November 2021

Annual Report on **Clinical Trials for New Drug Registration in China**

2020

Center for Drug Evaluation
National Medical Products Administration

English translation prepared by Tigermed, Yaxincheng and PharmaDJ

Abstract

Objective

In order to better understand the current status of clinical trials for new drug registrations in China; to disclose clinical trial progress information to the public; to provide reference for new drug research and development (R&D), resource allocation, drug review and approval for the industry; and to explore the use of informatization technology to improve the ability of intelligent supervision of drugs, the Center for Drug Evaluation (CDE) has conducted the first comprehensive summary and analysis of clinical drug trials in China according to data from the Drug Clinical Trial Registration and Information Disclosure Platform.

Methods

The annual report mainly summarizes and analyzes the overall trend changes, main characteristics and outstanding problems of clinical trials based on the information of drug clinical trials registered in 2020, from the perspective of type of sponsors, type of drugs, trial varieties, indications, trial phases, trials in special population, leading institution of clinical trials, time-consuming of initiating and completion, and compiles the *Annual Report on Clinical Trials for New Drug Registration in China (2020).*

Key Findings

1. Number of Clinical Trials for New Drug Registration

The total number of clinical trials registered on the Drug Clinical Trial Registration and Information Disclosure Platform increased by 9.1% year-on-year, with domestic sponsors accounting for over 70% of the total.

2. Drug Classification & Categories

Chemical drugs (approximately 73.6%) and biological products (23.8%) accounted for a relatively high percentage, and new therapies accounted for 4.3% of biological products. The highest percentage in the registration classification of chemical drugs, therapeutic biological products, biological products for prevention and traditional Chinese medicine (TCM) were all class 1, which were 71%, 65.4%, 46.0% and 61%, respectively; lack of diversity for targets was obvious, mainly for PD-1, VEGFR, PD-L1, etc. and cell therapy was still dominated by CD19 targets.

3. Clinical Trials Classification

Indications were largely concentrated in anti-tumor and anti-infection fields. The clinical trials of up to 91.6% of drugs were conducted only in China. Chemical drugs and biological products are still mainly developed in early stage in general. Phase I clinical trials accounted for 50.4% and 38.3%, respectively. Within the subject population, relatively few clinical trials were conducted in specific populations, with 3 and 33 clinical trials conducted in the elderly and pediatric populations, respectively, accounting for only 1.4% of total trial registrations for the year.

4. Implementing Efficiency of Clinical Trials

Less than half (45.4%) of the clinical trials registered in 2020 initiated subject recruitment within one year of approval. Clinical trials completed in 2020 were still concentrated in phase I clinical trials, with an average completion time of 95.7 days; only five phase III trials were completed, with an average completion time of 176.6 days.

5. Geographical Distribution of Clinical Trials

The leading and participating clinical trial institutions were still mainly in Beijing, Shanghai, Jiangsu Province, and Guangdong Province.

Conclusion

Clinical trials registered in 2020 were generally initiated by domestic sponsors and mainly carried out in China, with phase I clinical trials accounting for the highest percentage. Both the number of clinical trials and drug varieties in China have increased considerably. Class 1 new drugs accounted for a higher percentage, but the distribution of drug targets and indications fields was relatively concentrated, suggesting that the rapid development of clinical trials in China was accompanied by the lack of diversity. The analysis results such as clinical trial efficiency showed that there were also challenges, such as inefficient implementation after approval, minimal clinical trials of pediatric drugs and uneven geographical distribution of clinical trials throughout the country.

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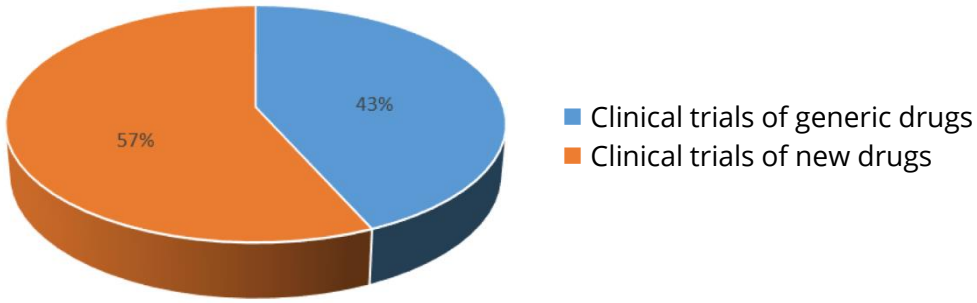
Chapter I Overview of Drug Clinical Trial Registration

A total of 2602 clinical trials were registered in 2020, an overall increase of 9.1% (2,386) from 2019.

