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# Current status of registry of vaccine clinical trials conducted by Korean investigators in ClinicalTrials.gov, database of US National Institutes of Health

**Purpose:** PubMed is not only includes international medical journals but also has a registration site for the ongoing clinical trials, such as ClinicalTrials.gov, under the supervision of US National Institutes of Health. We analyzed current status of vaccine clinical trials conducted by Korean investigators in database of ClinicalTrials.gov.

**Materials and Methods:** As of October 2012, there are total of 72 trials found on registry of vaccine clinical trials conducted by Korean investigators in database of ClinicalTrials.gov. These trials were analyzed and classified by conditions of vaccine clinical trials, biologicals or drugs used in vaccine clinical trials, status of proceeding research, and list of sponsor and collaborators.

**Results:** Total 72 trials of vaccine clinical trials conducted by Korean investigators are classified by groups of infection (64 trials), cancer (4 trials), and others (4 trials). Infections group shown are as follows: poliomyelitis, pertussis, diphtheria, tetanus, and *Haemophilus influenzae* type b (10), influenza (9), human papillomavirus infection (8), pneumococcal vaccine (6), herpes zoster (4), smallpox (4), hepatitis B (4), etc. One trial of each in lung cancer, breast cancer, prostate cancer, and colorectal cancer are shown in cancer group. One trial of each in Crohn's disease, ulcerative colitis, renal failure, and rheumatoid arthritis are shown in other group.

**Conclusion:** Vaccine clinical trials conducted by Korean investigators in ClinicalTrials.gov reflects the current status of Korean research on vaccine clinical trials at the international level and can indicate research progress. It is hoped that this aids the development of future vaccine clinical trials in Korea.

**Keywords:** Vaccines, Clinical trial, Database, ClinicalTrials.gov, US National Institutes of Health



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## Introduction

KoreaMed is the largest medical journal database that is used in Korea. As of October 2012, there were 40 articles found under vaccine, Korea and clinical trials and 84 articles under vaccine, Korea, clinical study refer to the key words, respectively [1]. However in PubMed, the largest medical journal database used worldwide, there were 109 articles and 171 articles referring to the same key words [2]. PubMed has a separate registration system for clinical trials, known as ClinicalTrials.gov, under the supervi-

sion of US National Institutes of Health [3]. The aims and scope of ClinicalTrials.gov are as follows: “ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world” [3].

We analyzed current status of vaccine clinical trials conducted by Korean investigators in database of ClinicalTrials.gov for the understanding the current status of Korean research on vaccine clinical trials at the international level.

## Materials and Methods

As of October 2012, there are 72 trials found on the registry of vaccine clinical trials conducted by Korean investigators in the database of ClinicalTrials.gov [3]. This represents about 1.6% of 4,480 vaccine clinical trials, the total trials on vaccine clinical trials all over the world, registered in ClinicalTrials.gov (Table 1) [3]. These Korean-led trials were analyzed and classified by conditions of vaccine clinical trials, biologicals or drugs used in vaccine clinical trials, status of proceeding research, and list of sponsor and collaborators.

## Results

### Classification by conditions of vaccine clinical trials conducted by Korean investigators in ClinicalTrials.gov (October 2012)

As of October 2012, 72 trials of vaccine clinical trials conducted by Korean investigators were classified by groups of infection, cancer, and others. The distributions under these categories are shown in Table 2 [3]. Infection group shown are as follows: 10 trials of poliomyelitis, pertussis, diphtheria, tetanus, and *Haemophilus influenzae* type b; 9 trials of seasonal influenza; 8 trials of human papillomavirus infection and associated cervical neoplasia; 6 trials of pneumococcal vaccine

and disease; 4 trials of herpes zoster; 4 trials of smallpox; 4 trials of hepatitis B; 3 trials of *Haemophilus influenzae* type b; 3 trials of varicella, rubella, mumps and measles; 2 trials of meningococcal disease; 2 trials of Japanese encephalitis; 1 trial of each in anthrax, cholera, and hepatitis A. One trial of each in non-small cell lung cancer, breast cancer, prostate cancer, and advanced colorectal cancer are shown in cancer group. One trial of each in Crohn’s disease and inflammatory bowel diseases, ulcerative colitis, hepatitis A, renal failure, and rheumatoid arthritis are shown in other group.

