difficulty		
						13	Cardiac	Ischemic heart disease		
						37	Cardiac	Nonspecific chest pain	Also ischemic heart disease	
A2171001	0027	1066	67	M	Metformin 2000, Glibenclamide 15	99	Cardiac	Inferior myocardial infarction	same	y
A2171001	0035	2333	61	F	Metformin 1500, Glibenclamide 10	189	Musculoskel	Bilateral carpal tunnel syndrome, left carpal tunnel		

Table 7.1.2.1.5
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
Treatment = Oral Agent(s)
Cutoff Date = 1 Sep 04

Trial	Center	Pt ID	Age (yrs)	Gender	Agent/Dose[1] (mg/day)	Time (days)[2]	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
								surgery		
A2171001	0035	3021	59	F	Metformin 500, Glibenclamide 5	323	Musculoskel	Hallux valgus		
A2171001	0035	0076	66	F	Metformin 1500, Glibenclamide 15	66	Musculoskel	Acute back pain	same	y
A2171001	0037	1080	71	M	Metformin 2500, Glibenclamide 15	71	Cardiac	Unstable angina pectoris		
A2171001	0045	3361	79	F	Metformin 1500, Glibenclamide 15	202	Metab	Hypoglycemia, unconsciousness	same	
					Metformin 1000, Glibenclamide 15	319	Neoplasm	Ovarian cancer, ascites	same	
A2171001	0046	0099	54	M	Metformin 2000, Glibenclamide 160 (sic)	63	GI	Cholecystitis		
A2171001	0059	1134	35	F	Metformin 500, Glimepiride 4	16	GI	Worsening epigastric pain, vomiting		
A2171001	0085	3005	72	F	Metformin 2000, Glimepiride 3	92	Infec	Skin abscess left hip, infected sebaceous gland scalp		
A2171001	0088	1193	68	M	Metformin 500, Glimepiride 3	11	Neuro	Cerebrovascular accident	Apoplexy	y
A2171001	0100	1229	68	F	Metformin 1500, Glibenclamide 15	186	GI	Abdominal pain of unknown origin		
A2171001	0108	1290	71	F	Metformin 1000, Glibenclamide 15	166	Cardiac	Angina pectoris	same	
A2171001	0109	1237	62	M	Metformin 2000, Glibenclamide 15	111	Cardiac	Myocardial infarction	Cardiac infarction	
A2171001	0112	3366	78	F	Metformin 2000, Glibenclamide 7.5	169	Neuro	Syncope	same	
					Metformin 2000, Glibenclamide 7.5, Isophane 14, Mixtard 52	582	Musculoskel	Polymyalgia rheumatica	same	
					Metformin 2000, Glibenclamide 7.5, Isophane 64, Mixtard 52	596	Metab	Hypoglycemia, syncope	same	
					Metformin 2000, Glibenclamide 7.5, Isophane 64, Mixtard 52	596	Musculoskel	Exacerbation of polymyalgia rheumatica	same	

Table 7.1.2.1.5
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
Treatment = Oral Agent(s)
Cutoff Date = 1 Sep 04

Trial	Center	Pt ID	Age (yrs)	Gender	Agent/Dose[1] (mg/day)	Time (days)[2]	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
					Metformin 2000, Glibenclamide 7.5, Isophane 64, Mixtard 60	751	Metab	Hyperglycemia	not in narrative	
A2171001	0129	1334	43	M	Metformin 1500, Glimepiride 3	156	Skin	Diabetic ulcer foot	same	y
A2171001	0134	1374	53	M	Metformin 500, Glibenclamide 20	7	Musculoskel	Prolapsed cervical disc	Intervertebral disc disorder	
					Metformin 1000, Glibenclamide 20	215 (31)	Infec	Pneumocystis carinii pneumonia	Pneumonia	
						215 (31)	Resp	Deterioration of lung function	Pneumonia	
A2171001	0138	1280	59	M	Metformin 1500, Glibenclamide 15	252	Vasc	Lower limb arteriopathy worsening		
A2171001	0140	0302	62	M	Metformin 2000, Glibenclamide 15	260	Accid/ Injur	Broken ribs	same	
A2171001	0140	1302	61	F	Metformin 1500, Glibenclamide 17.5	182 (17)	GI	Gastroesophageal pyrosis, esophageal spasm	Narrative reports diarrhea	
A2171001	0141	2068	84	M	Metformin 1500, Glibenclamide 10	684	Neoplasm	Basal cell carcinoma skin		
A2171001	0142	3057	67	M	Metformin 2000, Glibenclamide 20	196	Musculoskel	Multiple fractures		
A2171002	0002	7338	57	M	Metformin 2000, Glibenclamide 2.5	698	Repro/ Uro	Transurethral resection of prostate		
A2171002	0004	8010	64	F	Metformin 2500, Glibenclamide 12.5	?	GI	Epigastric hernia	Not in narrative	
					Metformin 2500, Glibenclamide 12.5	242	General	Chest pain	same	
A2171002	0005	5030	64	M	Metformin 2000, Glibenclamide 2.5	57	Cardiac	Persistent atrial flutter	same	
					Metformin 2000, Glibenclamide 2.5	89	Accid/ Injur	Car accident	same	y (death)
A2171002	0005	6029	50	F	Metformin 2000, Glibenclamide 7.5	84	GI	Acute pancreatitis		
A2171002	0005	6030	54	F	Metformin 1000, Glibenclamide 2.5	118	GI	Unspecified upper abdominal pain		
A2171002	0027	7365	58	F	Metformin 2000, Glibenclamide 15	213	Infec	Urosepsis		

Table 7.1.2.1.5
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
Treatment = Oral Agent(s)
Cutoff Date = 1 Sep 04

Trial	Center	Pt ID	Age (yrs)	Gender	Agent/Dose[1] (mg/day)	Time (days)[2]	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
A2171002	0029	5054	51	M	Metformin 2000, Glibenclamide 7.5	339	Cardiac	Heart attack	Acute anterior myocardial infarction	y
A2171002	0035	6057	54	F	Metformin 2000, Glibenclamide 7.5	48	Musculoskel	Bilateral carpal tunnel syndrome		
A2171002	0035	7330	52	F	Metformin 2000, Glibenclamide 7.5	210	GI	Food poisoning		
A2171002	0038	8025	66	M	Metformin 2000, Glibenclamide 7.5	680	Cardiac	Acute anteroseptal myocardial infarction		
A2171002	0045	5077	74	F	Metformin 1500, Glibenclamide 2.5	8 (100)	Cardiac	Myocardial infarction	same	Prev dc; death from this SAE
A2171002	0047	6086	59	M	Metformin 2000, Glibenclamide 10	83	Cardiac	Acute myocardial infarction	same	y (death)
A2171002	0047	7342	69	F	Metformin 2000, Glibenclamide 10	608	Repro/ Uro	Prolapsed uterus		
A2171002	0047	8322	67	M	Metformin 2000, Glibenclamide 10	106	GI	Acute cholecystitis, esophagitis	Same terms included in narrative for lung fibrosis on CXR	
A2171002	0049	5089	53	M	Metformin 2000, Glibenclamide 7.5	230	Eye	Eye movement disorder	Strabismus mentioned in narrative for decline in FEV1	
A2171002	0051	5093	63	M	Metformin 2000, Glibenclamide 7.5	369	Neuro	Vestibular neuritis		
A2171002	0051	6096	59	M	Metformin 2000, Glibenclamide 10	121	Musculoskel	Hammer toe		
A2171002	0056	8050	61	M	Metformin 2000, Glibenclamide 5	295	Eye	Ischemic optic neuropathy		
						?	Musculoskel	Right sided coxarthrosis		
						145	Neuro	Peripheral paresis of right facial nerve		
A2171002	0058	6117	53	F	Metformin 2000, Glibenclamide 7.5	54	GI	Abdominal discomfort		
A2171002	0073	6145	46	M	Metformin 2000, Glibenclamide 10	57	Cardiac	Congestive heart failure	same	y
A2171002	0074	5151	54	M	Metformin 2000, Glibenclamide 2.5	613	Resp	Dyspnea	Same term mentioned in narrative for abnormal CXR	
						632	Repro/ Uro	Renal calculus	Kidney pain mentioned in narrative for abnormal CXR	
A2171002	0074	5152	73	M	Metformin 1000,	730	Vasc	Narrowing left renal artery		