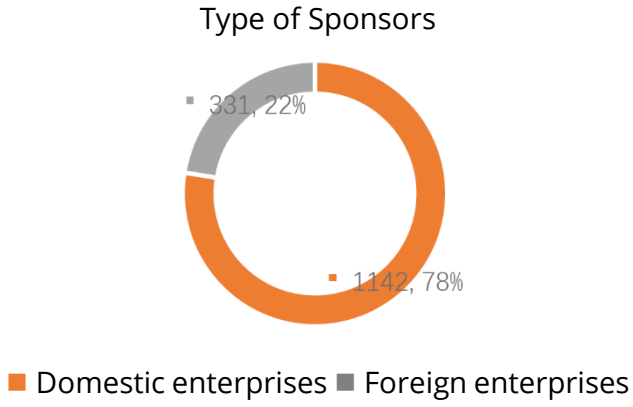
The number of clinical trial registrations was higher for new drugs than for generic drugs, accounting for 57% (1473) and 43% (1129), respectively, in 2020.



Chapter II Analysis of Basic Characteristics of Clinical Trials

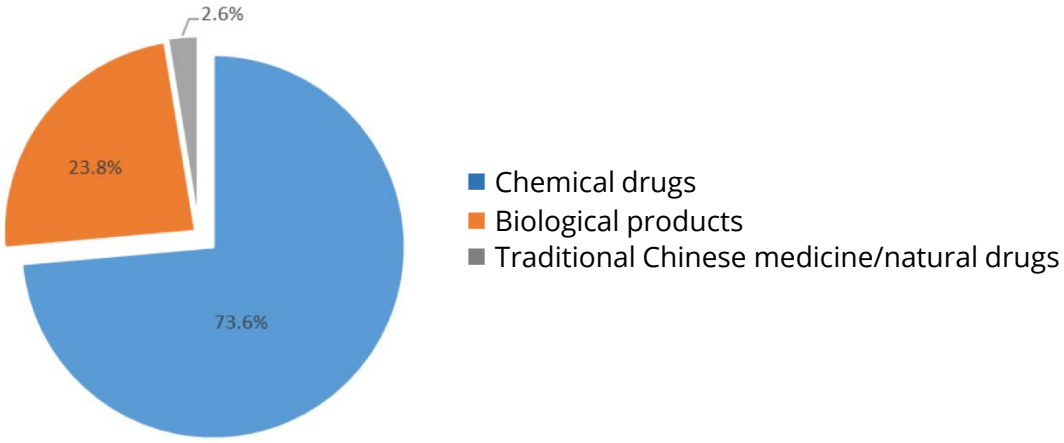
I. Type of Sponsors

The types of sponsors were analyzed in accordance with the type of acceptance number, i.e., those with the initial letter J were counted as foreign sponsors, while the others were domestic sponsors. Trials registered in 2020 were mainly initiated by domestic enterprises, with foreign enterprises accounting for less than 30% of all sponsors.