### Used biologicals or drugs in vaccine clinical trials conducted by Korean investigators in ClinicalTrials.gov (October 2012)

The formulation of ingredients or preparation name of vaccine biological or drugs used in 72 clinical trials are listed in Table 3 [3].

### Status of proceeding of vaccine clinical trials conducted by Korean investigators in ClinicalTrials.gov (October 2012)

The progress of clinical trials as of October 2012, are shown in Table 4 [3]. There are 37 trials of completed clinical trials, 17 trials recruiting, 11 trials non-recruiting, 2 trials not yet recruiting, 1 trial enrolling by invitation, 1 terminated trial, and 3 trials of unknown progress. This means that out of 72 clinical trials reported only 37 trials were completed and rest are still ongoing, of which 1 trial was terminated and progression of 3 trials are unknown. Among the completed trials, 13 trials have reports of final results.

### List of sponsor and collaborators of vaccine clinical trials conducted by Korean investigators in ClinicalTrials.gov (October 2012)

List of sponsors and collaborators in 72 vaccine clinical trials are shown in Table 5 [3].

**Table 1.** Number of papers and clinical trials of vaccine related key words of vaccine, Korea, and clinical trials in PubMed database of US National Library of Medicine and ClinicalTrials.gov<sup>a)</sup> database of US National Institutes of Health (October 2012)

Items	No.
Published papers related key words of vaccine, Korea, and clinical trials in PubMed database of US National Library of Medicine	109
Published papers related key words of vaccine, Korea, and clinical study in PubMed database of US National Library of Medicine	171
Registry of clinical trials related key words of vaccine and Korea (conducted by Korean investigators) in ClinicalTrials.gov <sup>a)</sup> database of US National Institutes of Health (A)	72
Registry of clinical trials related key words of vaccine in ClinicalTrials.gov <sup>a)</sup> database of US National Institutes of Health (B)	4,480
A/B (%)	1.6

<sup>a)</sup><http://clinicaltrials.gov/> [3].

**Table 2.** Classification by conditions of vaccine clinical trials conducted by Korean investigators in ClinicalTrials.gov<sup>a)</sup>

Group	Conditions	No.
Infection	Influenza, seasonal, infection, avian flu	9
	HPV infection, HPV-16/18 Infections and associated cervical neoplasia, cervical intraepithelial neoplasia	8
	Pneumococcal vaccine, disease, <i>Streptococcus pneumoniae</i>	6
	Rotavirus gastroenteritis, rotavirus vaccine	6
	Meningitis, meningococcal disease	2
	Herpes zoster	4
	Smallpox	4
	<i>Haemophilus influenzae</i> type b infection	3
	Diphtheria, tetanus, pertussis, poliomyelitis, <i>Haemophilus influenzae</i> type b	
	Diphtheria, tetanus, pertussis	2
	Diphtheria, tetanus	1
	Poliomyelitis, pertussis; diphtheria, tetanus	4
	Poliomyelitis	1
	Poliomyelitis, diphtheria, pertussis, tetanus, <i>Haemophilus influenzae</i> type b disease	2
	Japanese encephalitis, Japanese encephalitis virus disease	2
	Rubella, varicella, mumps, measles	
	Rubella, varicella, mumps, measles; measles-mumps-rubella-varicella vaccine	2
	Measles, mumps, rubella diseases	1
	Anthrax	1
	Cancer	Cholera
Hepatitis A		1
Hepatitis B		4
Non-small cell lung cancer		1
Breast cancer		1
Prostatic cancer		1
Advanced colorectal cancer		1
Others	Crohn's disease	1
	Inflammatory bowel disease, Crohn's disease, ulcerative colitis, hepatitis A	1
	Renal failure	1
	Rheumatoid arthritis	1
Total		72

HPV, human papillomavirus.

<sup>a)</sup><http://clinicaltrials.gov/> [3].

## Discussion

The 72 clinical trials conducted by Korean investigators represents about 1.6% of 4,480 vaccine clinical trials, the total vaccine clinical trials all over the world registered in Clinical-Trial.gov. This is a very low percentage, something that Korea will have to improve in the future.