Table 7.1.2.1.5
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
Treatment = Oral Agent(s)
Cutoff Date = 1 Sep 04

Trial	Center	Pt ID	Age (yrs)	Gender	Agent/Dose[1] (mg/day)	Time (days)[2]	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
					Glibenclamide 2.5					
					Metformin 2000, Glibenclamide 2.5	14	Vasc	Worsening right inferior limb arteritis		
A2171002	0083	5165	58	F	Metformin 2000, Glibenclamide 2.5	63	Neoplasm	Small cell bronchus carcinoma	Bronchial carcinoma	y
A2171002	0085	5169	74	F	Metformin 2000, Glibenclamide 10	124	Musculoskel	Lumbalgia		
A2171002	0092	5189	59	M	Metformin 2000, Glibenclamide 10	138	Vasc	Stenosis carotid artery		
A2171002	0096	5202	48	M	Metformin 2000, Glibenclamide 5	165	Musculoskel	Pectoralis muscle inflammation		
A2171002	0096	5203	62	M	Metformin 2500, Glibenclamide 5	58	Cardiac	Cardiac infarction	Heart infarction	y (death)
A2171002	0141	8027	69	F	Metformin 2000, Glibenclamide 7.5	26	Neuro	Hydrocephalus acquired worsening		
					Metformin 2000, Glibenclamide 10	335	Neuro	Hydrocephalus acquired worsening		
A2171002	0141	8032	62	M	Metformin 2000, Glibenclamide 10	533	Cardiac	Cardiac arrhythmia, angina		
A2171002	0141	8037	49	F	Metformin 2000, Glibenclamide 10	454	Repro/ Uro	Dysfunctional uterine hemorrhage		
A2171002	0142	7041	65	M	Metformin 2000, Glibenclamide 10	220	Cardiac	Worsening of angina		
A2171002	0142	7406	46	M	Metformin 2000, Glibenclamide 5	188	Neoplasm	Colon adenocarcinoma		
						258	GI	Biliary colic		
A2171002	0142	7409	53	M	Metformin 2000, Glibenclamide 2.5	5	Vasc	Intermittent claudication worsening		
					Metformin 2000, Glibenclamide 12.5	321	Infec	Suture line abscess right leg		
A2171002	0142	8379	56	F	Metformin 2000, Glibenclamide 10	98	Repro/ Uro	Renal lithiasis		
A2171017	1003	1002	70	M	Glipizide 10, Metformin 2000, Rosiglitazone 8	209	Cardiac	Recurrent angina		
A2171017	1036	1002	55	M	Rosiglitazone 8, Metformin 2000, Glimepiride 7.5	218	Neuro	Subarachnoid hemorrhage		
A2171017	1037	1002	51	M	Glipizide 20, Metformin 2000, Rosiglitazone 4	68	Cardiac	Angina		

Table 7.1.2.1.5
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Adult Type 2 Diabetics
Sorting by Patient
Treatment = Oral Agent(s)
Cutoff Date = 1 Sep 04

Trial	Center	Pt ID	Age (yrs)	Gender	Agent/Dose[1] (mg/day)	Time (days)[2]	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
A2171030	1032	3085	64	M	Metformin 1000, Glipizide 10, Isophane 49, Regular 19	93	Cardiac	Myocardial infarction (event also in SQ table)		

Includes Studies 1001, 1002, 1005, 1007, 1009, 1017, 1022, 1026, 1027, 1028, 1029, 102E, 103, 1030, 1036, 104, 104E, 106, 107, 108, 109, 110, 111
1 Dose at time of adverse event
2 Duration of exposure in days at time of event. If event occurred after discontinuation, the number of days after discontinuation is included in parentheses
3 Applicant's assigned term
4 Term used by investigator or patient; nb- applicant provided SAE narratives only for pulmonary SAEs and SAEs that led to death or discontinuation
5 If patient withdrew due to this adverse event, noted with a "y"
Source: Applicant's Table 6.3.1.1, Section 2.7.4, pgs 1903-2296

Table 7.1.2.1.6
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Pediatric Patients
Sorting by Patient
Treatment = Inhaled Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Pt ID	Age (yrs)	Gender	Dose[1] (mg)	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
106	5082	6093	14	F	8	165	Metab	Diabetic ketoacidosis		
107	5083	7499	17	M	6	8	Metab	Hypoglycemia, dehydration		
						8	GI	Emesis		
107	5084	7336	13	M	18	133	Musculoskel	Fracture tibia and fibula		
107	5090	7455	13	M	4	133	Metab	Hypoglycemia	Mentioned in narrative for decline in TLC	
						133	GI	Nausea, vomiting	Mentioned in narrative for decline in TLC	
111	5064	6103	16	M	20	622	Metab	Diabetic ketoacidosis	same	y
111	5064	6105	15	F	17	20	Metab	Diabetic ketoacidosis		
					18	604 (40)	Metab	Recurrent diabetic ketoacidosis		
111	5064	6517	13	F	10	46	Metab	Diabetic ketoacidosis		
111	5064	6519	16	F	18	308	GI	Pancreatitis	same	y
					18	308	Metab	Diabetic ketoacidosis	same	

Table 7.1.2.1.6
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Pediatric Patients
Sorting by Patient
Treatment = Inhaled Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Pt ID	Age (yrs)	Gender	Dose[1] (mg)	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
111	5091	3373	12	M	17	575	GI	Nausea, vomiting, food poisoning		
111	5091	3374	12	M	15	418	Infec	Viral syndrome		
					15	418	Metab	Diabetic ketoacidosis		
111	5091	6074	16	F	10	796	Metab	Diabetic ketoacidosis		
					13	19	Metab	Ketonuria		
					13	19	GI	Vomiting		
111	5091	6076	15	M	18	80	Metab	Diabetic ketoacidosis		
					18	80	Infec	Vomiting, viral syndrome, gastroenteritis		
111	5091	6474	13	F	18	85	Metab	Diabetic ketoacidosis		
111	5091	6475	16	M	9	91	Metab	Diabetic ketoacidosis		
					9	91	Infec	Viral syndrome		
111	5092	6487	16	M	12	751	Accid/ Injur	Bicycle accident		
111	5093	7039	16	F	13	986 (13)	Metab	Diabetic ketoacidosis		
111	5093	7040	14	M	14	394	Infec	Nausea, vomiting		
111	5093	7392	16	F	7	269	Psych	Suicidal tendencies		
					7	346	Psych	Suicidal tendencies, intentional overdose alcohol and acetaminophen		
111	5094	7094	14	M	13	277	Infec	Stomach flu	Not mentioned in narrative for hypoglycemia	
					14	599	Metab	Hypoglycemia	same	
111	5095	3334	7	M	8	240	Metab	Hypoglycemia	same	
111	5096	3358	12	M	21	585	Metab	Hypoglycemia, partial seizure	same	
111	5096	3359	10	M	8	435	Metab	Hypoglycemia, seizure	same	
111	5098	3048	10	M	6	569	Metab	Hypoglycemia, seizures		
					9	380	Metab	Hypoglycemia, seizure	same	
111	5108	7077	16	F	23	825 (21)	Psych	Exacerbation of depression		
					24	825 (21)	Metab	Diabetic ketoacidosis		
					26	825 (102)	Psych	Depressive disorder		
					25	691	Psych	Depressive disorder		
A2171009	5088	3381	7	F	8	78	Metab	Hypoglycemia, unresponsiveness		
A2171009	5095	3339	11	M	20	49	Psych	Suicidal ideation		
A2171009	5096	3021	10	F	19	46	Metab	Hypoglycemic event, possible seizures		

