



Summary

Analysis of 5,167 industry-sponsored trials and 126,980 study sites registered between October 2005 and September 2007 at the US-based clinical trials register, www.ClinicalTrials.gov.

California, Florida, Texas and New York State are the most preferred States.

US cities represent about half of the leading one hundred cities worldwide.

New York Metropolitan standing out as the leading city globally -- followed by Atlanta, (Paris), Chicago, Phoenix, Houston, Los Angeles, San Diego, Dallas and San Antonio.

Next Issue

April 2008, Volume 1, Issue 4

The Trail of Sponsored Clinical Trials

Free Subscription

Register at
<http://www.ClinicalTrialMagnifier.com>

Most Preferred Sponsored Clinical Trial Locations in the United States

By Johan PE Karlberg, MD, PhD

Clinical Trials Centre, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, PR China

Abstract

Despite rapidly increasing competition internationally, the United States is still ahead of Europe and all emerging testing countries in the testing of new medicines. This report, based on 5,167 industry-sponsored trials and 126,980 study sites (registered on www.ClinicalTrials.gov between October 2005 and September 2007), examines the contribution of the United States to the worldwide clinical testing of new medicines. US cities represent half of all global study sites, representing many more sites per trial as well as per population with 195 sites/million. This is more than in any other country. Of the top 100 cities worldwide for registered study sites, the US comprises about half. The southern US dominates with the most study sites, highest density of sites per million population and highest growth in the number of study sites. California, Florida, Texas and New York are the leading states with the New York Metropolitan area standing out as the leading city globally -- followed by Atlanta, (Paris), Chicago, Phoenix, Houston, Los Angeles, San Diego, Dallas and San Antonio.

Introduction

The International Conference on Harmonisation's Good Clinical Practice (ICH GCP) guidelines regulating clinical trial conduct of new medicines was adopted by drug regulatory authorities in the US, EC and Japan in 1996.¹ The impact of these international quality standards has been enormous, allowing pharmaceutical companies to collect trial data worldwide rather than only in established regions. As a result, more and more industry-sponsored trials are now conducted in emerging testing regions, especially in Eastern Europe (including Russia), Asia and Latin America.^{2,3} Since mid-2005, as a condition of consideration for publication, the International Committee of Medical Journal Editors (ICMJE) has required interventional patient-controlled clinical trials to be registered in a public trial registry before the onset of patient enrolment.^{4,5} Trial listings on the largest international trial registry, the US-based www.ClinicalTrials.gov register, were downloaded on November 1, 2007 to identify the most active sponsored clinical trial countries by means of the largest number of study sites and growth in study sites.⁶ The analysis data set comprised 5,167 industry-sponsored active or completed trials and 126,980 study sites registered between October 2005 and September 2007. This study was used to identify the contribution of US States

and cities to sponsored clinical trials, compared with other countries and cities worldwide. The overall objective was to identify the magnitude of contribution and level of dominance of the United States in clinical testing of new medicines.

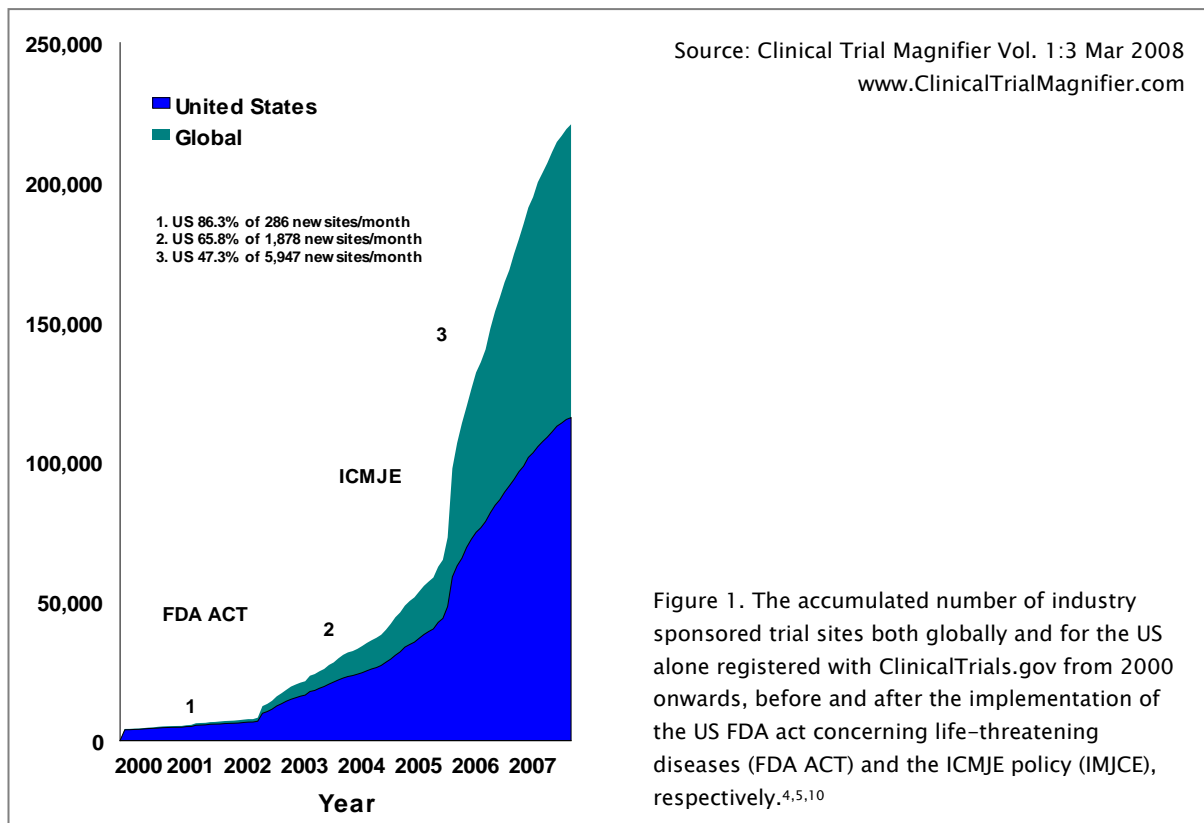
Methods

See pages 37–38.

Results

Based on registrations over the two years studied, the US was involved in 2,770 (53.6%) studies and 58,933 (46.4%) study sites. A total of 4,356 (84.3%) sponsored clinical trials were in the established trial countries of North America, Western Europe, Australia and New Zealand, at 101,345 (79.8%) study sites. This compared to 1,833 (35.5%) protocols and 15,635 (20.1%) sites in emerging trial countries.

A total of 5,167 trials and 126,980 study sites remained for analysis, with an average of 24.6 sites per protocol. Respectively, there were 1,978, 2,232 and 957 phase II, III and IV trials. Main reasons for deleting a trial were those registered before October 2007 (n=6,841), trials sponsored by a non-for-profit organization (n=2,096 studies), phase I trials



(n=1,519), and trials with no country site address (n=873). The Year 1 sub-set data comprised 2,597 protocols and 74,071 study sites. The Year 2 sub-set data comprised 2,570 protocols and 52,909 study sites.

A significant increase in registered trial sites

Figure 1 shows the increase in the number of registered industry-sponsored trial sites. Some 5,000 new sites were registered every month, with close to half in the US. Both curves initially show a linear shape followed by a drop in monthly registrations from early 2007 because not all study sites had yet been registered for the latest trials.

Most preferred regions

Table 1 indicates the number of registered study sites for each of the four US census Regions and nine Regional Divisions, with figures also included for Puerto Rico. All four Regions are involved in the majority of the 2,770 studies conducted in the US; note that one trial can be conducted in more than one location giving a summary percentage over 100%, thus 64.9% of all US studies were carried out in the Midwest Region and 75% in the South Region. The average number of sites per study differed regionally, from 11.8 sites in the South Regions to 5.0 in the Northeast Region. The South Region had most study sites both in absolute numbers (24,564; 41.7%) and in sites/million population (237). The South contributed an extra 4,343 study sites over the population size-adjusted US average of 195 sites per million inhabitants. The South Atlantic and West South Central Regional Divisions had the highest overall number of sites per million population (247 and 237, respectively). The Midwest and Northeast Regions had the lowest number of study

sites per million population (167 and 169, respectively), with the East North Central and the Mid-Atlantic Regional Divisions contributing the least based on their populations. The South Region showed the highest relative growth (74.3%) in the number of sites between Years 1 and 2, most notably the West South Central Regional Division (79.3%). Conversely, the New England and East North Central Divisions showed the slowest growth in study site number; respectively at 68.4% and 69.7%. The overall negative growth in the number of sites – not in the number of trials – is due to the fact that the most recently registered trials have not yet registered all sites.

Most preferred States

Table 2 indicates the number of registered sponsored trials and study sites for all 50 US States, plus the District of Columbia and Puerto Rico. Ranking is based both on the number of study sites over the two year period, as well as over the two individual years. Ranking between the top nine States did not change over the two periods. Only four States changed their ranking by three or more places. The number of studies, number of sites per protocol and number of protocols were all significantly ($p < 0.0001$) correlated with population size, at $r = 0.94$, 0.90 and 0.88 , respectively. The number of sites was significantly (< 0.0001) explained by both number of protocols and population size in a multiple regression analysis with a total R-square of 0.91. All top 10 States had on average of more than 1.8 sites per protocol, compared with less than 1.4 for all 10 States with the lowest number of sites. The average number of study sites per million population was 195, ranging between 25 and 542. For most States it ranged between 100 and 300. Among the ten most populous States, the highest density of sites per million population (> 250) was in

Table 1. The number of study sites registered with ClinicalTrials.gov between October 2005 to September 2006 (Year 1) and October 2006 and September 2007 (Year 2) for the various US Regions and Regional Divisions.