Considering these trials by the goal of vaccine, prevention of infection was 90.0% (64 trials), cancer 5.5% (4 trials), others 5.5% (4 trials), in which the prevention of infection was the predominant goal. The categories of infection can be divided into poliomyelitis, pertussis, diphtheria, tetanus and *Haemophilus influenzae* type b (10 trials), seasonal influenza (9),

human papillomavirus infection and associated cervical neoplasia (8), pneumococcal vaccine and disease (6), of herpes zoster (4), smallpox (4), hepatitis B (4), *Haemophilus influenzae* type b (3), varicella, rubella, mumps and measles (3), meningococcal disease (2), Japanese encephalitis (2), anthrax (1), cholera (1), and hepatitis A (1). Cancers can be categorized into trials on non-small cell lung cancer (1), breast cancer (1), prostate cancer (1), and advanced colorectal cancer (1). Others included Crohn's disease (1), inflammatory bowel disease, ulcerative colitis and hepatitis A (1), renal failure (1), and rheumatoid arthritis (1)

The 72 clinical trials can be divided by disease category of PubMed, there are some overlap (number of trials): arbovirus

**Table 3.** Biologicals or drugs in vaccine clinical trials conducted by Korean investigators in ClinicalTrials.gov<sup>a)</sup>

No.	Biologicals/Drugs
1	13-valent pneumococcal conjugate vaccine; 7-valent pneumococcal conjugate vaccine
2	Meningococcal (groups A, C, Y, and W-135) polysaccharide diphtheria toxoid conjugate vaccine (Menactra); tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine adsorbed
3	Novartis MF59-adjuvanted influenza subunit vaccine; Sandoz Korea MF59-adjuvanted influenza subunit vaccine
4	Novartis MenACWY-CRM
5	IDflu (split virion inactivated influenza vaccine); Vaxigrip (split virion inactivated influenza vaccine)
6	Synflorix
7	Zoster vaccine live (Zostavax)
8	<i>Haemophilus influenzae</i> type b conjugate vaccine
9	Cervarix
10	Infanrix-IPV
11	JE vaccine, Vero cell-derived JE vaccine
12	Euvax B vaccine
13	GSK Biologicals' Rotarix (human/rotavirus vaccine)
14	Live attenuated Japanese encephalitis chimeric virus vaccine; Japanese encephalitis live attenuated vaccine (SA14-14-2 vaccine)
15	HPV-16/18 VLP/AS04 vaccine (Cervarix)
16	Infanrix-IPV + Hib; Infanrix IPV; Hiberix; Synflorix; Rotarix
17	Prevenar
18	Priorix; Varilrix; GSK Biologicals' vaccine 208136
19	DTPa-IPV; DTPa; Imovax Polio
20	Pentaxim (DTaP IPV//PRP-T combined vaccine); Tetraxim (DTaP IPV combined vaccine); ActHIB (PRP tetanus conjugate vaccine)
21	GSK Biologicals' HPV-16/18 L1/AS04
22	Rotavirus vaccine, live, oral, pentavalent
23	Tetraxim: combined adsorbed diphtheria, tetanus, acellular pertussis, and enhanced inactivated polio
24	Poliomyelitis vaccine (inactivated)-Poliorix
25	Smallpox vaccine CJ-50300
26	Smallpox vaccine CJ-50300
27	DTaP-IPV combined vaccine
28	Cell-culture derived smallpox vaccine
29	Smallpox vaccine CJ-50300
30	Rotavirus vaccine
31	Adacel (adsorbed diphtheria, tetanus toxoids and component pertussis combined)
32	Measles, mumps, rubella and varicella (Oka-Merck) virus vaccine live (ProQuad); M-M-R II; Varivax
33	23-valent polysaccharide pneumococcal vaccine
34	Gardasil
35	VGX-3400
36	MG1109 step 1, step 2
37	GSK Biologicals' hepatitis A
38	Fluarix
39	GSK Biologicals' Synflorix (pneumococcal vaccine GSK1024850A); Wyeth-Lederle's Prevenar; GSK Biologicals' Hiberix
40	Pneumococcal vaccine GSK1024850A (Synflorix); Prevenar; GSK Biologicals' Hiberix
41	Priorix; Merck's M-M-R-II, measles, mumps, and rubella virus vaccine (also known as M-M-R Vax Pro); Kinrix; Varivax
42	Herpes zoster vaccine GSK1437173A
43	Herpes zoster vaccine GSK1437173A
44	Influenza vaccine GSK2321138A; Fluarix; influenza vaccine GSK2604409A
45	Live attenuated human rotavirus vaccine
46	L-BLP25 or BLP25 liposome vaccine (Stimuvax)