1 Dose at time of adverse event
2 Duration of exposure in days at time of event. If event occurred after discontinuation, the number of days after discontinuation is included in parentheses
3 Applicant's assigned term

Table 7.1.2.1.6
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Pediatric Patients
Sorting by Patient
Treatment = Inhaled Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Pt ID	Age (yrs)	Gender	Dose[1] (mg)	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]

4 Term used by investigator or patient; nb- applicant provided SAE narratives only for pulmonary SAEs and SAEs that led to death or discontinuation
5 If patient withdrew due to this adverse event, noted with a "y"
Source: Applicant's Table 6.3.1.1, Section 2.7.4, pgs 1903-2296

Table 7.1.2.1.7
Serious Adverse Event Listing
All Clinical Pharmacology, Phase 2 and Phase 3 Clinical Trials in Pediatric Patients
Sorting by Patient
Treatment = SQ Insulin
Cutoff Date = 1 Sep 04

Trial	Center	Pt ID	Age (yrs)	Gender	Dose[1] (U/day)	Time[2] (days)	Body System	Applicant's Assigned Term[3]	Investigator's Term (if different)[4]	D/C?[5]
107	5063	7419	17	F	Isophane 84, Regular 82	156	Metab	Diabetic ketoacidosis		
107	5079	7479	16	M	Isophane 65, Regular 74	91	Metab	Diabetic ketoacidosis		
						91	GI	Hematemesis		
107	5098	7073	13	F	Isophane 80, Regular 20	201	Metab	Severe hypoglycemic event, seizures	same	
A2171009	5082	3347	7	M	Zinc suspension 22, Regular 20	36	Metab	Hypoglycemic, seizure	same	
A2171009	5096	3022	11	M	Isophane 28, Regular 8	92	Infec	Herpes zoster		

1 Dose at time of adverse event
2 Duration of exposure in days at time of event. If event occurred after discontinuation, the number of days after discontinuation is included in parentheses
3 Applicant's assigned term
4 Term used by investigator or patient; nb- applicant provided SAE narratives only for pulmonary SAEs and SAEs that led to death or discontinuation
5 If patient withdrew due to this adverse event, noted with a "y"
Source: Applicant's Table 6.3.1.1, Section 2.7.4, pgs 1903-2296

Table 7.1.2.1.8
Serious Adverse Event Listing
Nondiabetic Subjects
Sorting by Patient
All Treatments
Cutoff Date = 1 Sep 04

Trial	Center	Pt ID	Age	Gender	Dose[1]	Time[2] (days)	Body System	Preferred Term[3]	Investigator AE Term[4]	D/C?[5]
A2171005	5139	0076	71 yrs	M	Crossover inhaled and SQ; last treatment SQ 9 U	Single dose Study Day 19, after 8 day washout, ACS Study Day 21, MI Study Day 23	Cardiac	Acute myocardial infarction, hypotension	same	
A2171005	5139	0085	67 yrs	M	Crossover inhaled and SQ; last treatment inhaled insulin 3 mg	Single dose Study Day 13, after 3 day washout; event Study Day 13	Cardiac	Myocardial infarction	same	
A2171022	1039	Nonsubject 01	1 day	M	Inhaled insulin 7 (to mother)	From conception through appr 25 days in utero	General	Drug exposure in utero		y (death)
							Cardiac	Cardiomegaly, congestive heart failure, cardiogenic shock		
							Metab	Fetal macrosomia		

Includes Studies 1001, 1002, 1005, 1007, 1009, 1017, 1022, 1026, 1027, 1028, 1029, 102E, 103, 1030, 1036, 104, 104E, 106, 107, 108, 109, 110, 111
1 Dose at time of adverse event
2 Duration of exposure in days at time of event. If event occurred after discontinuation, the number of days after discontinuation is included in parentheses
3 Applicant's assigned term
4 Term used by investigator or patient
5 If patient withdrew due to this adverse event, noted with a "y"
Source: Applicant's Table 6.3.1.1, Section 2.7.4, pgs 1903-2296

10.5 Serious Adverse Event Narratives

These narratives relate to Section 7.1.2 of the main body of the review. Patients are identified by their study number, then their center number, then their patient ID number.

Serious Accidents and Injuries

A2171002-0002-7337: 69 yo man with Type 2 DM, treated with inhaled insulin and metformin. On day 673 of inhaled insulin treatment, fell while using a mall escalator and experienced head trauma with loss of consciousness lasting a few seconds. Hospitalized on neurosurgery ward for two weeks, then transferred to rehabilitation. Applicant states no history of hypoglycemia prior to the fall. No blood glucose values in narrative. Inhaled insulin permanently discontinued on day of fall.

A2171022-1006-0302: 37 yo man with Type 1 DM, treated with inhaled insulin and subcutaneous isophane insulin. On Day 31 of inhaled insulin, patient had a motorcycle accident; did not have recorded hypoglycemia prior to the accident. In the emergency room, had psychomotor agitation and was given 40 mL of 50% glucose. BG prior to administration of glucose not in narrative, but narrative states that patient recovered from hypoglycemia that evening. Had left clavicular rhegma which required shoulder immobilization; was discharged later that night. On day 192 of inhaled insulin, patient had a hypoglycemic episode with a blood glucose of 27 mg/dL at 1846. At 2030, was taken to the ER, where he had a BG of 34 mg/dL. Received 500 cc 10% dextrose in ER; within 30 minutes, BG was 142. Discharged to home that evening.

103E-5005-0063: 58 yo woman with Type 2 diabetes, treated with inhaled insulin and zinc suspension insulin. On day 180 of inhaled insulin treatment, patient had a "moderate" episode of syncope while driving, and had an MVA. Specific injuries not mentioned. Blood sugar status not mentioned. While in the ER after the MVA, pneumonia noted. Treated with clindamycin. Hospitalized for 17 days.

Serious Cardiac Adverse Events

A2171001-0093-1209: 64 yo man with Type 2 DM, treated with inhaled insulin. Episodes of angina on inhaled insulin days 56 and 94. On day 109, dyspnea, burning chest pain, vertigo. Left anterior descending coronary artery (LAD) stenosis noted; successful percutaneous transluminal coronary angioplasty (PTCA) study day 116. At end of trial, also had decline in FEV1 (3.76-3.09 L) and DLco (30.9-22.7 mL/min/mmHg).