Division	Region	Year 1	Year 1	Year 2	Year 2	Total	Total	Sites/	Growth*		Population [§]	Sites/	Extra**
		Protocols	Sites	Protocols	Sites	Protocols	Sites	Protocol	Protocols	Sites	Million	Million	Sites
		N	N	N	N	N	N	N	%	%		N	N
New England	Northeast	601	1,566	517	1,071	1,118	2,637	2.4	86.0	68.4	14.3	185	-147
Mid-Atlantic	Northeast	957	4,270	874	3,030	1,831	7,300	4.0	91.3	71.0	44.7	163	-1,414
Total	Northeast	1,028	5,836	957	4,101	1,985	9,937	5.0	93.1	70.3	58.9	169	-1,560
West South Central	South	821	3,801	775	3,014	1,596	6,815	4.3	94.4	79.3	28.8	237	1,204
South Atlantic	South	924	8,183	885	5,954	1,809	14,137	7.8	95.8	72.8	57.1	247	2,991
East South Central	South	614	2,109	553	1,503	1,167	3,612	3.1	90.1	71.3	17.8	203	149
Total	South	1,051	14,093	1,027	10,471	2,078	24,564	11.8	97.7	74.3	103.7	237	4,343
West North Central	Midwest	645	2,093	617	1,604	1,262	3,697	2.9	95.7	76.6	19.9	185	-193
East North Central	Midwest	851	4,323	774	3,015	1,625	7,338	4.5	91.0	69.7	46.3	159	-1,689
Total	Midwest	923	6,416	876	4,619	1,799	11,035	6.1	94.9	72.0	66.2	167	-1,881
Pacific	West	841	5,154	852	3,686	1,693	8,840	5.2	101.3	71.5	48.5	182	-622
Mountain	West	665	2,468	610	1,821	1,275	4,289	3.4	91.7	73.8	20.8	206	223
Total	West	918	7,622	924	5,507	1,842	13,129	7.1	100.7	72.3	69.4	189	-400
Total	Puerto Rico	78	164	57	104	135	268	2.0	73.1	63.4	3.9	68	-501
Total	United States	1,388	34,131	1,382	24,802	2,770	58,933	21.3	99.6	72.7	302.1	195	0

* Percentage increase: (number in Year 2)/(number in Year 1)*100

** Extra sites based on the US average of 195.06 sites per million population

Florida, Texas and North Carolina. Lowest density (<150) was in Illinois and New York State.

Most preferred cities

Table 3 shows the ranking of the most preferred cities in the US by the number of sponsored trials and study sites. The 50 cities contributed 25,431 sites, accounting for 43.2% of all US sites. Five of the cities were in Florida, four in Texas, and three each in California, North Carolina and Ohio. San Jose, Fort Worth, El Paso and Milwaukee. Four of the 25 most populous US cities (>550,000 population) were not ranked while relatively small US cities with populations

below 250,000 such as Durham, Rochester, Spokane, Winston-Salem, Richmond, Little Rock, Salt Lake City, Charleston and West Palm Beach all ranked among the top 50 US cities. The US accounts for 56 of the top 100 trial cities globally, and 13 of the top 20. Among the top 20 most active trial cities are also Paris, Moscow, Barcelona, Madrid, Berlin, Buenos Aires and Toronto.

US compared with other countries

Figure 2 indicates the 60 most preferred sponsored clinical trials locations, by States in the US along with other countries. Germany has the highest number of study sites, followed by California, France, Florida,

Table 2. The number of study sites registered with ClinicalTrials.gov between October 2005 to September 2006 (Year 1) and October 2006 and September 2007 (Year 2) for all 50 States in the US, plus District of Columbia and Puerto Rico. Ranking is based on the total number of registered study sites and number of sites for Years 1 and 2, respectively.

Rank Total Sites	Rank Year 1 Sites	Rank Year 2 Sites	State	Year 1	Year 1	Year 2	Year 2	Total	Total	Sites per	Protocols %	Sites %	Growth* Sites Rank	Population ^a Million	Sites per	
				Protocols N	Sites N	Protocols N	Sites N	Protocols N	Sites N	Protocol N					Million N	Million Rank
1	1	1	California	789	3,844	783	2,749	1,572	6,593	4.2	99.2	71.5	27	36.5	181	33
2	2	2	Florida	694	3,351	654	2,411	1,348	5,762	4.3	94.2	71.9	26	18.1	319	2
3	3	3	Texas	746	2,591	711	2,111	1,457	4,702	3.2	95.3	81.5	7	18.1	260	7
4	4	4	New York	667	1,850	606	1,323	1,273	3,173	2.5	90.9	71.5	28	23.5	135	40
5	5	5	Pennsylvania	622	1,549	540	1,147	1,162	2,696	2.3	86.8	74.0	20	12.4	217	19
6	6	6	Ohio	575	1,396	488	1,007	1,063	2,403	2.3	84.9	72.1	25	11.5	209	22
7	7	7	North Carolina	557	1,298	477	963	1,034	2,261	2.2	85.6	74.2	17	8.9	255	8
8	8	8	Illinois	542	1,149	450	756	992	1,905	1.9	83.0	65.8	42	12.8	148	37
9	9	9	Georgia	474	1,033	399	722	873	1,755	2.0	84.2	69.9	32	9.4	187	29
10	11	10	Arizona	408	821	358	616	766	1,437	1.9	87.7	75.0	15	6.2	233	11
11	10	13	New Jersey	475	871	366	560	841	1,431	1.7	77.1	64.3	46	8.7	164	36
12	13	11	Virginia	410	811	360	609	770	1,420	1.8	87.8	75.1	14	7.6	186	31
13	12	14	Michigan	426	821	329	559	755	1,380	1.8	77.2	68.1	33	6.0	229	13
14	15	12	Tennessee	377	759	315	567	692	1,326	1.9	83.6	74.7	16	6.0	220	17
15	14	15	Missouri	411	759	361	557	772	1,316	1.7	87.8	73.4	21	5.8	225	15
16	16	17	Washington	392	739	314	495	706	1,234	1.7	80.1	67.0	38	6.4	193	26
17	17	18	Alabama	379	730	302	489	681	1,219	1.8	79.7	67.0	39	4.6	265	5
18	18	19	Massachusetts	425	713	342	484	767	1,197	1.6	80.5	67.9	35	6.4	186	30
19	20	16	South Carolina	361	653	300	541	661	1,194	1.8	83.1	82.8	6	4.3	276	3
20	19	20	Maryland	370	671	336	476	706	1,147	1.6	90.8	70.9	31	5.6	204	24
21	21	21	Indiana	339	609	289	445	628	1,054	1.7	85.3	73.1	22	6.3	167	35
22	22	22	Colorado	356	585	294	434	650	1,019	1.6	82.6	74.2	18	4.8	214	20
23	23	23	Oregon	306	482	265	380	571	862	1.5	86.6	78.8	9	3.7	233	12
24	25	24	Louisiana	291	449	226	363	517	812	1.6	77.7	80.8	8	4.3	189	27
25	24	25	Kentucky	292	453	233	341	525	794	1.5	79.8	75.3	13	4.2	189	28
26	26	27	Connecticut	278	423	217	308	495	731	1.5	78.1	72.8	24	3.5	209	23
27	27	28	Oklahoma	277	404	211	305	488	709	1.5	76.2	75.5	11	3.6	198	25
28	28	26	Minnesota	272	393	235	309	507	702	1.4	86.4	78.6	10	5.2	136	39
29	31	29	Kansas	238	355	208	268	446	623	1.4	87.4	75.5	12	2.8	225	14
30	29	31	Utah	248	373	176	247	424	620	1.5	71.0	66.2	40	2.6	243	9
31	32	30	Wisconsin	250	348	189	248	439	596	1.4	75.6	71.3	29	5.6	107	45
32	30	32	Arkansas	251	357	171	235	422	592	1.4	68.1	65.8	43	2.8	211	21
33	34	33	Nebraska	191	255	162	222	353	477	1.4	84.8	87.1	2	1.8	270	4
34	33	34	Nevada	193	270	145	184	338	454	1.3	75.1	68.1	34	2.5	182	32
35	35	35	Iowa	143	197	125	146	268	343	1.3	87.4	74.1	19	3.0	115	43
36	36	36	Dist. Columbia	155	188	112	127	267	315	1.2	72.3	67.6	36	0.6	542	1
37	37	39	New Mexico	131	170	102	109	233	279	1.2	77.9	64.1	47	2.0	143	38
38	38	38	Rhode Island	129	168	91	110	220	278	1.3	70.5	65.5	44	1.1	260	6
39	39	40	Mississippi	111	167	90	106	201	273	1.4	81.1	63.5	48	2.9	94	48
40	40	42	Puerto Rico	78	164	57	104	135	268	2.0	73.1	63.4	49	3.9	68	50
41	41	37	Idaho	117	142	96	120	213	262	1.2	82.1	84.5	5	1.5	179	34
42	43	41	Montana	83	100	93	105	176	205	1.2	112.0	105.0	1	0.9	217	18
43	42	43	West Virginia	74	102	58	66	132	168	1.3	78.4	64.7	45	1.8	92	49
44	44	44	Maine	75	97	55	64	130	161	1.2	73.3	66.0	41	1.3	122	42
45	45	45	North Dakota	69	87	47	62	116	149	1.3	68.1	71.3	30	0.6	234	10
46	47	46	Vermont	75	82	51	55	126	137	1.1	68.0	67.1	37	0.6	220	16
47	46	48	New Hampshire	80	83	48	50	128	133	1.0	60.0	60.2	50	1.3	101	46
48	49	47	Hawaii	64	70	49	51	113	121	1.1	76.6	72.9	23	1.3	94	47
49	48	50	Delaware	60	76	39	39	99	115	1.2	65.0	51.3	52	0.9	135	41
50	50	49	South Dakota	43	47	36	40	79	87	1.1	83.7	85.1	4	0.8	111	44
51	51	51	Alaska	17	19	11	11	28	30	1.1	64.7	57.9	51	0.7	45	51
52	52	52	Wyoming	7	7	4	6	11	13	1.2	57.1	85.7	3	0.5	25	52