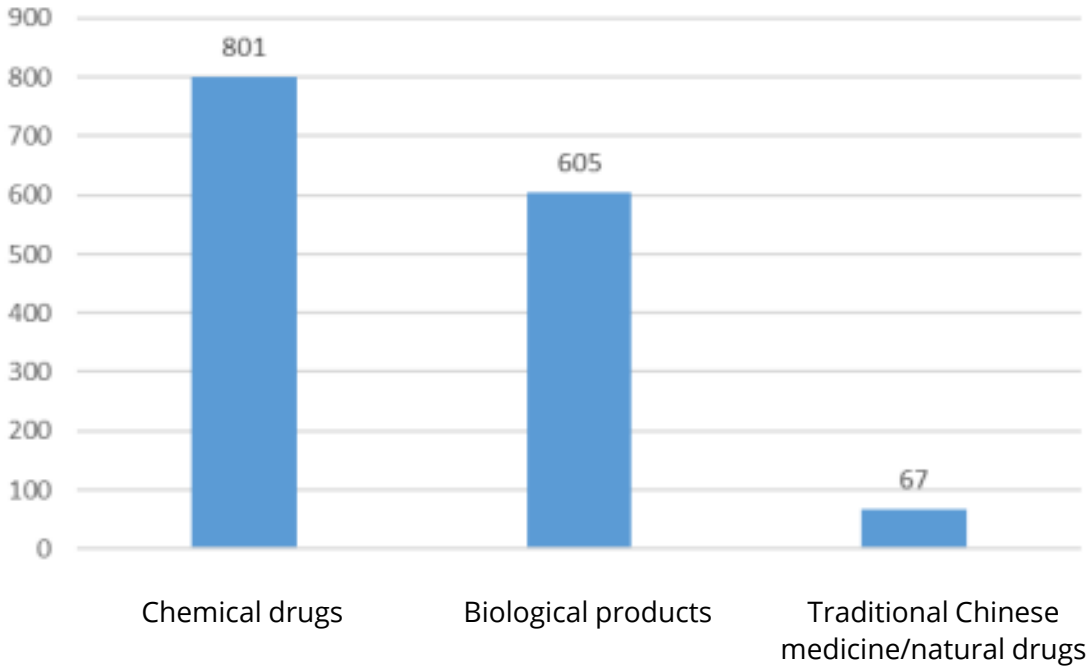


II. Type of Drugs

Clinical trials for chemical drugs still accounted for the highest percentage in 2020, 73.6%. Biological products accounted for 23.8%, and the TCM accounted for 2.6%.



Chemical drugs were registered most in 2020 at a total of 801 (54.4%), followed by biological products and TCM at 605 (41.1%) and 67 (4.5%), respectively.



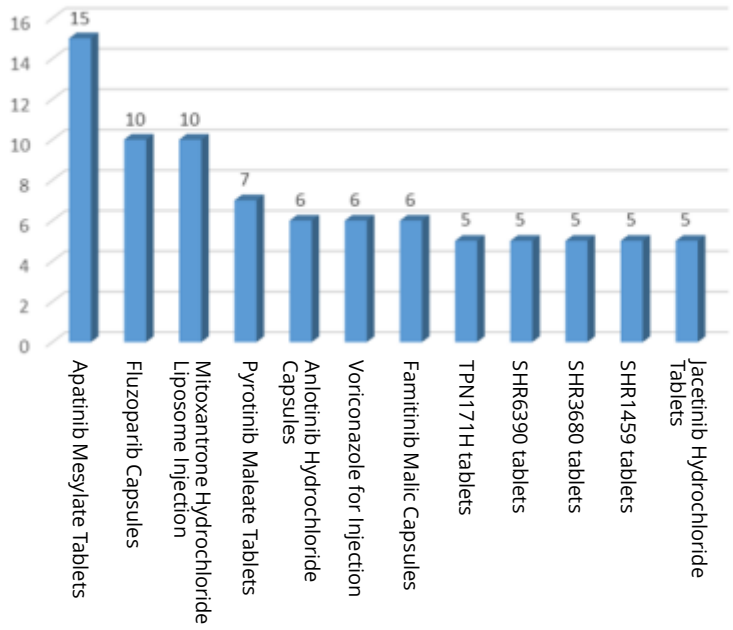
III. Drugs and Targets Involved in Clinical Trials

1. Drugs Involved in Non-bioequivalence Clinical Trial

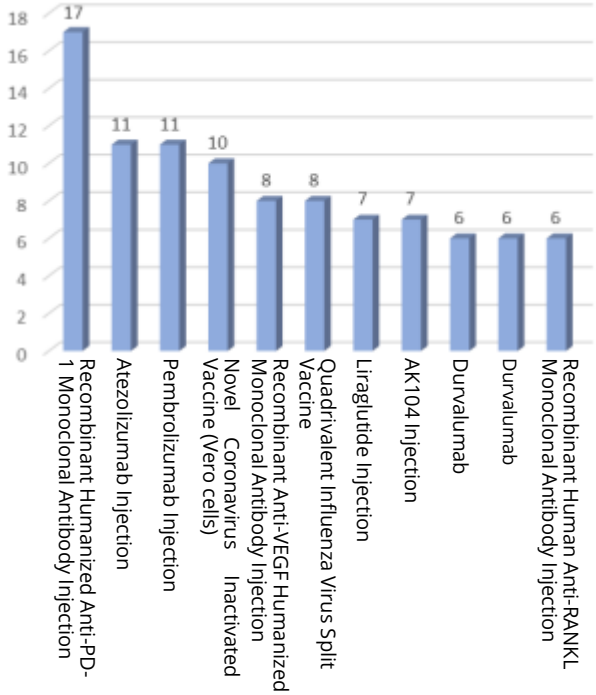
The number of drugs (drug names in accordance with the clinical trial approval documents) involved in the 1473 non-BE/consistency evaluation clinical trials in 2020 were statistically analyzed by different drug types respectively.