A2171005-5139-0076: 71 yo nondiabetic man with chronic bronchitis enrolled in PK study with salbutamol coadministration. Received a single dose of inhaled insulin on Study Days 1 and 6, both followed by salbutamol. On Study Day 19, received a single injection of 9 u regular insulin SQ, preceded by salbutamol. On Study Day 21, experienced diaphoresis and chest pressure; cardiac enzymes negative. On Study Day 23, had myocardial infarction with CABG that same day; experienced postoperative hypotension. Discharged on Study Day 31.

A2171005-5139-0085: 67 yo nondiabetic man with chronic bronchitis enrolled in PK study with salbutamol coadministration. Received a single dose of inhaled insulin on Study Days 1 and 13, and a single dose of SQ insulin on Study Day 9. On Study Day 13, after inhaled insulin administration, became diaphoretic after a large meal. Went to ER and was diagnosed with an MI with elevated enzymes. Catheterization revealed diffuse minimal irregularities, with a circumflex coronary vessel thrombus. Treated with coumadin. Discharged on Study Day 20.

103E-5002-0010: 39 yo man with Type 2 DM treated with inhaled insulin and zinc suspension insulin. Narrative states that on day 1110, coronary arteriosclerosis was reported, but precise event not described. Patient had previously undergone pulmonary consultation for cough, wheezing and decline in lung diffusion capacity for carbon monoxide (DLco). On Study Day 1110, experienced "ongoing moderate coronary artery disorder". Was discontinued from study on Day 1172 due to coronary artery disorder.

111-5034-8035: 66 yo man with Type 2 DM, treated with inhaled insulin and NPH. On day 727, while recovering from a cystourethroscopy, pt experienced a severe myocardial infarction. Four days later, he underwent CABG; discharged to home 5 days after CABG.

111-5049-8378: 67 yo man with Type 2 DM, treated with inhaled insulin. Inhaled insulin was discontinued on day 637 in preparation for CABG, which was performed 5 days later. Narrative states that "event of worsening coronary artery disease was considered resolved" 8 days post-CABG.

111-5055-0581: 70 yo man with Type 2 DM, treated with inhaled insulin and metformin. On day 717 of inhaled insulin treatment, patient was diagnosed with severe congestive heart failure with severe global hypokinesia, EF of 33%, large apical thrombus, enlarged left atrium. Two months later, ECG showed inferior MI. Narrative states that eight months after CHF diagnosed, was considered resolved. Patient also had decline in FEV1, FVC, and TLC.

111-5060-0664: 56 yo man with Type 2 DM, treated with inhaled insulin, metformin and glyburide. On day 132 of inhaled insulin treatment (84 in Study 109 and 48 in Study 111), patient was admitted to hospital with chest pain and diagnosed by ECG with acute MI. Inhaled insulin was discontinued temporarily. Underwent CABG and was discharged 6 days after MI. Pt had another MI 44 days later and was permanently discontinued from study.

111-5060-0672: see Serious Neoplastic Events

111-5060-8110: 53 yo man with Type 2 DM, treated with inhaled insulin and UL. On day 562 of inhaled insulin administration, patient presented with new onset unstable angina and borderline elevations in cardiac enzymes. Inhaled insulin was discontinued on admission. Three days later, cardiac catheterization revealed severe proximal LAD occlusion with a possible dissection of the LAD. Pt underwent CABG that day. He was discharged to home 5 days later.

111-5062-0642: 49 yo man with Type 2 DM, treated with inhaled insulin monotherapy. Patient began study with abnormal PFTs (mild peripheral airways obstruction). On day 113 of inhaled

insulin administration, patient experienced dyspnea on exertion. On day 181 of inhaled insulin administration, PFTs showed a significant decline in DLco from baseline. Inhaled insulin was discontinued after 282 days of administration. Twenty-two days after discontinuation of inhaled insulin, coronary angiography revealed occlusion of the high first diagonal branch, an 80% mid-circumflex lesion, and a complex 90% stenosis of the right coronary artery. PTCA dilated the right coronary and circumflex arteries; shortness of breath improved. PFTs done 24 days after PTCA revealed improvements in FVC and FEV1, but DLco is not mentioned.

111-5076-0700: 65 yo man with Type 2 DM, treated with inhaled insulin, glyburide and metformin. On day 335 of inhaled insulin administration, patient awoke with left arm pain, which did not respond to sublingual nitroglycerin. The next morning, he awoke with similar pain and presented to the ER. He was admitted with a diagnosis of myocardial infarction, with a peak serum creatine phosphokinase (CPK) of 448 U/L. ECG showed inferior ischemic changes; echocardiogram showed "minimal" left ventricular dysfunction, EF 50-59%, moderate aortic stenosis (AoS). He was treated with heparin, integrilin and oxygen. Inhaled insulin was discontinued and never restarted. Seven days after admission, he underwent 4-vessel CABG and aortic valve replacement (AoVR).

Serious Gastrointestinal Adverse Events

A2171002-0142-8380: 70 yo man with Type 2 DM, treated with inhaled insulin and metformin. On day 25 of inhaled insulin, developed severe acute biliary pancreatitis, which resolved on Study Day 50. Investigator felt event due to biliary lithiasis. At time of event, alanine aminotransferase (ALT), total bilirubin (bili), gamma-glutamyl transferase (GGT) and alkaline phosphatase (alk phos) were within normal limits (wnl). Patient permanently discontinued on Study Day 57 due to this event.

A2171022-1010-0537: 48 yo man with Type 1 DM, treated with inhaled insulin and subcutaneous insulin glargine. On day 314 of inhaled insulin, admitted to hospital with nausea, vomiting and hypoglycemia. Diagnosed with gastroenteritis. Inhaled insulin temporarily discontinued while patient in hospital. Hospitalized for four days; discharged and readmitted one day later for recurrent nausea, vomiting and hypoglycemia. Gastroenteritis resolved 4 days later. Patient also had developed high titers of anti-insulin antibodies.

111-5064-6519: 16 yo girl with Type 1 DM, treated with inhaled insulin and UL. On day 308 of inhaled insulin administration, the patient was admitted to the hospital with severe abdominal pain, nausea and vomiting. She was diagnosed with pancreatitis and diabetic ketoacidosis. Amylase was 309 U/L (nl range for lab not reported; std ref range 60-180 U/L, Harrison's 16th Ed) and lipase was 839 U/L (std ref range 0-160 U/L, Harrison's 16th Ed). Serum glucose was 247 mg/dL, beta-hydroxybutyrate was 3.5 mmol/L (uln 3.0), and serum bicarbonate was 12 mmol/L. Inhaled insulin was permanently discontinued on admission by the primary investigator due to "lack of efficacy". Abdominal ultrasound was normal; etiology of pancreatitis not determined. Patient was discharged 7 days after admission.

Serious Metabolic Adverse Events

A2171009-5088-3381: 8 yo girl with Type 1 DM, treated with inhaled insulin and subcutaneous isophane insulin. On Day 78 of inhaled insulin administration, after lunch, went to school nurse complaining that she didn't feel well; became unresponsive and fell to the floor. Fingerstick glucose 28 mg/dL. Paramedics administered IV glucose en route to ER. Patient had had several low blood sugars during the week prior to the event. Discontinued from study on Day 78.

A2171009-5096-3021: 10 yo girl with Type 1 DM, treated with inhaled insulin and subcutaneous isophane insulin. On Day 46 of inhaled insulin, patient awoke her mother at 0429; patient appeared confused and lethargic. BG 50; given half can of cola. At 0443, BG 346, but still confused and lethargic. At 0455, BG 72. Mother called doctor, who told mother to give 1 mg glucagon. At 0552, patient still confused and lethargic. Mother drove child to ER; child vomited en route. Head CT negative; BG 128 mg/dL. Admitted to neurology ward; felt to possibly have had seizures; recovered and was discharged the following day.