* Percentage increase: (number in Year 2)/(number in Year 1)*100

Canada and Texas. Among the 60 listed locations, 30 are in US States and 30 in other countries. Figure 2 also compares the number of sites contributing over 135 sites per million population, with all 30 US States in the ranking. Only six of the 30 countries reached this level, namely Denmark (186 sites/million), Belgium (181), Canada (161), Sweden (158), Norway (151) and Finland (144). Established countries such as the “big five” in Europe contributed fewer than 100 sites per million population, with Italy (57), UK (63), Spain (82), Germany (95) and France (99). Many of the emerging trial regions had even fewer sites registered (20 or below) per million population, notably China (1), India (1), Brazil (7), Mexico (11), Russia (16), South Korea (18) and Ukraine (20).

Discussion

Over the past few decades the pharmaceutical industry has faced new challenges in clinical testing of new medicines. Regulatory authorities have – for good reasons – recurrently introduced new requirements and more rigorous regulations, which have drastically extended clinical testing. We see more clinical trials for each test compound, as well as more sites per study.^{1,10,11} Another challenge is the dramatic reduction in success rate of new compounds entering the clinical testing phase, currently reported at just 1/11.^{12,13} This and other factors have induce rapid changes in disease focus of drug development.¹⁴ A steady increase in the number of pharmaceutical and biotech companies further strains the competitive environment, forcing

Table 3. The number of study sites registered with ClinicalTrials.gov between October 2005 to September 2006 (Year 1) and October 2006 and September 2007 (Year 2) for the top 50 US cities ranked among the top cities globally. Ranking is based on the total number of registered study sites and number of sites for Years 1 and 2, respectively.

Rank*	Rank*	Rank*			Year 1	Year 1	Year 2	Year 2	Total	Total	Sites per	Growth**	
Total Sites	Year 1 Sites	Year 2 Sites	State	City	Protocols N	Sites N	Protocols N	Sites N	Protocols N	Sites N	Protocol N	Protocols %	Sites %
1	1	1	New York	New York	501	1,004	438	716	939	1,720	1.8	87.4	71.3
2	2	2	Georgia	Atlanta	410	738	344	531	754	1,269	1.7	83.9	72.0
4	4	6	Illinois	Chicago	405	581	319	419	724	1,000	1.4	78.8	72.1
5	5	3	Arizona	Phoenix	339	553	291	437	630	990	1.6	85.8	79.0
6	6	5	Texas	Houston	362	487	341	428	703	915	1.3	94.2	87.9
7	7	8	California	Los Angeles	323	471	293	378	616	849	1.4	90.7	80.3
8	8	7	California	San Diego	322	456	297	391	619	847	1.4	92.2	85.7
9	9	14	Texas	Dallas	310	444	277	349	587	793	1.4	89.4	78.6
10	11	10	Texas	San Antonio	309	424	281	368	590	792	1.3	90.9	86.8
14	12	15	Florida	Tampa	260	419	237	339	497	758	1.5	91.2	80.9
16	15	17	Pennsylvania	Philadelphia	318	390	255	302	573	692	1.2	80.2	77.4
18	17	19	Massachusetts	Boston	291	378	225	274	516	652	1.3	77.3	72.5
19	19	18	Missouri	Saint Louis	290	370	237	275	527	645	1.2	81.7	74.3
21	21	23	Alabama	Birmingham	243	323	203	247	446	570	1.3	83.5	76.5
22	22	24	Florida	Miami	250	321	213	247	463	568	1.2	85.2	76.9
23	24	21	Ohio	Cincinnati	247	309	216	253	463	562	1.2	87.4	81.9
26	25	27	Michigan	Detroit	211	305	166	213	377	518	1.4	78.7	69.8
27	26	28	Florida	West Palm Beach	206	303	167	209	373	512	1.4	81.1	69.0
28	27	29	Maryland	Baltimore	226	299	190	207	416	506	1.2	84.1	69.2
31	31	30	Indiana	Indianapolis	225	269	177	207	402	476	1.2	78.7	77.0
32	33	32	Oregon	Portland	220	263	177	192	397	455	1.1	80.5	73.0
33	36	35	Oklahoma	Oklahoma City	211	247	157	188	368	435	1.2	74.4	76.1
36	39	33	Colorado	Denver	191	218	166	189	357	407	1.1	86.9	86.7
39	37	43	Ohio	Cleveland	200	228	154	170	354	398	1.1	77.0	74.6
41	38	47	Pennsylvania	Pittsburgh	180	224	140	157	320	381	1.2	77.8	70.1
42	44	44	Florida	Jacksonville	182	211	147	169	329	380	1.2	80.8	80.1
43	47	41	Texas	Austin	176	201	150	174	326	375	1.2	85.2	86.6
47	46	48	Arizona	Tucson	166	204	133	156	299	360	1.2	80.1	76.5
49	41	57	North Carolina	Winston-Salem	194	214	133	141	327	355	1.1	68.6	65.9
50	40	63	Utah	Salt Lake City	195	215	117	135	312	350	1.1	60.0	62.8
52	52	49	Virginia	Richmond	166	192	138	152	304	344	1.1	83.1	79.2
53	48	56	California	San Francisco	160	198	131	142	291	340	1.2	81.9	71.7
54	43	68	Arkansas	Little Rock	187	213	116	127	303	340	1.1	62.0	59.6
57	61	50	North Carolina	Charlotte	147	178	130	151	277	329	1.2	88.4	84.8
59	53	66	Nevada	Las Vegas	154	191	113	131	267	322	1.2	73.4	68.6
60	62	59	Tennessee	Nashville	160	178	128	138	288	316	1.1	80.0	77.5
61	57	69	Distr. Columbia	Washington Dc	154	187	112	127	266	314	1.2	72.7	67.9
62	50	71	Washington	Seattle	173	193	114	121	287	314	1.1	65.9	62.7
63	64	61	Kentucky	Louisville	143	170	121	136	264	306	1.2	84.6	80.0
64	70	55	Nebraska	Omaha	143	158	124	144	267	302	1.1	86.7	91.1
65	58	74	Ohio	Columbus	167	187	109	115	276	302	1.1	65.3	61.5
66	65	65	South Carolina	Charleston	154	169	115	132	269	301	1.1	74.7	78.1
68	67	62	New York	Rochester	154	162	129	136	283	298	1.1	83.8	84.0
69	72	64	Kansas	Kansas City	129	152	122	134	251	286	1.1	94.6	88.2
72	76	73	Minnesota	Minneapolis	133	149	108	118	241	267	1.1	81.2	79.2
74	73	76	Florida	Orlando	135	151	101	111	236	262	1.1	74.8	73.5
75	74	79	North Carolina	Durham	145	151	102	107	247	258	1.0	70.3	70.9
80	75	97	Tennessee	Memphis	122	150	80	85	202	235	1.2	65.6	56.7
81	82	82	Washington	Spokane	116	137	91	97	207	234	1.1	78.4	70.8
82	83	84	New Mexico	Albuquerque	114	135	91	96	205	231	1.1	79.8	71.1

* Global ranking

the industry to extend clinical trials beyond established trial regions. This globalization process has evolved over the past decade since the introduction of the ICP GCP guidelines providing an internationally-recognized quality assurance platform for trial conduct.^{1,2}

Criteria for selecting study sites differs among companies but commonly takes into consideration several factors such as patient population size, trial experience, regulatory framework, language skills, cost and potential market size. Although emerging regions with a low gross domestic product (GDP) offer competitive trial budgets, selection is primarily based on non-financial issues, most importantly that an investigator can deliver sufficient subjects in time and in full compliance with the protocol.

Perhaps these are some of the reasons we see that the US accounts for more than half of the top 100 cities worldwide, based on the number of registered study sites. The New York Metropolitan area stands out as the leading city globally -- followed by Atlanta, (Paris),

Chicago, Phoenix, Houston, Los Angeles, San Diego, Dallas and San Antonio. The US States of California, Texas and New York State stand out not only with the highest number of study sites, but also with six cities among the top 10 globally. With a population of 18 million, Florida has 5,762 registered sites, similar to the number of sites in France which has a much larger population of 61 million. Florida also has more sites than the UK, Spain and Italy, which have populations 2-3 times larger. Interestingly, there are regional variations in the US, with more testing done in the South Region, notably Florida, Texas and the Carolinas, than in the Midwest and Northeast.