(Continued to the next page)

**Table 3.** (Continued from the previous page) Biologicals or drugs in vaccine clinical trials conducted by Korean investigators in ClinicalTrials.gov<sup>a)</sup>

No.	Biologicals/Drugs
47	Liquid CAIV-T
48	Stimuvax
49	Rotarix
50	Purified hepatitis B surface antigen
51	Stimuvax (L-BLP 25 or BLP25 liposome vaccine)
52	LBVH0101 (Hib vaccine); Hiberix vaccine
53	GX-188
54	Autologous dendritic cell
55	Influenza vaccine (Flumist)
56	Epaxal Berna (virosomal hepatitis A vaccine)
57	Herpes zoster vaccine GSK1437173A
58	CP-690,550
59	Pneumococcal polysaccharide vaccine
60	HPV-16/18 L1/AS04
61	LBVH0101 (Hib vaccine); Hiberix vaccine
62	Biological: rPA vaccine containing alhydrogel
63	Euvichol cholera vaccine
64	GC1107; SK Td vaccine
65	VGX 310
66	A mixed plasmid DNA (HB-110)
67	Adjuvanted influenza A (H1N1) vaccine; un-adjuvanted influenza A (H1N1) vaccine
68	RotaTeq
69	Gardasil
70	GSK Biologicals' Infanrix
71	Genetic: HB-110
72	TK cell

JE, Japanese encephalitis; HPV, human papillomavirus; DTPa-IPV, diphtheria, tetanus, acellular pertussis and inactivated poliomyelitis vaccine; PRP-T, polysaccharide conjugated to tetanus toxoid.

<sup>a)</sup><http://clinicaltrials.gov> [3].

**Table 4.** Status of vaccine clinical trials conducted by Korean investigators in ClinicalTrials.gov<sup>a)</sup>

Status	No.
Completed	37
Recruiting	17
Active, not recruiting	11
Not yet recruiting	2
Enrolling by invitation	1
Terminated	1
Unknown	3
Total	72

<sup>a)</sup><http://clinicaltrials.gov/> [3].

infections (2), arthritis (1), arthritis, rheumatoid (1), autoimmune diseases (1), bacterial infections (15), bacterial meningitis (1), brain diseases (2), breast diseases (1), breast neoplasms (1), bronchial neoplasms (2), calcium metabolism

disorders (5), carcinoma (4), carcinoma *in situ* (2), carcinoma, bronchogenic (2), carcinoma, non-small-cell lung (2), central nervous system diseases (11), central nervous system infections (11), cervical intraepithelial neoplasia (2), chickenpox (2), cholera (1), chronic disease (1), *Clostridium* infections (9), colitis (1), colitis, ulcerative (1), colonic diseases (2), colorectal neoplasms (1), connective tissue diseases (1), cough (8), Crohn's disease (2), digestive system diseases (13), digestive system neoplasms (1), diphtheria (11), DNA virus infections (15), encephalitis (2), encephalitis, Japanese (2), enterovirus infection (13), flavivirus infections (2), gastroenteritis (7), gastrointestinal diseases (8), gastrointestinal neoplasms (1), genital diseases, female (1), genital diseases, male (1), genital neoplasms, male (1), Gram-negative bacterial infections (12), Gram-positive bacterial infections (11), haemophilus infections (1), *Haemophilus influenzae* (5), hepadnaviridae infections (4), hepatitis (6), hepatitis A (6), hepatitis B (4),