A2171022-1001-0009: 37 yo man with Type 1 DM, treated with inhaled insulin and subcutaneous isophane insulin. On Day 197 of inhaled insulin, was found unconscious in the early morning hours by his wife. She called paramedics, who administered IV glucose. BG by paramedics was 1.1 mmol/L (20 mg/dL) at 0445. Regained consciousness and was stable within one hour of receiving IV glucose. The previous evening at 1930, pt had had BG of 1.8 mmol/L (33 mg/dL), which he had self-treated. BG at 0130 had been 12.7 mmol/L (231 mg/dL); nighttime isophane dose 10 units. Discontinued inhaled insulin on Study Day 202.

A2171022-1015-0837: 37 yo man with Type 1 DM, treated with inhaled insulin and subcutaneous insulin glargine. On day 82 of inhaled insulin administration, had a "moderate" hypoglycemic event with a BG of 38 mg/dL, which resolved after eating breakfast. On day 84 of inhaled insulin administration, at 0430, patient had hypoglycemia and loss of consciousness. EMS measured BG at 35 mg/dL; transported to hospital. Narrative states that patient had administered supper insulin based on his post-supper value, rather than on his pre-supper value.

A2171022-1025-1424: 32 yo man with Type 1 DM, treated with inhaled insulin and subcutaneous insulin glargine. In the early morning of day 244 of inhaled insulin administration, had a headache accompanied by confusion and a change in affect. Patient felt hypoglycemic and ate 15-20 gms of carbohydrate at 0630 without checking BG; BG at 0730 after food was 99 mg/dL. Mental status changes persisted and patient was admitted to the hospital for hypoglycemia and seizure; details of seizure activity not provided. Hypoglycemia and seizure resolved that day. EEG on Study Day 245 showed excessive "low" wave discharges in the left hemisphere, particularly in the temporal lobe, interpreted as c/w underlying focal cerebral dysfunction. CT of head on Study Day 246 was "benign". MRI head normal (nl) on Study Day 248.

A2171022-1026-1489: 22 yo man with Type 1 DM, treated with inhaled insulin and subcutaneous isophane insulin. On Study Day 482, while driving to work and before eating breakfast, patient became hypoglycemic and had a motor vehicle accident "when he was unable to stop his vehicle". He was disoriented after the accident and was transported to the hospital by

A2171027-5148-1329: 43 yo man with Type 1 DM, treated with inhaled insulin and isophane insulin. On day 4 of inhaled insulin, consumed a 20 oz beer at a hockey game at 2000. At 2105, became dizzy, sweaty, confused and began to mumble; he then lost consciousness for 25 minutes. EMS called; on their arrival, BG 18 mg/dL. EMS treated pt with IV glucose; pt recovered and was not hospitalized.

A2171029-1059-2607: 45 yo man with Type 2 DM, treated with inhaled insulin and insulin glargine. On day 223 of inhaled insulin treatment, while patient was undergoing a gallium scan as part of a pulmonary evaluation, patient began twitching and had a BG of 25 mg/dL, followed by a seizure. Time of day of event not mentioned, but occurred after breakfast. He was treated with glucose and hospitalized; discharged later that day with a reduction in inhaled insulin dose.

A2171029-1093-3854: 64 yo woman with Type 2 DM treated with inhaled insulin and isophane. On day 14 of inhaled insulin, patient had no oral intake except some juice at 1200. At 2200, pt's daughter found pt unconscious; daughter called EMS. BG by EMS 38 mg/dL; EMS gave IV glucose and transported patient to hospital. Discharged early the next morning. On day 22 of inhaled insulin, after a day of relatively good oral intake, pt became unconscious at night and EMS was called. BG by EMS at 2122 was 35 mg/dL. EMS gave IV glucose; pt recovered and was not taken to hospital. Inhaled insulin dose decreased.

A2171029-1093-3857: 62 yo man with Type 2 DM treated with inhaled insulin and isophane. On day 316 of inhaled insulin treatment, patient lost consciousness sometime after lunch, and remained unconscious for approximately 7 hours. When patient lost consciousness, he fell and injured his front teeth. Prelunch BG had been 78 mg/dL. After recovering consciousness, patient ate carbohydrate; he did not go to hospital, but saw his primary care physician the next day. On day 336 of inhaled insulin treatment, patient lost consciousness from 1400 and 1600. Pt had not had lunch. EMS was called; BG at 1500 was 31 mg/dL. Treated with IV glucose; no report of transfer to hospital.

A2171030-1015-1393: 72 yo man with Type 2 DM treated with inhaled insulin and isophane. On day 9 of inhaled insulin treatment, after eating at a restaurant, developed nausea and vomiting. Did not take evening insulin for fear of becoming hypoglycemic. Admitted that night with DKA. Reportedly treated with regular SQ insulin sliding scale; DKA resolved 2 days later.

106-5025-6592: 36 yo man with Type 1 DM, treated with inhaled insulin and extended zinc suspension insulin. On day 98 of inhaled insulin treatment, patient took extra inhaled insulin (3 mg extra at supper and 2 mg extra at bed). He also consumed two beers prior to bed. The next morning, he was found unresponsive, convulsing and sweating. Patient's girlfriend administered glucagon; ten minutes later BG was 386 mg/dL. In extension study 111, on day 508 of inhaled insulin treatment, patient went out in the evening with friends and had alcohol. After returning home, his serum glucose was 453 mg/dL at 2215, and he took 18 mg of inhaled insulin. At 0140 the next morning, he awoke and checked his blood sugar, which was 229 mg/dL. He gave himself 24 U of insulin glargine and 6 mg of inhaled insulin and went back to sleep. At 0700, he was found in bed convulsing; paramedics called. Serum glucose 20 mg/dL; D50 given.

Transported to ER; released later that day. On day 558 of inhaled insulin administration, pt had several drinks before bed. At 0540, patient awoke, sat in a chair, refused to return to bed, and then had a seizure and bit his tongue. Paramedics called; BG 38 mg/dL. IV dextrose given; patient did not regain consciousness and was transported to ER. In ER, he regained consciousness and was discharged later that day.

106-5030-6883: 53 yo woman with Type 1 DM, treated with inhaled insulin and extended zinc suspension insulin. On day 31 of inhaled insulin treatment, at 0900, patient was found unconscious by her roommate. Blood glucose was 20 mg/dL; paramedics administered IV dextrose at the scene. In the ER, patient's body temperature was 90 degrees Fahrenheit rectally. She was treated with additional dextrose, and was released to home that day.

106-5060-6966: 36 yo man with Type 1 DM, treated with inhaled insulin and extended zinc suspension insulin. On the morning of day 33 of treatment with inhaled insulin, after experiencing morning hypoglycemia for several days, the patient was found unresponsive by his wife. He was treated with glucagon and awoke within 15 minutes. Bedtime extended zinc insulin was moved from bedtime to morning. On the morning of day 39 of inhaled insulin, patient was found comatose with a blood sugar of 14 mg/dL. His wife administered 1 mg of glucagon. After three hours, patient's blood sugar "had stabilized". Patient permanently discontinued study in response to this event.