Why are France, Germany and the UK, homes to large pharmaceutical companies, domestically conducting fewer trials than the US? Firstly, the US is the pharmaceutical industry's leading market, so new drug approval by the US Food and Drug Administration is consequently a priority. Secondly, the industry has access to key clinical investigators and a well-established, highly professional clinical trial contract

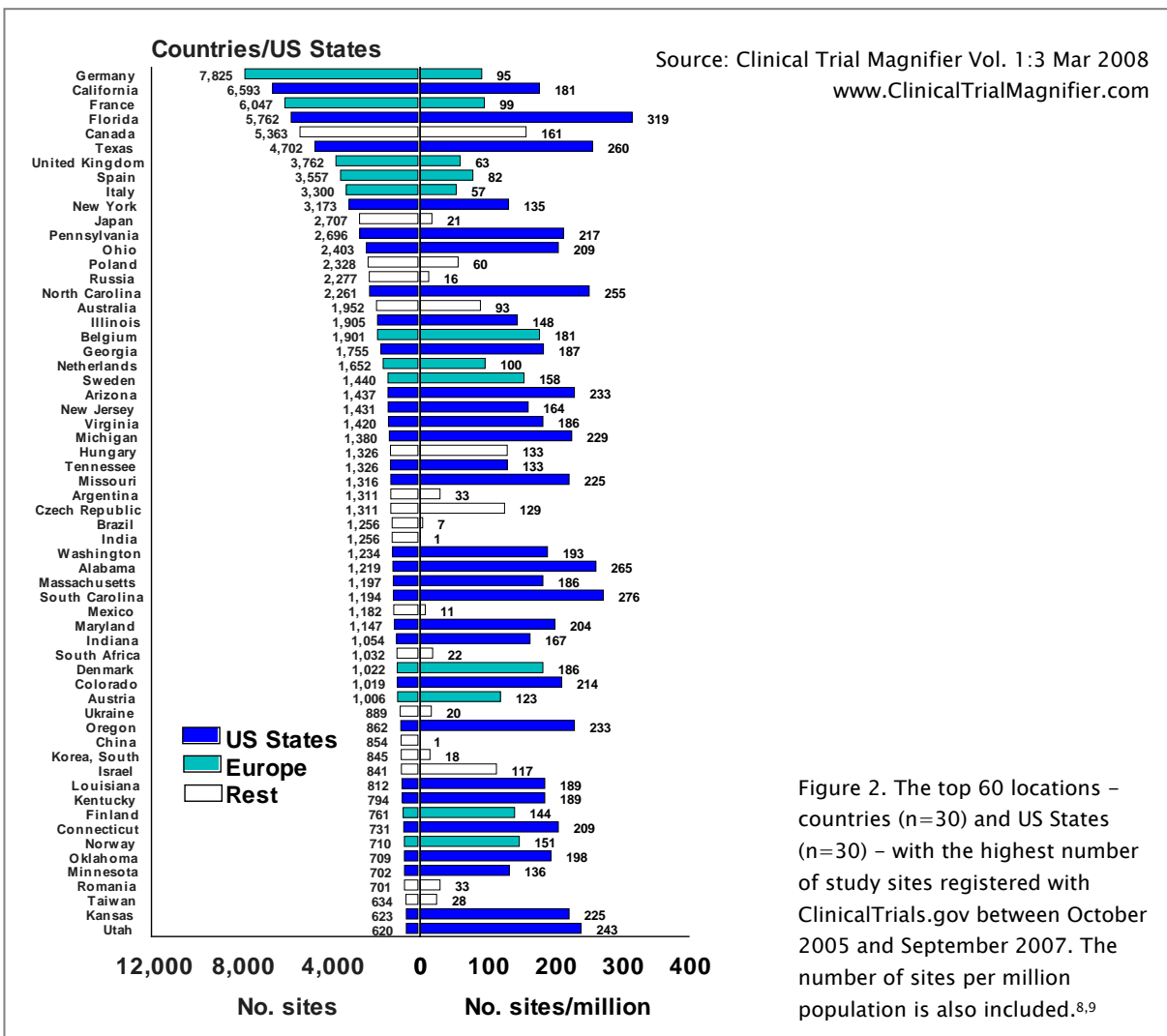


Figure 2. The top 60 locations – countries (n=30) and US States (n=30) – with the highest number of study sites registered with ClinicalTrials.gov between October 2005 and September 2007. The number of sites per million population is also included.^{8,9}

research organization service industry in the US. Since the mid-1990s, virtually all US clinical academic institutions have established administrative clinical trial centers – “Offices of Clinical Trials” – that offer ‘one-stop-shop’ solutions for clinical trial contract, budget and other additional services such as research pharmacy and accredited core laboratories. Such efficient infrastructure is vital for the industry to meet important quality assurance demands and timelines. This is still largely absent in other geographic regions, whether established or emerging.

Still, about one out of five clinical study sites registered with ClinicalTrials.gov are in emerging countries,^{3,6} demonstrating that sponsored clinical research on new medicines has become global. But even large emerging countries such as China, India, Brazil, Mexico, Russia, South Korea and Ukraine still have far fewer clinical trial sites per million population (<10%) than the US. Those countries evidently have large growth potential in the clinical trial arena, although they must develop a clinical trial infrastructure equivalent to the US to become more competitive and not simply only compete by low cost and large patient pools. A reasonably large potential market for the pharmaceutical industry is also of key importance for a country’s transition from emerging to established clinical trial status.

In conclusion, the US accounts for about half of all industry-sponsored clinical trial sites globally, and also contributes around half of the top 100 cities worldwide, based on the number of registered study sites. Clearly, the US is an extremely strong position in clinical testing of new medicines, remaining predominant over Europe and emerging countries despite rapidly increasing international competition from low-cost countries, many with large patient pools. Due to vital added values in the US, no significant change in this dominance seems likely.

Acknowledgement

This study could not have been completed without the implementation of the ICMJE policy and the existence of the ClinicalTrials.gov trial register.

References

1. ICH Harmonised Tripartite Guideline for Good Clinical Practice E6 The International Conference on Harmonisation, 1996. Available on line at <http://www.ich.org/>.
2. The globalization of clinical trials: a growing challenge in protecting human subjects:

executive summary (2001). *J Int Bioethique* 2003;14:165–9.

3. Thiers F, Sinskey AJ, Berndt ER. Trends in the globalization of clinical trials. *Nature Rev Drug Discov* 2008;7:13–4.
4. De Angelis C, Drazen JM, Frizelle FA, et al. Clinical trial registration: a statement from the International Committee of Medical Journal Editors. *N Engl J Med* 2004;351:1250–1.
5. De Angelis C, Drazen JM, Frizelle FA, et al. Is This Clinical Trial Fully Registered? A Statement from the International Committee of Medical Journal Editors. *N Engl J Med* 2005;352:2436–8.
6. Karlberg JPE. Globalization of Sponsored Clinical Trials. *Nature Rev Drug Discov*. In Press.
7. Statistical Analysis System, Version 9.1.3. SAS Institute, Cary, North Carolina, US, 2007.
8. United States -- States; and Puerto Rico. 2006 Population Estimates. U.S. Census Bureau, Population Division. Available on line at <http://factfinder.census.gov>.
9. UNFPA State of World Population 2007. United Nations Population Fund. Available on line at <https://www.unfpa.org>.
10. Guidance for Industry Information Program on Clinical Trials for Serious or Life-Threatening Diseases and Conditions. Division of Drug Information, Center for Drug Evaluation and Research, United States Food and Drug Administration, 2002. Available online at <http://www.fda.gov/cder/guidance/index.htm>.
11. Pediatric Research Equity Act of 2003. Federal Food, Drug, and Cosmetic Act. US FDA. Available on line at <http://www.fda.gov>.
12. Kola, I. & Landis, J. Can the pharmaceutical industry reduce attrition rates? *Nature Rev. Drug Discov*. 3, 711–715 (2004).
13. Drug Development Science Obstacles and Opportunities for Collaborations. Association of American Medical Colleges and the US. Food and Drug Administration. 2005. Available on line at <https://services.aamc.org>.
14. Karlberg JPE. Disease focus in drug development. *Nature Rev Drug Discov*. In press.

Methods

The ICMJE policy applies to any clinical trial commencing enrolment after July 1, 2005. Since the policy’s introduction, the pharmaceutical industry has consistently registered over 2,700 new phase II–IV trials annually with the US-based clinical trial register www.ClinicalTrials.gov, compared with 336 previously. Virtually all of world’s leading pharmaceutical companies

now register at ClinicalTrials.gov⁶ – making it a truly global register of industry-sponsored phase II–IV clinical trials. Trials registered before 2005 were overwhelmingly conducted in the US, with life-threatening disease studies predominant. This dominance has reduced since 2005, stabilizing at about 47% of study sites located to the US, with 18% of diseases studied being life-threatening.⁶ Trials registered between July and September 2005 are partially biased, because they not only include new trials planned, but also ongoing/completed trials, which has to be registered before September 13, 2005 to comply with the new ICMJE policy. From October 2005 onwards, however, registrations provided a satisfactory overview of sponsored clinical trial activity according to region, country, sponsor, therapeutic areas and diseases.

Data capture: Data was captured at ClinicalTrials.gov for all “Industry Sponsored” trials on November 1, 2007. Essential information was extracted by a tailor-made SAS program (Statistical Analysis System).⁷ The dataset was subsequently analyzed using SAS.

Extracted information: Register id, date of first registration, date of last update, study phase (phase I–IV), type of study (observational or experimental), primary and secondary sponsors, therapeutic/disease area, study site location (i.e. country and city, with institution rarely listed), global sample size, status of the trial, and test medication or test device.

Analysis Dataset: The following inclusion/exclusion criteria restricted the analysis dataset to industry sponsored clinical trials:

- Interventional studies, not observational studies, were included.
- True industry sponsored trials were included, not trials with a non-for-profit organization registered as the prime sponsor.
- Initiated or completed trials were included, not withdrawn trials.
- Only phase II–IV trials were included, not phase I trials, since they do not yet require registration under the ICMJE policy.
- Trials with information about the location of the study site(s) were included, but not protocols not providing any site address.
- While initiated trials were included, trials under planning were not.