**Table 5.** Sponsors and collaborators in seventy two vaccine clinical trials in ClinicalTrials.gov<sup>a)</sup>

Sponsors and collaborators	No.
Asan Medical Center	2
Binex	1
Boryung Pharmaceutical Co., Ltd.	1
Bukwang Pharmaceutical	1
Chung-Ang University	1
CJ Cheiljedang Corporation	4
EMD Serono	2
EuBiologics Co., Ltd.	1
Ewha Womans University	3
Gachon University Gil Medical Center	1
Genexine Co., Ltd.	2
GlaxoSmithKline	23
Green Cross Corporation	4
Inha University Hospital	1
Inje University	2
Inovio Pharmaceuticals	2
Instituto Universitario IVI	1
International Vaccine Institute	1
Konkuk University Hospital	1
Korea Cancer Center Hospital	1
Korea University	1
Korean Center for Disease Control and Prevention	1
Kosin University Gospel Hospital	1
Kyunghee University Medical Center	1
LG Life Sciences	2
MedImmune LLC	1
Merck	7
Merck KGaA	2
National Cancer Center, Korea	1
Novartis	3
Novartis Vaccines	3
Pfizer	1
Samsung Medical Center	2
Sanofi-Aventis	7
Seoul National University Hospital	6
Severance Hospital	2
Soonchunhyang University Hospital	1
Tehran University of Medical Sciences	1
The Catholic University of Korea	2
VGX International, Inc.	1
Wonkwang University	1
Wyeth is now a wholly owned subsidiary of Pfizer	2
Yonsei University	2

<sup>a)</sup><http://clinicaltrials.gov/> [3].

hepatitis B, chronic (2), hepatitis, chronic (2), hepatitis, viral, human (6), herpes zoster (6), herpesviridae infections (6),

hypocalcemia (5), inflammatory bowel diseases (2), influenza in birds (2), influenza, human (14), intestinal diseases (3) intestinal neoplasms (1), Japanese encephalitis (2), joint diseases (1), kidney diseases (1), kidney failure, chronic (1), liver diseases (6), lung diseases (4), lung neoplasms (2), measles (3), meningitis (2), meningitis, bacterial (1), meningitis, meningococcal (1), meningococcal infections (2), menopause (1), metabolic diseases (5), mouth diseases (3), mumps (3), musculoskeletal diseases (1), myelitis (7), *Neisseria meningitidis* infection (2), neisseriaceae infections (2), neoplasms, glandular and epithelial (2), neurologic manifestations (5), neuromuscular diseases (7), non-small cell lung cancer (2), orthomyxoviridae infections (14), papilloma (2), papilloma-virus infections (1), paramyxoviridae infections (3), parotitis (3), cicornaviridae infections (13), pneumococcal infections (1), pneumonia (2), poliomyelitis (7), poxviridae infections (4), precancerous conditions (1), prostatic diseases (1), prostatic neoplasms (1), rectal diseases (1), renal insufficiency (1), renal insufficiency, chronic (1), respiratory tract diseases (23), respiratory tract infections (21), respiratory tract neoplasms (2), rheumatic diseases (1), RNA virus infections (31), rotavirus infections (1), rubella (3), salivary gland diseases (3), sialadenitis (3), skin diseases (1), smallpox (4), spinal cord diseases (7), stomatognathic diseases (3), streptococcal infections (1), tetanus (12), tetany (12), thoracic neoplasms (2), tumor virus infections (1), ulcer (1), urogenital neoplasms (1), urologic diseases (1), uterine cervical diseases (1), uterine cervical dysplasia (1), uterine cervical neoplasms (3), uterine diseases (1), vaccina (1), vibrio infections (1), virus diseases (41), and whooping cough (9).

The types of vaccines are also analyzed in Table 3. There were mostly studies of new products for licensure as well as some established products for efficacy studies. The centers in which the studies took place had a wide distribution from hospitals to pharmaceutical companies.

Looking at the current status of the studies, trials were completed, 31 were still in progress (sum of recruiting, active, not recruiting, not yet recruiting, and enrolling by invitation), 1 was terminated, and 3 were unknown. Among the completed trials, 13 trails have reports of final results. This data shows that the studies need continuing observation of study process for final results.

Vaccine clinical trials conducted by Korean investigators in ClinicalTrial.gov, an internationally acknowledged databases, reflects the current status of Korean research on vaccine clinical trials at the international level and can indicate research

progress. It is hoped that this aids the development of future vaccine clinical trials in Korea [3].

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