107-5007-7988: 19 yo woman with Type 1 DM, treated with inhaled insulin and isophane insulin. Had 12 reported severe hypoglycemic events. The first nine of these events were during a 3-week winter break from college. In these events, the patient's mother had difficulty waking the patient, and the patient responded to orange juice administered by the mother. In most cases, no blood sugar was measured prior to orange juice administration. The investigator felt that it was possible that patient had not been tightly controlling her blood sugars while away from home, with resultant hypoglycemic episodes when she resumed her intensive regimen while back at home. However, the three later events did have blood sugars measured at the time of the event; these values were 45, 49 and 43 mg/dL. All events were in the morning.

107-5052-7181: 53 yo man with Type 1 DM, treated with inhaled insulin and isophane insulin. On day 23 of inhaled insulin treatment, while driving home from work, patient became hypoglycemic and had a motor vehicle accident at around midnight, running into a ditch. He had not taken his evening isophane, but had taken his usual inhaled insulin dose at around 2000. The patient called his son, who drove the patient home. At 0600 the next morning, blood glucose was 67 mg/dL. The patient had also had three other episodes of hypoglycemia within the four weeks prior to the accident.

107-5083-7499: 17 yo boy with Type 1 DM, treated with inhaled insulin and isophane insulin. On day 8 of inhaled insulin administration, after playing basketball for 5 minutes, the patient became dizzy and vomited. Blood glucose measured 39 mg/dL. Pt consumed 2 glasses of orange juice, cake and milk. One hour later, BG 22 mg/dL. Patient's mother administered glucagon, and paramedics administered IV glucose. Pt hospitalized for hypoglycemia, vomiting and dehydration.

107-5127-7221: 30 yo woman with Type 1 DM, treated with inhaled insulin and isophane insulin. On the morning of day 19 of inhaled insulin treatment, patient had a grand mal seizure witnessed by her parents. Was given glucagon at the scene and recovered from the seizure. Blood sugar was not measured at the time of the event, but investigator felt seizure was due to hypoglycemia, and seizure responded to glucagon. On day 486 of inhaled insulin administration, at 2200, her roommate witnessed the patient become unconscious and then have a seizure. The roommate called an ambulance; patient's BG while still unconscious was 29 mg/dL. She regained consciousness after IV glucose, and she was not transported to the hospital. No change was made in her insulin regimen. On day 522 of inhaled insulin administration, the patient "passed out" and had a witnessed seizure at home. She was transported to the ER, where she was given IV glucose and discharged to home. No change was made in her inhaled insulin regimen. On day 527 of inhaled insulin administration, patient "fell unconscious" and had a seizure, that was witnessed by her roommate. The roommate called an ambulance; patient was treated with IV glucose, but was not transported to the hospital. No change in insulin regimen in response to event. On day 615 of inhaled insulin administration, patient was found at home by a friend; patient was unconscious and having a seizure. Treatment not mentioned. On day 632 of inhaled insulin administration, at 0400, patient had a blood sugar of <36 mg/dL and a seizure. An ambulance was called and the pt was treated with IV glucose. At 0600, her BG was 171 mg/dL. She was not admitted to the hospital and her insulin was not changed. On day 654, patient discontinued study. Although the reason for discontinuation was listed as "other", and not as "adverse event", the investigator's reason for discontinuation was "too many serious hypoglycemias (sic) caused by the study drug".

109-5071-0483: 66 yo man with Type 2 DM, treated with inhaled insulin monotherapy. On day 12 of inhaled insulin administration, at around 1800, took 6 mg inhaled insulin, but delayed eating. At appr 1900, wife noted patient to be perspiring profusely and unable to obey simple commands. Patient was taken to ER, where BG was 2.1 mmol/L (38 mg/dL). He was given IV dextrose and furosemide. He was released to home and inhaled insulin was resumed the next day.

111-5017-8450: 73 yo man with Type 2 DM, treated with inhaled insulin and isophane insulin. On day 469 of inhaled insulin administration, after taking his granddaughter to the park in the afternoon, he became disoriented and confused while driving home. He attempted to pull off to the side of the road, thought he applied his brakes, and had a motor vehicle accident. Paramedics measured a serum glucose of 52 mg/dL. He was given IV D50 with immediate response. In the ER, he was found to have a chest wall contusion, but no fractures. His inhaled insulin dose was reduced and he was discharged from the ER that night. He had also had a severe hypoglycemic event requiring emergency room treatment 3 days previously, and had a HbA1c of 5.9%.

111-5025-6592: see 106-5025-6592

111-5030-6883: 54 yo woman with Type 1 DM, treated with inhaled insulin and isophane insulin. On day 92 of inhaled insulin administration in Study 111, patient was found in her car on the side of the road at around 1800. She had sluggish speech and told paramedics that she

was diabetic and had not eaten. She was given oral dextrose; BG after measured 20 mg/dL. Taken to ER where she had altered level of consciousness. In the critical care unit, she was given 50 cc of dextrose; BG 39 mg/dL. Was discharged later that day. On day 111 of inhaled insulin in Study 111, had loss of consciousness and BG 29 mg/dL. Paramedics gave oral dextrose with reversal of symptoms. Four days later, was seen in the ER again with BG 20 mg/dL. Three days after that, was seen in ER again with BG 20 mg/dL and unresponsiveness; responded to D50.

111-5052-7180: 34 yo man with Type 1 DM, treated with inhaled insulin and isophane insulin. On day 103 of inhaled insulin administration in Study 111, patient began crying and speaking incoherently. Blood sugar was 30 mg/dL. Transported to hospital by paramedics; admitted. EEG and CT nl. ECG borderline ventriculomegaly. Discharged 2 days later.

111-5061-7793: 44 yo woman with Type 1 DM, treated with inhaled insulin and isophane insulin. On day 726 of inhaled insulin administration, patient did a large amount of house cleaning and ate soup for lunch. At 1430, she took a nap, and was found unconscious at 1800. An ambulance transported the patient to the hospital; blood sugar values at the time of the event are not mentioned. Patient received D50 in the ER and was discharged the same day. The narrative states that inhaled insulin treatment continued unchanged, but inhaled insulin was discontinued 10 days later.

111-5061-7794: 31 yo woman with Type 1 DM, treated with inhaled insulin and isophane insulin. In the early morning of day 303, patient had a severe hypoglycemic episode with unconsciousness and incontinence. She had not taken inhaled insulin at bedtime, but she had taken isophane insulin. She was transported to the ER, and received D50 in the ambulance. Blood sugar prior to transport was 38 mg/dL. The narrative does not mention hospital admission. On day 314 of inhaled insulin administration, patient awakened in the early morning, and was disoriented and not fully conscious. At 0445, her husband administered juice and licorice, but the patient remained disoriented. At 0449, the patient's blood sugar was 47 ng/dL. The husband gave the patient a glucagon injection, and the patient recovered by 0513. Inhaled insulin was not changed in response to these events.

111-5061-7797: 46 yo man with Type 1 DM, treated with inhaled insulin and isophane insulin. On day 479 of inhaled insulin administration, patient experienced gastroenteritis with nausea. He did not eat that day, and took his premeal inhaled insulin and hs inhaled and SQ isophane insulins. The next morning, at 0300, patient awoke feeling nauseated and weak. He got up to measure his blood sugar, fell down to the floor, and was unconscious for 5-10 seconds. His glucose measured 38 mg/dL. He drank two glasses of orange juice and felt better. At 0900, his blood sugar was 165 mg/dL. His inhaled insulin dose was not changed in response to the event.