Trials first registered between October 2005 and September 2007 giving two full years of data were included. The number of trials registered in September 2005 increased temporarily by about 400% due to one specific ICMJE policy, namely the September 2005 deadline date for registration of ongoing studies. This was why only trials registered from October 2005 onwards were included in the final analysis.

Statistical analysis was not only performed for the whole data set, but also for all studies first registered between October 2005 and September 2006 (Year 1), and all studies first registered between October 2006 and September 2007 (Year 2).

Identifications of cities: Some US cities stretch over more than one State. For instance, Kansas City straddles both Missouri and Kansas, and is represented by two separate legal jurisdictions. Study sites in cities in more than one State are here grouped in the States, rather than one single city. Study sites in metropolitan areas/suburbs of large cities such

as New York, Sydney, Paris, Johannesburg and Madrid are grouped in their respective cities. Both countries and US States are well defined in the register, since pull-down menus are used at registration. However, many cities are not spelled uniformly. For instance, Saint Louis (US) is variously recorded as Saint Louis, St Louis, St. Louis and St.Louis. In Russia, St. Petersburg is alternatively recorded as Leningrad, Saint Petersburg, Saint–Petersburg, St Petersburg, St. Petersburg, St. Petersburg, St.Petersburg, St.–Petersburg and St–Petersburg. In Sweden, Goteborg is referred to as Ga–Teborg, Goeteborg, Goteboerg, Goteborg, Goteburg, Gotenborg, Gotheburg, Gothenberg, Gothenburg and Gothenburgh. Our tailor-made SAS program coded such spelling variations for all major cities globally.

For some countries like the United States, close to all (97.9%) study site location addresses were identified and subsequently checked of their existence and spelling. For other countries a slightly lower proportion of site addresses were not coded by city, such as the UK (87.9%) and France (84.7%), usually because they were in small towns and villages outside large cities and metropolitan areas.

Identifications of cities: Some US cities stretch over more than one State. For instance, Kansas City straddles both Missouri and Kansas, and is represented by two separate legal jurisdictions. Study sites in cities in more than one State are here grouped in the States, rather than one single city. Study sites in metropolitan areas/suburbs of large cities such as New York, Sydney, Paris, Johannesburg and Madrid are grouped in their respective cities. Both countries and US States are well defined in the register, since pull-down menus are used at registration. However, many cities are not spelled uniformly. For instance, Saint Louis (US) is variously recorded as Saint Louis, St Louis, St. Louis and St.Louis. In Russia, St. Petersburg is alternatively recorded as Leningrad, Saint Petersburg, Saint–Petersburg, St Petersburg, St. Petersburg, St. Petersburg, St.Petersburg, St.–Petersburg and St–Petersburg. In Sweden, Goteborg is referred to as Ga–Teborg, Goeteborg, Goteboerg, Goteborg, Goteburg, Gotenborg, Gotheburg, Gothenberg, Gothenburg and Gothenburgh. Our tailor-made SAS program coded such spelling variations for all major cities globally.

For some countries like the United States, close to all (97.9%) study site location addresses were identified and subsequently checked of their existence and spelling. For other countries a slightly lower proportion of site addresses were not coded by city, such as the UK (87.9%) and France (84.7%), usually because they were in small towns and villages outside large cities and metropolitan areas.



Clinical Trial Magnifier
www.ClinicalTrialMagnifier.com
editorialboard@ClinicalTrialMagnifier.com

Editorial Board

Clinical Trials Centre



Li Ka Shing Faculty of Medicine
The University of Hong Kong
Queen Mary Hospital
8/F, Clinical Pathology Building
102 Pokfulam Road
Hong Kong
Phone: (852) 2855 4664
Fax: (852) 2974 1248
E-mail : ctcentre@hkucc.hku.hk
Home page: <http://www.hku.hk/ctc/>

Commentary

Requirements for Running Clinical Trials in Mainland China and in Hong Kong

Dear Dr. Karlberg,

First, let me congratulate you on the Clinical Trial Magnifier publication. It is an outstanding resource of information, and I appreciate the efforts of you and your colleagues to produce it.

Secondly, I have a few questions for you regarding your experience at the Clinical Trials Centre at the University of Hong Kong. The reason for my questions is that I am developing a database of information on public disclosure requirements for clinical trials (registration and results) around the globe. I am trying to determine whether sponsors view Hong Kong differently, and thus whether I need an entry in the database for Hong Kong that is separate from China as a whole – only because that may be the way sponsors think of it.

Your comments would be most appreciated.

Best regards,

John McKenney
President, SEC Associates, Inc.
Raleigh, NC 27615, USA
www.secassociates.com

Dear Mr. McKenney,

Thank you for the letter and for the relevant questions. The database of information on public disclosure requirements for clinical trials (registration and results) around the globe that you are establishing will certainly be highly appreciated by various parties involved in clinical research. We will answer your questions below.

Johan PE Karlberg, MD, PhD
Professor and Director
Henry Yau, MBA, BSc
Assistant Director and B&D Manager
Clinical Trials Centre
Li Ka Shing Faculty of Medicine
The University of Hong Kong
Hong Kong SAR

Q: Is there any difference between running clinical trials in Mainland China and in Hong Kong?

At this point in time, do you feel that clinical trial sponsors and CROs regard running clinical trials in Hong Kong any differently than running clinical trials in Mainland China? Or, do you see no difference?

Alternatively, has your experience been that sponsors no longer think of Hong Kong as distinct from mainland China, therefore they should be included as a single integrated section of the database?

A: There are large differences in conducting clinical trials in Hong Kong and in Mainland China.

In order to initiate a new drug trial in Hong Kong you only need to obtain an approval from the Hong Kong Department of Health and no approval is needed from the State Food and Drug Administration (SFDA) in Beijing, China. Medical devices and cell therapy trials are not regulated in Hong Kong and require only an IRB approval.

In Mainland China all clinical trials of medical devices, vaccines, drugs and herbal products must be approved by the SFDA, and all trial documents must be submitted in Chinese. Rather than simply adopting the ICH GCP guidelines, Mainland China has developed its own GCP guidelines, and all trials must be conducted in SFDA-accredited hospitals. The accreditation process is extensive and as such the only of its kind worldwide.

In 2007 our university hospital in Hong Kong was accredited in seven therapeutic areas, which means that we now can contribute clinical trial data for drug registration purpose in Mainland China.

Importantly, Hong Kong as with the rest of Asia has accepted the ICH GCP guidelines. Since the introduction of the ICH GCP Guideline in 1996 we have seen a steady stream of sponsors and CROs allocating clinical trials to Hong Kong in a similar pace as in other emerging regions. However, this development has been relatively slow in Mainland China, mostly due to the long regulatory approval process; many times early global clinical trials have already been completed before an approval has been obtained in Mainland China.

Today, about 50% of all trials in China registered with www.clinicaltrials.gov are multi-national in nature and the other 50% are local registration trials usually with a fixed and rather small sample size.

The IRBs in Hong Kong review protocols independently and do not necessarily only accept protocols that have been approved by overseas regulatory authorities.

Additionally, all professional business in Hong Kong is conducted in English. With the exception of informed consent forms, which need to be translated into Chinese, there is no requirement to translate other clinical trial related documents as the case is in Mainland China – whether for ethics or regulatory approval purpose.

For the above reasons, most sponsors and CROs view Hong Kong and Mainland China very differently. Having separate entries for Hong Kong and Mainland China in your database will be useful to the database users.

Q: Does Hong Kong require registration of clinical trials?

In your experience, do Ethics Committees in Hong Kong require registration of clinical trials in ChiCTR for protocol approval (even though registration is supposed to be voluntary)?

A: There is no governmental or institutional requirement to register a clinical trial conducted in Hong Kong in a local or overseas trial register. Company-sponsored clinical trials are usually registered by sponsors in the US trial register (www.clinicaltrials.gov). Our university has however established our own trial register (www.hkclinicaltrials.com), since we would like to inform the local community about ongoing research projects and provide interested subjects the possibilities to participate.

Our IRB applications are made electronically. If an investigator and a sponsor agree to register a trial with our trial register, relevant trial information will be uploaded automatically. At present our trial register includes about 600 of the 1,000 IRB applications handled by our IRB over the past 2.5 years.

The new drug registration process is also quite simple in Hong Kong. Marketing approvals are normally granted for new drugs which have already been approved by at least two developed countries such as the US and EC countries. No local registration trial is required in Hong Kong.

Investigator Network Focus

Thailand Clinical Research Collaboration Network

Clinical Research Collaboration Network – CRCN – founded in 2000

The Clinical Research Collaboration Network (CRCN) is a not-for-profit academic clinical research organization founded in 2000 by the Consortium of Thai Medical Schools and Health System Research Institute, Thailand. CRCN is the only academic clinical research network formally established in Thailand, with the continued core support of the Consortium of Thai Medical Schools.

CRCN Objectives

CRCN aims to improve health care quality and effectiveness by providing core multicenter clinical research services to all medical schools (currently 17) and affiliated hospitals of the Ministry of Public Health Hospitals in Thailand. The focus is on locally relevant as well as related global health service issues. Additionally, CRCN provides clinical research capacity development to hospitals within the network.

CRCN Project Operation

With a centrally located office in Bangkok, CRCN provides full multicenter clinical study services, including research consultation, study design, study management, monitoring, data management, statistical services, medical writing and regulatory services for both investigator-initiated and sponsor-initiated clinical projects. CRCN has recently expanded its network and services to locally-conducted global clinical projects with the implementation of clinical data management and project monitoring services.

CRCN Network

By networking with clinical research teams within the 30 plus clinical professional organizations in Thailand, CRCN has continued to produce research outputs and large clinical databases (15 databases in 2007). This information is accessible for translation into health services policy, more research and can be used for clinical practice guidelines.

CRCN Organization

CRCN became better known as an academic clinical research network in 2002 with the opening of an office. CRCN is a secretary office of the Consortium of Thai Medical Schools–Research Committee, which consists of the associate dean for research affairs of all 17 medical schools. Each medical school will have a clinical research center (CRC) and all 17 CRC's will form a CRC network to be a platform of promotion of multicenter clinical research.


500 to 160,000 study subjects

For the past five years, there have been fifteen multicenter clinical databases collected by clinical expert research teams and there are approximately 5–8 new multicenter clinical research studies being facilitated by CRCN each year. The studies vary in size (number of subjects varies from 500 to 160,000) and number of participating hospitals which can be from 5–50. There are more than 40 scientific publications in local and international journals.

Pyatat Tatsanavivat, MD
Professor and Director
Clinical Research Collaboration Network
Bangkok, Thailand
<http://www.crcn.in.th>




Dr. Pyatat Tatsanavivat with CRCN members visiting the Clinical Trials Centre, The University of Hong Kong in February 2008.



Clinical Trial Magnifier
www.ClinicalTrialMagnifier.com
editorialboard@ClinicalTrialMagnifier.com

Editorial Board
Clinical Trials Centre



Li Ka Shing Faculty of Medicine
 The University of Hong Kong
 Queen Mary Hospital
 8/F, Clinical Pathology Building
 102 Pokfulam Road
 Hong Kong
 Phone: (852) 2855 4664
 Fax: (852) 2974 1248
 E-mail : ctcentre@hkucc.hku.hk
 Home page: <http://www.hku.hk/ctc/>

New Trial Registrations (Table 1 of 3)

The most recent industry sponsored clinical trials testing drugs, biological or medical devices registered with www.ClinicalTrials.gov; registered from March 1, 2008 and still not activated (Planning) or recruiting (Requiring) subjects on March 30, 2008.

Status	Link/ID	Type	Phase	Sponsor	Size (n)	Min age	Max age	Condition
PLANNING	NCT00633269	Drug	1	AstraZeneca	6	18 Yr	N/A	Neoplasm Metastasis
PLANNING	NCT00634660	Drug	1	Biomarin	35	16 Yr	50 Yr	Phenylketonuria
PLANNING	NCT00632424	Drug	1	Bristol-Myers Squibb	36	18 Yr	N/A	Advanced Solid Tumors
PLANNING	NCT00634088	Drug	1	Bristol-Myers Squibb	60	18 Yr	N/A	Metastatic Breast Cancer
PLANNING	NCT00644488	Drug	1	Bristol-Myers Squibb	24	20 Yr	N/A	Prostate Cancer
PLANNING	NCT00633126	Drug	1	Cerexa	8	12 Yr	17 Yr	Infection
PLANNING	NCT00640328	Drug	1	Genmab	324	18 Yr	55 Yr	Relapsing Remitting Multiple Sclerosis
PLANNING	NCT00640497	Biological	1	Henogen	12	18 Yr	N/A	Acute Graft Versus Host Disease
PLANNING	NCT00638989	Drug	1	Medimmune	24	19 Yr	55 Yr	Healthy
PLANNING	NCT00635596	Biological	1	Micromet	30	18 Yr	N/A	Solid Tumors
PLANNING	NCT00646165	Drug	1	Mundipharma	45	18 Yr	N/A	Relapsed B-Cell Chronic Lymphocytic Leukemia
PLANNING	NCT00637338	Biological	1	Pfizer	100	18 Yr	70 Yr	Diabetes Mellitus, Type 2
PLANNING	NCT00638742	Drug	1	Pfizer	30	N/A	N/A	Ocular Hypertension
PLANNING	NCT00644839	Drug	1	Pfizer	28	18 Yr	55 Yr	Obesity
PLANNING	NCT00645021	Drug	1	Pfizer	24	18 Yr	65 Yr	Hepatic Insufficiency
PLANNING	NCT00636558	Drug	1	Viralytics	26	18 Yr	N/A	Prostate Cancer
PLANNING	NCT00641225	Drug	1	Wyeth	46	18 Yr	70 Yr	Rheumatoid Arthritis
PLANNING	NCT00637247	Drug	2	Amplimed	124	18 Yr	N/A	Pancreatic Neoplasms
PLANNING	NCT00642811	Drug	2	AstraZeneca	80	18 Yr	N/A	Stable Coronary Artery Disease
PLANNING	NCT00645788	Drug	2	Bayer	240	18 Yr	N/A	Cystic Fibrosis
PLANNING	NCT00632749	Drug	2	Boehringer Ingelheim	169	18 Yr	N/A	Leukemia, Myeloid, Acute
PLANNING	NCT00633464	Drug	2	Bristol-Myers Squibb	80	18 Yr	N/A	Metastatic Breast Cancer
PLANNING	NCT00633789	Drug	2	Bristol-Myers Squibb	300	18 Yr	N/A	Pancreatic Cancer
PLANNING	NCT00646425	Drug	2	Cerimon	56	12 Yr	80 Yr	Non-Infectious Uveitis
PLANNING	NCT00640484	Drug	2	Chiesi	60	40 Yr	75 Yr	Chronic Obstructive Pulmonary Disease
PLANNING	NCT00640965	Drug	2	D-Pharm	40	18 Yr	85 Yr	Migraine
PLANNING	NCT00636818	Drug	2	Eli Lilly	40	18 Yr	N/A	Attention Deficit Hyperactivity Disorder
PLANNING	NCT00642174	Drug	2	Eli Lilly	40	18 Yr	74 Yr	Coronary Artery Disease
PLANNING	NCT00636610	Drug	2	Genentech	150	18 Yr	N/A	Metastatic Colorectal Cancer
PLANNING	NCT00642603	Drug	2	Hoffmann-La Roche	230	18 Yr	N/A	Colorectal Cancer
PLANNING	NCT00643565	Drug	2	Hoffmann-La Roche	45	2 Yr	17 Yr	Sarcoma
PLANNING	NCT00633295	Drug	2	Novartis	15	18 Yr	N/A	Gastrointestinal Stromal Tumors (GIST)
PLANNING	NCT00637923	Drug	2	Romark	60	18 Yr	N/A	Chronic Hepatitis C
PLANNING	NCT00642993	Drug	2	Schering-Plough	300	18 Yr	N/A	Body Weight
PLANNING	NCT00634933	Drug	2	Wyeth	216	18 Yr	N/A	Active Rheumatoid Arthritis
PLANNING	NCT00641056	Drug	3	Amylin	456	18 Yr	N/A	Type 2 Diabetes Mellitus
PLANNING	NCT00634049	Drug	3	Basilea Ceutica	100	18 Yr	N/A	Invasive Fungal Infections
PLANNING	NCT00637377	Drug	3	Bayer	1200	50 Yr	N/A	Macular Degeneration
PLANNING	NCT00633893	Drug	3	Bristol-Myers Squibb	2500	18 Yr	N/A	Venous Thrombosis
PLANNING	NCT00636168	Drug	3	Bristol-Myers Squibb	950	18 Yr	N/A	High Risk Stage Iii Melanoma
PLANNING	NCT00643201	Drug	3	Bristol-Myers Squibb	5000	18 Yr	N/A	Venous Thrombosis
PLANNING	NCT00643851	Drug	3	Bristol-Myers Squibb	600	18 Yr	77 Yr	Type 2 Diabetes
PLANNING	NCT00635089	Drug	3	Ception	172	5 Yr	N/A	Eosinophilic Esophagitis
PLANNING	NCT00638690	Drug	3	Cougar	1158	18 Yr	N/A	Castration-Resistant Prostate Cancer
PLANNING	NCT00641719	Drug	3	Eli Lilly	300	20 Yr	80 Yr	Diabetic Neuropathies
PLANNING	NCT00642304	Drug	3	Hoffmann-La Roche	200	18 Yr	N/A	Anemia
PLANNING	NCT00642460	Drug	3	Hoffmann-La Roche	108	2 Yr	17 Yr	Juvenile Idiopathic Arthritis
PLANNING	NCT00642967	Drug	3	Hoffmann-La Roche	250	18 Yr	N/A	Anemia
PLANNING	NCT00642616	Drug	3	Mannkind	474	18 Yr	70 Yr	Diabetic Type 2
PLANNING	NCT00640588	Drug	3	Novartis	30	18 Yr	N/A	Hepatitis B, Chronic

New Trial Registrations (Table 2 of 3)

The most recent industry sponsored clinical trials testing drugs, biological or medical devices registered with www.ClinicalTrials.gov; registered from March 1, 2008 and still not activated (Planning) or recruiting (Requiring) subjects on March 30, 2008.