111-5064-6103: 16 yo boy with Type 1 DM, treated with inhaled insulin and UL. On day 622 of inhaled insulin administration, patient developed nausea and vomiting shortly after midnight. His bedtime blood sugar had been 305 mg/dL. He was hospitalized with diabetic ketoacidosis, with a blood sugar of 705 mg/dL, beta-hydroxybutyrate of 12.8 mM/L, and large ketones in the urine. He was treated with IV fluids, potassium and regular insulin. Inhaled insulin was

discontinued. Two days later, he was discharged on lispro insulin and UL. He was discontinued from study due to this event.

111-5064-6519: see Serious Gastroenterologic Adverse Events

111-5064-6524: 16 yo boy with Type 1 DM, treated with inhaled insulin and UL. On day 294 of inhaled insulin administration, patient began vomiting at suppertime, and did not take his evening doses of either insulin. Admitted to the hospital with DKA on day 295 of inhaled insulin administration. Patient had large ketones in the urine, serum blood glucose >600 mg/dL, serum bicarbonate 8 mM/L, blood pH 7.19. Treated with fluids, potassium and regular insulin IV. Had renal insufficiency; creatinine value not reported. Withdrawn from study due to this event. Narrative states patient had problems with noncompliance. Applicant's serious adverse event listing also states that patient had another serious episode of DKA on day 66 of inhaled insulin administration, but this event is not discussed in the narrative.

111-5066-7741: 41 yo woman with Type 1 DM, treated with inhaled insulin and isophane insulin. On day 323 of inhaled insulin administration, at 0230, while in bed, she was found by her husband to be incoherent, screaming, "cross-eyed" and clammy. The husband measured her blood sugar at 22 mg/dL, then injected glucagon without response. The glucagon was later found to have expired. An ambulance was called; the attendant administered oral glucose gel and then a glass of milk. At 0450, the patient's BG was 116 mg/dL. Her inhaled insulin was not changed.

111-5066-7745: 29 yo man with Type 1 diabetes, treated with inhaled insulin and extended zinc suspension insulin. On day 190 of inhaled insulin administration, at 0400, the patient awoke from sleep sweating, shaking and disoriented. Blood sugar was 35 mg/dL. Girlfriend gave patient orange juice, but he did not respond, and he began to have a seizure with tonic-clonic movements. An ambulance was called, and the attendants gave the patient IV dextrose; he was coherent within 15 minutes and remained at home. Inhaled insulin was not changed.

111-5070-6896: 30 yo woman with Type 1 DM, treated with inhaled insulin and isophane insulin. On the morning of day 137 of inhaled insulin administration, the patient's mother found the pt unresponsive. The mother put jam on the patient's tongue, and the patient aroused somewhat, but did not become coherent. The patient was transported to the ER by ambulance; she received 50% dextrose in the ER. By 1135, the patient's BG was 255 mg/dL, and she was discharged to home following lunch. Both her inhaled insulin and isophane insulin were reduced in response to this event.

111-5070-6898: 42 yo woman with Type 1 DM, treated with inhaled insulin and extended zinc suspension insulin. On day 304 of inhaled insulin administration, patient experienced a hypoglycemic event from 0030-0800 hours. Her husband reported that she was convulsing, combative and stuporous. Blood sugars were not measured during the event. Her husband did not bring her to the hospital, but gave her a glass of juice and watched her through the night. Patient's prebreakfast glucose that morning was 38 mg/dL. The patient went to work the next day, but had a headache, was sweaty and felt tired. Both her inhaled insulin and isophane insulin

doses were decreased in response to this event. The status of her marriage after the event was not mentioned.

111-5081-6446: 18 yo woman with Type 1 DM, treated with inhaled insulin and extended zinc suspension insulin. On day 230 of inhaled insulin administration, at 0100, the patient's blood glucose was 74 mg/dL; she took her extended zinc insulin, but did not take her bedtime inhaled insulin. She went to bed at 0200. At 1600, she had not awakened, and her roommates became concerned and tried to wake her. She awoke but was incoherent. Her roommates tried to test her blood sugar, but dropped and broke her meter. Paramedics transported the patient to the ER, where she was treated the patient with 50% dextrose. After dextrose, blood sugar was 130 mg/dL. She was discharged to home from the ER.

111-5082-3341: 11 yo girl with Type 1 DM, treated with inhaled insulin and insulin glargine. On day 831 of inhaled insulin administration, the patient did not eat supper. At 2144, her BG was 375 mg/dL, and she received 40 units of insulin glargine. The next morning at 0028, her blood sugar was 58 mg/dL; intervention not mentioned. At 0830, she was unarousable. Her mother gave her glucagon and called paramedics. At 0847, after glucagon, BG was 117 mg/dL. At 0900, she had a seizure and was transported to the hospital. She was treated with IV fluids, observed overnight, and discharged the next day. Inhaled insulin was not changed; glargine dose reduced.

111-5082-3346: 10 yo boy with Type 1 DM, treated with inhaled insulin and insulin glargine. On day 657 of inhaled insulin administration, patient had gastroenteritis with diarrhea and vomiting. His blood sugars fluctuated through the day; inhaled insulin was continued. Prior to bedtime, he experienced a hypoglycemic episode and was taken by ambulance to the hospital, where his BG was 27 mg/dL. He was admitted and treated with IV glucose. His inhaled insulin and insulin glargine doses were reduced in response to this event. He was discharged to home two days after admission.

111-5082-3347: 8 yo boy with Type 1 DM, treated with inhaled insulin and extended zinc suspension insulin. On day 346 of inhaled insulin administration, the patient had a large late breakfast at 0920, with his usual pre-breakfast dose of 6 mg inhaled insulin. At 1300 (no lunch yet), the patient's mother observed the patient having a seizure. BG measured at 60 mg/dL. Mother administered glucagon and took patient to hospital, where he was admitted. He was treated with intravenous fluids and intravenous insulin. He was discharged the next day and his inhaled insulin was resumed.

111-5082-3348: 9 yo boy with Type 1 DM, treated with inhaled insulin and insulin glargine. On day 310 of inhaled insulin administration, after attending a football daycamp that ended at 1600, he called his mother when he arrived home and told her that he did not feel well. His mother arrived home at 1800 and found the patient standing in the shower, confused, flailing his arms, and unable to stand on his left leg. BG was 39 mg/dL. He was taken to the ER, where his BG was 59 mg/dL. He was admitted to the hospital and treated with IV dextrose 5% (sic) and normal saline. A head CT at 1920 revealed a left middle cranial fossa arachnoid cyst, but was otherwise "negative". He was discharged to home the next day. On inhaled insulin day 445, the

patient exercised strenuously for several hours, and had three meals and three snacks. At bedtime, his blood sugar was 82 mg/dL; he ate an ice cream sundae and took 7 units of insulin glargine. At 0100 the next morning, he was found "foaming at the mouth", limp, and unresponsive. His pupils were dilated and he had severe sweating. BG was 46 mg/dL; mother administered glucagon and glucose increased to 140 mg/dL. Paramedics administered orange juice and glucose gel and transported the patient to the ER. Upon arrival, his BG was 119 mg/dL, but dropped to 38 mg/dL at 0213. He was treated with intravenous glucose, and released at 0500. Inhaled insulin was not changed, but glargine was reduced. Head CT in ER revealed unchanged left middle cranial fossa arachnoid cyst. On day 578 of inhaled insulin treatment, while at a sleepover at a friend's house, his friend's mother heard noises from the bedroom and called 911. The principle investigator believed these noises to be seizure activity. Paramedics gave the patient glucagon and transported him to the hospital. BG was 40 mg/dL. He was admitted and treated with IV fluids and dextrose. He was discharged one day after this event.