Status	Link/ID	Type	Phase	Sponsor	Size (n)	Min age	Max age	Condition
PLANNING	NCT00644969	Drug	3	Pfizer	120	18 Yr	75 Yr	Smoking
PLANNING	NCT00640601	Drug	4	AstraZeneca	500	18 Yr	65 Yr	Schizophrenia
PLANNING	NCT00638157	Drug	4	Cubist	60	18 Yr	N/A	Infective Endocarditis
PLANNING	NCT00634569	Biological	4	Grifols	30	2 Yr	16 Yr	Primary Immune Deficiency Diseases
PLANNING	NCT00642668	Drug	4	Hoffmann-La Roche	200	18 Yr	N/A	Anemia
PLANNING	NCT00640393	Drug	4	Innovaderm	98	18 Yr	N/A	Psoriasis Vulgaris
PLANNING	NCT00634920	Drug	4	Novartis	250	18 Yr	N/A	Chronic Allograft Nephropathy
PLANNING	NCT00646737	Drug	4	Novartis	168	18 Yr	65 Yr	Kidney Transplantation
PLANNING	NCT00641004	Drug	4	Otsuka Co	30	18 Yr	65 Yr	NSAID Induced Gastropathy
PLANNING	NCT00637780	Drug	4	Pfizer	12	6 Yr	17 Yr	Arthritis, Juvenile Rheumatoid
PLANNING	NCT00635609	Drug	4	Warner Chilcott	100	12 Yr	N/A	Acne Vulgaris
PLANNING	NCT00640720	Device	4	Cordis	200	18 Yr	80 Yr	Peripheral Artery Disease
PLANNING	NCT00643474	Device	NA	Hoffmann-La Roche	1000	35 Yr	75 Yr	Diabetes Mellitus, Type 2
RECRUITING	NCT00635284	Drug	1	Abraxis	42	18 Yr	N/A	Solid Tumors
RECRUITING	NCT00633841	Biological	1	Affiris	24	50 Yr	80 Yr	Alzheimer's Disease
RECRUITING	NCT00637702	Drug	1	Array	24	18 Yr	N/A	Solid Tumors
RECRUITING	NCT00637039	Drug	1	AstraZeneca	30	18 Yr	N/A	Advanced Solid Malignancies
RECRUITING	NCT00636519	Biological	1	Cangene	36	18 Yr	55 Yr	Healthy Volunteers
RECRUITING	NCT00642538	Drug	1	Mannkind	20	18 Yr	70 Yr	Diabetes Mellitus, Type 2
RECRUITING	NCT00635830	Biological	1	Merck	40	9 Yr	26 Yr	HPV Infection
RECRUITING	NCT00636207	Drug	1	Merck	48	18 Yr	65 Yr	Asthma
RECRUITING	NCT00642798	Drug	1	Merck	16	18 Yr	45 Yr	Diabetes Mellitus Non-Insulin-Dependent
RECRUITING	NCT00642954	Drug	1	Merck	44	18 Yr	N/A	Relapsed/Refractory Multiple Myeloma
RECRUITING	NCT00635557	Drug	1	Myriad	30	18 Yr	N/A	Glioblastoma Multiforme
RECRUITING	NCT00637221	Drug	1	Neuropharm	12	18 Yr	45 Yr	Fragile X Syndrome
RECRUITING	NCT00633997	Drug	1	Novartis	32	30 Yr	65 Yr	Diabetes Mellitus, Type 2
RECRUITING	NCT00645346	Biological	1	Novartis	130	18 Yr	40 Yr	Invasive Group B Streptococcus (GBS) Disease
RECRUITING	NCT00635193	Drug	1	PdI	150	18 Yr	N/A	Primary Peritoneal Cancer
RECRUITING	NCT00644124	Drug	1	Sanofi-Aventis	50	18 Yr	N/A	Lymphoma, Non-Hodgkin
RECRUITING	NCT00643981	Biological	1	Tca Cellular Therapy	10	18 Yr	80 Yr	Coronary Arteriosclerosis
RECRUITING	NCT00640185	Drug	2	Abbott	150	18 Yr	60 Yr	Attention Deficit-Hyperactivity Disorder
RECRUITING	NCT00640419	Drug	2	Abbott	105	6 Yr	12 Yr	Attention Deficit Hyperactivity Disorder
RECRUITING	NCT00645177	Drug	2	Abbott	102	18 Yr	N/A	Metastatic Breast Cancer
RECRUITING	NCT00632242	Drug	2	Archemix Corp	28	18 Yr	75 Yr	Von Willebrand Disease Type-2b
RECRUITING	NCT00643448	Drug	2	AstraZeneca	80	20 Yr	80 Yr	Atrial Fibrillation
RECRUITING	NCT00640523	Drug	2	Biocryst	26	18 Yr	N/A	Chronic Lymphocytic Leukemia (CLL)
RECRUITING	NCT00638755	Drug	2	Capnia	20	19 Yr	65 Yr	Perennial Allergic Rhinitis
RECRUITING	NCT00633152	Drug	2	Cerexa	150	18 Yr	N/A	Bacterial Infection
RECRUITING	NCT00640705	Drug	2	Cerimon	308	18 Yr	75 Yr	Ankle Sprain
RECRUITING	NCT00638716	Drug	2	Conjuchem	90	25 Yr	N/A	Type 2 Diabetes Mellitus
RECRUITING	NCT00642902	Drug	2	EMD Serono	292	18 Yr	60 Yr	Relapsing Multiple Sclerosis
RECRUITING	NCT00642148	Drug	2	GlaxoSmithKline	300	40 Yr	N/A	Chronic Obstructive Pulmonary Disease
RECRUITING	NCT00642473	Drug	2	Hoffmann-La Roche	34	18 Yr	N/A	Non-Small Cell Lung Cancer
RECRUITING	NCT00642733	Drug	2	Hoffmann-La Roche	30	18 Yr	N/A	Pancreatic Cancer
RECRUITING	NCT00642824	Drug	2	Hoffmann-La Roche	40	18 Yr	N/A	Lung Cancer
RECRUITING	NCT00642941	Drug	2	Hoffmann-La Roche	180	12 Yr	N/A	Sarcoma
RECRUITING	NCT00638378	Drug	2	Incyte	41	18 Yr	N/A	Metastatic Prostate Cancer
RECRUITING	NCT00639002	Drug	2	Incyte	37	18 Yr	N/A	Multiple Myeloma
RECRUITING	NCT00644787	Drug	2	Janssen	154	20 Yr	N/A	Pain
RECRUITING	NCT00639249	Drug	2	M's Science	60	18 Yr	80 Yr	Ischemic Stroke

New Trial Registrations (Table 3 of 3)

The most recent industry sponsored clinical trials testing drugs, biological or medical devices registered with www.ClinicalTrials.gov; registered from March 1, 2008 and still not activated (Planning) or recruiting (Requiring) subjects on March 30, 2008.

Status	Link/ID	Type	Phase	Sponsor	Size (n)	Min age	Max age	Condition
RECRUITING	NCT00642681	Drug	2	Mannkind	50	18 Yr	80 Yr	Upper Respiratory Infections
RECRUITING	NCT00636792	Drug	2	Millennium	75	18 Yr	N/A	Follicular Lymphoma
RECRUITING	NCT00644878	Drug	2	Novartis	160	18 Yr	N/A	Chronic Myelogenous Leukemia
RECRUITING	NCT00635622	Drug	2	Osel	40	18 Yr	40 Yr	Bacterial Vaginosis
RECRUITING	NCT00635232	Drug	2	Pharmacoepia	375	18 Yr	70 Yr	Hypertension
RECRUITING	NCT00640146	Drug	2	Progenics	260	18 Yr	N/A	Opioid-Induced Constipation
RECRUITING	NCT00642707	Drug	2	Progenics	40	18 Yr	N/A	HIV Infection
RECRUITING	NCT00633659	Drug	2	Sangart	12	N/A	N/A	Chronic Critical Lower Limb Ischemia
RECRUITING	NCT00639158	Drug	3	Abbott	460	18 Yr	N/A	Mixed Dyslipidemia
RECRUITING	NCT00637273	Drug	3	Amylin	500	18 Yr	N/A	Type 2 Diabetes Mellitus
RECRUITING	NCT00633932	Drug	3	AstraZeneca	555	20 Yr	N/A	Reflux Esophagitis
RECRUITING	NCT00634114	Drug	3	AstraZeneca	240	20 Yr	N/A	Reflux Esophagitis
RECRUITING	NCT00640562	Drug	3	AstraZeneca	290	18 Yr	65 Yr	Depression
RECRUITING	NCT00632814	Drug	3	Bayer	40	1 Year	12 Yr	Hemophilia A
RECRUITING	NCT00637494	Drug	3	Corcept	450	22 Yr	75 Yr	Psychosis
RECRUITING	NCT00641745	Drug	3	Dainippon Sumitomo	600	18 Yr	75 Yr	Schizoaffective Disorder
RECRUITING	NCT00641537	Drug	3	EMD Serono	1100	18 Yr	65 Yr	Relapsing-Remitting Multiple Sclerosis
RECRUITING	NCT00640510	Drug	3	Eli Lilly	30	20 Yr	64 Yr	Schizophrenia
RECRUITING	NCT00635219	Drug	3	H Lundbeck	660	18 Yr	75 Yr	Major Depressive Disorder
RECRUITING	NCT00642577	Drug	3	Hoffmann-La Roche	210	18 Yr	N/A	Colorectal Cancer
RECRUITING	NCT00642850	Drug	3	Hoffmann-La Roche	200	18 Yr	N/A	Anemia
RECRUITING	NCT00639678	Drug	3	Human Genome	320	18 Yr	N/A	Healthy
RECRUITING	NCT00641667	Drug	3	Janssen	63	20 Yr	N/A	Cancer
RECRUITING	NCT00645099	Drug	3	Janssen-Cilag	456	18 Yr	65 Yr	Schizophrenia
RECRUITING	NCT00640822	Drug	3	Leo	735	18 Yr	N/A	Psoriasis Vulgaris
RECRUITING	NCT00634192	Drug	3	Novartis	50	6 Yr	N/A	Pseudomonas Infections
RECRUITING	NCT00636961	Drug	3	Novartis	24	40 Yr	75 Yr	Chronic Obstructive Pulmonary Disease
RECRUITING	NCT00646542	Drug	3	Novartis	300	18 Yr	85 Yr	Diabetes Mellitus, Type 2
RECRUITING	NCT00635427	Biological	3	Shire	102	2 Yr	N/A	Gaucher Disease, Type 1
RECRUITING	NCT00644007	Drug	3	Sk	112	19 Yr	N/A	Erectile Dysfunction
RECRUITING	NCT00635063	Drug	3	Sosei	150	18 Yr	N/A	Pain
RECRUITING	NCT00638911	Drug	4	Boehringer Ingelheim	9435	18 Yr	N/A	Hypertension
RECRUITING	NCT00641082	Drug	4	Bukwang	72	18 Yr	60 Yr	Chronic Hepatitis B
RECRUITING	NCT00644332	Drug	4	CV	200	18 Yr	N/A	Chronic Angina
RECRUITING	NCT00635128	Biological	4	GlaxoSmithKline	959	9 Yr	13 Yr	Poliomyelitis
RECRUITING	NCT00634543	Drug	4	Janssen	176	18 Yr	75 Yr	Diabetic Neuropathies
RECRUITING	NCT00635349	Drug	4	Janssen	172	40 Yr	75 Yr	Osteoarthritis
RECRUITING	NCT00640042	Drug	4	King	2000	21 Yr	N/A	Pain
RECRUITING	NCT00631917	Drug	4	Novartis	640	50 Yr	N/A	Hypertension
RECRUITING	NCT00639691	Biological	4	Novartis	50	6 Yr	N/A	Asthma
RECRUITING	NCT00642356	Drug	4	Novartis	172	30 Yr	75 Yr	Parkinson's Disease
RECRUITING	NCT00646503	Drug	4	Novartis	150	18 Yr	N/A	Hepatitis B, Chronic
RECRUITING	NCT00634842	Drug	4	Novo Nordisk	236	18 Yr	N/A	Type 2 Diabetes Mellitus
RECRUITING	NCT00643604	Drug	4	United	25	18 Yr	70 Yr	Hypertension, Pulmonary
RECRUITING	NCT00643929	Drug	NA	GlaxoSmithKline	150	N/A	N/A	Ocular Safety
RECRUITING	NCT00646477	Device	3	TYCO	24	18 Yr	75 Yr	Obstructive Sleep Apneas Syndrome
RECRUITING	NCT00643461	Device	NA	3M	45	19 Yr	N/A	Dental Caries
RECRUITING	NCT00635375	Device	NA	GE Healthcare	82	N/A	1 Month	Hyperbilirubinemia
RECRUITING	NCT00636987	Device	NA	St Jude Medical	360	18 Yr	N/A	Mitral Valve Incompetence
RECRUITING	NCT00638846	Device	NA	Vistakon	660	18 Yr	45 Yr	Vision Correction
RECRUITING	NCT00639353	Device	NA	Vistakon	100	18 Yr	39 Yr	Astigmatism
RECRUITING	NCT00639379	Device	NA	Vistakon	110	18 Yr	45 Yr	Vision Correction

Subscribers' characteristics

The Clinical Trial Magnifier has 4,614 subscribers (March 30, 2008). The subscribers' characteristics are provided in the following tables.

Industry – 20%
Academia – 55%
MD/PhD – 73%
Professor – 26%
Senior Management – 16%
Global distribution – 122 countries

Work Environment - all subscribers					
Work Environment	N	%	Sub-groups	N	%
Pharmaceutical	449	9.7			
Biotech	179	3.9			
CRO	182	3.9			
Consultant Organization	117	2.5	Industry	927	20.1
University - Clinical	1964	42.6			
University - Non-clinical	575	12.5			
Health Care Organization	427	9.3			
Private Practitioner	191	4.1	Academia/Health Care	3,157	68.4
Governmental Regulatory	64	1.4			
Governmental Other	138	3.0	Governmental	202	4.4
Media	35	0.8	Media	35	0.8
Patient	15	0.3			
Patient Relative	3	0.1			
Healthy Volunteer	5	0.1	Research Subject	23	0.5
Other	270	5.9	Other	270	5.9
Total	4,614	100.0	Total	4,614	100.0
University Degree - except study subjects and relatives					
University Degree - Highest	N	%	Sub-groups	N	%
Medical Doctor and PhD/MD	1539	33.5			
Medical Doctor	924	20.1			
PhD or alike	886	19.3	MD and/or PhD	3,349	72.9
MBA	63	1.4			
Master Medical Area	250	5.4			
Master Other Area	261	5.7	Master	574	12.5
BSc or alike	533	11.6	BSc	533	11.6
Other	135	2.9	Other	135	2.9
Total	4,591	99.5	Total	4,591	100.0

Subscribers' characteristics (continuation)

Work Title - except study subjects and relatives					
Work Title	N	%	Sub-groups	N	%
President, CEO, Managing Director	148	3.2			
VP, Director	142	3.1			
Medical Director	79	1.7			
Project Manager, Leader	229	5.0			
Director Medical Affaires	33	0.7			
Lawyer/Legal Assistant	12	0.3			
Associate Director	71	1.5	Senior Management	714	15.6
Business & Development Manager/Assistant	35	0.8			
QA, QC Officer	18	0.4			
Medical Statistician	49	1.1			
Medical Writer	49	1.1			
Computer System Analyst/Assistant	9	0.2			
Clinical Data Specialist/Manager	45	1.0			
Project Manager	150	3.3			
Supervisor	32	0.7			
Manager	143	3.1			
Clinical Research Associate, Monitor (CRA)	127	2.8	Management & Operation	657	14.3
Consultant, Private	74	1.6			
Journalist	13	0.3			
Investor	15	0.3	Other Profession	102	2.2
Professor, Academic Post	1214	26.4			
Medical Doctor, Practitioner	925	20.1			
Nurse	47	1.0			
Clinical Research Coordinator/Nurse	293	6.4			
Pharmacist	66	1.4			
Technician	21	0.5	Clinical Profession	2,566	55.9
Other Titles	552	12.0	Others	552	12.0
Total	4,591	100.0	Total	4,591	100.0
Geographic Region - except study subjects and relatives					
Geographic Region	N	%	Sub-groups	N	%
North America	1328	28.9			
Latin America	189	4.1	Americas	1,517	33.0
Europe	1361	29.6			
East Europe & Russia, Ukraine, Turkey	562	12.2	Continental Europe	1,923	41.9
Middle East	149	3.2			
Africa	127	2.8	M. East & Africa	276	6.0
Asia	721	15.7			
Oceania	154	3.4	Asia & Oceania	875	19.1
Total	4,591	100.0	Total	4,591	100.0

WE GIVE YOU 10 REASONS TO CONSIDER HONG KONG FOR YOUR NEXT **MEDICAL DEVICE TRIAL**

1. **Leading trial city:** Hong Kong is the third most active industry-sponsored clinical trial city in Asia after Seoul and Taipei.
2. **Trial Experience:** Hong Kong has a long and impressive track record of conducting global clinical trials. Since the introduction of the ICH GCP guideline in 1996, Hong Kong has participated in over 1,400 global clinical trials, all requiring ICH GCP compliance.
3. **Regulatory Framework:** Medical devices and medical device trials are non-government regulated and require only ethics committee approval. The whole study approval process takes approximately 1 month for a standard trial.
4. **Ethics Committee (EC/IRB):** The 41 public hospitals in Hong Kong are organized into seven clusters. The cluster ethics committees operate according to international standards – e.g., the Declaration of Helsinki and ICH GCP – and also according to a unified operational guideline. Our cluster IRB, which is registered with the US Office for Human Research Protections (OHRP), handles 300 protocols annually. IRB meetings are scheduled every two weeks.
5. **Clinical Research Excellence:** Hong Kong has two medical schools with many years of high quality clinical research output and has for this reason taken scientific leadership in Asia. This means access to qualified investigators.
6. **Infrastructure:** With a population approaching 7 million, Hong Kong has an excellent infrastructure in terms of transportation, work force and legal framework.
7. **Health Care:** Hong Kong has an outstanding health care system as indicated by one of the lowest infant mortality rates (2-3/1000) and the longest life expectancy (80 for males and 86 for females) in the world. There are 41 public hospitals which provide 90% of the medical care in Hong Kong at low cost. All public hospital records are computerized and stored in a central computer.
8. **Leading Clinical Trial Centre:** The University of Hong Kong has a leading Clinical Trials Centre (CTC) in the region with 205 ongoing global clinical trials including 35 medical device trials in early 2008. CTC has the experience, expertise and ability to assist with trials from start to finish, from protocol development to close out.
9. **Streamlined Sites:** CTC has established a trial network – ClinCluster – which allows standardization of contracts, budgets and ethics committee applications for multi-centre trials in Hong Kong.
10. **Language Skills, Trained Staff:** Hong Kong has two official languages, English and Chinese. The English language is used in higher education, professional business and many important sectors of society. Hospital records are all in English.

For further information about the possibility to conduct medical device trials in Hong Kong please contact Tiffany Bauguess MS, Special Project Manager, Clinical Trials Centre, The University of Hong Kong. tiffanyb@hkucc.hku.hk. Tiffany has nine years working experiences in the medical device industry in California, US before joining the Clinical Trials Centre in early 2008.

MOST PREFERRED SPONSORED CLINICAL TRIAL LOCATIONS IN THE UNITED STATES



Most Active

US States: California, Florida, Texas and New York State

US Cities: New York, Atlanta, Chicago, Phoenix, Houston,
Los Angeles, San Diego, Dallas, San Antonio and Tampa