111-5087-7011: 17 yo boy with Type 1 DM, treated with inhaled insulin and isophane insulin. On day 1156 of inhaled insulin administration, he awoke with BG 45 mg/dL. He drank juice, then administered isophane and inhaled insulins, then ate breakfast. At school, he attended a vigorous gym class. At 0900, he was confused and disoriented. He was given two juices and transported to the ER. He was treated and released later that day. He did not recall the event. Neither insulin was changed in response to this event.

111-5088-3384: 7 yo girl with type 1 DM, treated with inhaled insulin and isophane insulin. On day 190 of inhaled insulin administration, BG at 2115 was 456 mg/dL. By study regimen, pt should have received snack followed by 1 mg inhaled and 5 units isophane insulins, and study site should have been called for BG >400 mg/dL. Blood sugar should have been checked 2.5-3 hours postdose. However, pt was not given snack and was given 3 mg inhaled and 5 u isophane. Site was not called. In the early morning of the next day, patient experienced a seizure and her sister awakened the patient's parents. BG was 47 mg/dL at 0243. Parents gave patient juice and called paramedics. BG at 0253 was 57 mg/dL; by 0304, BG was 205 mg/dL. Patient was not transported to the hospital.

111-5089-3025: 10 yo girl with Type 1 DM, treated with inhaled insulin and NPH. On day 41 of inhaled insulin administration, patient stopped keeping BG and dosing logs. On day 53, patient stopped taking her lunchtime insulin while at school. On day 67, she began to vomit and was hospitalized for DKA. She was treated with intravenous insulin, and DKA resolved 3 days later. Inhaled insulin was permanently discontinued on hospital admission.

111-5091-3008: 11 yo boy with Type 1 DM, treated with inhaled insulin and extended zinc suspension insulin. On day 140 of inhaled insulin administration, patient received 4 mg of inhaled insulin and 14 units of extended zinc suspension insulin at 2200. At midnight, pt experienced a seizure. Mother administered glucagon and patient "stabilized". In ER at 0230, BG was 46 mg/dL; IV fluids started. By 0500, BG was 138 mg/dL. Pt had morning inhaled insulin and ate breakfast, then was released to home. No action was taken with regard to inhaled insulin.

111-5094-7094: 14 yo boy with Type 1 DM, treated with inhaled insulin and extended zinc suspension insulin. On day 598 of inhaled insulin administration, at 2000, patients BG was 65 mg/dL. At 2200, he ate two chocolate chip pancakes and took 3 mg of inhaled insulin. The next morning, at 0700, he was pale, combative and incoherent with a BG of 33 mg/dL. Paramedics treated patient with IV saline and 25 gms D50. 30 minutes after treatment, BG was 255 mg/dL, and "the event was considered resolved".

111-5095-3334: 7 yo boy with Type 1 DM, treated with inhaled insulin and extended zinc suspension insulin. On day 596 of inhaled insulin administration, family was advised to increase insulin dose (type of insulin not specified) for a BG of 300 mg/dL. On days 598 and 599, pt had low blood sugar readings; family was advised to decrease insulin back to prior regimen. At 2100 on day 599, patient was brought to the ER for hypoglycemia (BG not mentioned). He was admitted, treated with intravenous fluids, and released the next day. Inhaled insulin was temporarily discontinued, but later resumed. Zinc suspension insulin dose reduced.

111-5096-3358: 12 yo boy with Type 1 DM, treated with inhaled insulin and extended zinc suspension insulin. On day 584 of inhaled insulin administration, at 1800, the patient had a blood sugar of 55 mg/dL and was given a snack and 3 mg of inhaled insulin. At 2247, BG was 81; pt given juice. The next morning at 0900, pt appeared confused. BG was 59 mg/dL and pt was given juice. He sat on the floor and began to cry. He stopped crying, and his legs then began to twitch. At 0934, his BG was 78 mg/dL. The mother called the study site; the investigator felt the patient might have been having a partial seizure. At 1015, pt taken to ER; BG 109 mg/dL, but speech slurred. At 1120, pt vomited and had a bowel movement. Pt was given an antibiotic "as a precaution". By 1330, pt was able to recognize people and verbalize coherently. He was admitted to the hospital. A neurologist ruled out meningitis, and felt the event had been a partial seizure due to hypoglycemia. Patient was discharged to home the next day.

111-5096-3359: 10 yo boy with Type 1 DM, treated with inhaled insulin and extended zinc suspension insulin. On day 435 of inhaled insulin administration, at 0500, the patient had a seizure m/b profuse perspiration, gurgling, "eyes that rolled back", and a rigid upper body. Did not respond to glucagon injection and glucose gel. Paramedics called; measured glucose at 46 mg/dL. Upon arrival at ER, BG 204 mg/dL. Treated with IV fluids and glucagon. Had 2 episodes of vomiting and one episode of diarrhea. Admitted to hospital; "event was considered resolved the same day". Inhaled insulin dose was not changed in response to this event.

111-5098-3048: 9 yo boy with Type 1 DM, treated with inhaled insulin and glargine insulin. On day 380 of inhaled insulin administration, at 0600, he was found having a seizure in the shower. Manifestations included whole body jerking, blue lips, and inability to speak. The patient was taken to the ER, where his blood glucose was 85 mg/dL at 0620. MRI and EEG normal. He was discharged later that day. On day 669 of inhaled insulin administration, at 0611, patient's blood glucose was 52 mg/dL at 0611; at 0615, he had a seizure. Two hours after the seizure, he saw the study investigator, who reduced his insulin glargine, but did not change his inhaled insulin.

He then vomited. He was transported to the ER by ambulance, where a CT revealed subarachnoid hemorrhage within the right sylvian fissure. He was transferred to the intensive care unit and then underwent a left frontotemporal craniotomy with clipping of a left middle cerebral artery aneurysm. Inhaled insulin was permanently discontinued on admission. Six days later, he experienced cerebral vasospasm; the narrative does not mention symptoms. On that day, he also was diagnosed with aspiration pneumonia. During this hospitalization, he also experienced a subdural hematoma and a pulmonary embolism. He was transferred to a rehabilitation center 75 days after the subarachnoid bleed, and was discharged to home 22 days later. His final neurologic status was not mentioned in the narrative.

Serious Reproductive and Urologic Events

A2171007-5141-0006: 29 yo woman with Type 2 pregestational DM, treated with inhaled insulin, enrolled in PK/PD study in pregnant patients with gestational or pregestational DM. Enrolled at 36 weeks EGA. On Study Day 1, received a single 3 mg dose of inhaled insulin. On Study Day 6, was admitted to the hospital for her second planned study admission. She did not receive another dose of inhaled insulin. About 1.5 hours after admission, had rupture of amniotic membranes. Fetal heart rate was reported as "good", but speculum examination revealed prolapsed umbilical cord. Underwent emergent C-section that night and was delivered of a 4 lb 11 oz male infant, APGAR (activity, pulse, grimace, appearance, respiration) scores 6 at 1 minute and 8 at 5 minutes. The mother was withdrawn from the study. On post-treatment day 29, the patient presented with a 24 hour history of headache, and MRI revealed a sagittal sinus thrombus. Admitted and received intracranial thrombolytic therapy and peripheral anticoagulation. Recovered and was discharged one week later.

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