For 91% of TCM drugs, only one clinical trial was performed. Huoling Shengji Granules, Tanreqing Oral Solution, and Kechang Granules, underwent two trials.

Most of the top 10 chemical drugs in trials were anti-tumor drugs. Apatinib mesylate tablets underwent the largest number of clinical trials (n=15), followed by mitoxantrone hydrochloride liposome injection and fluzoparib capsules (n=10 for each).



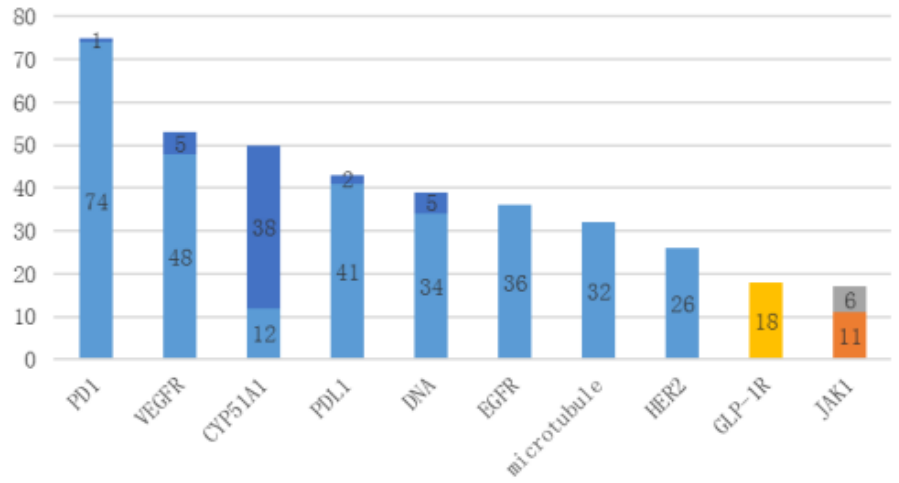
Most of the top 10 biological products in trials were therapeutic biological products. The recombinant humanized anti-PD-1 monoclonal antibody injection underwent the largest number of trials (n=17), followed by atezolizumab injection and pembrolizumab injection (n=11 for each); preventive biological products involved two varieties, novel coronavirus inactivated vaccine (vero cell) and quadrivalent influenza virus split vaccine, undergoing ten and eight clinical trials, respectively.



2. Targets Distribution

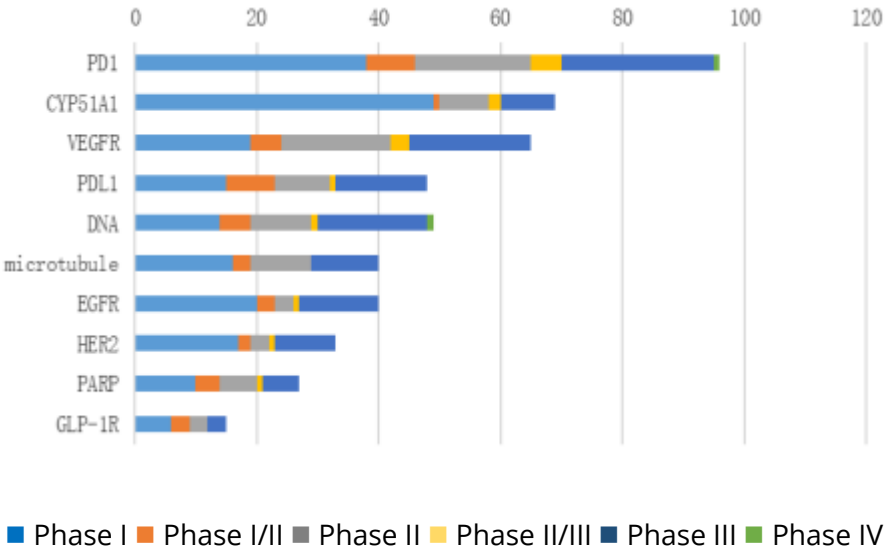
The top 10 targets of drug varieties with registered clinical trials were PD-1, CYP51A1, VEGFR and PD-L1 etc. The number of varieties involved is up to 75, 53, 50 and 43, respectively. Among the top 10 targets, the drug indications of 9 targets were concentrated in the same indications field, and over 90% of the drug indications of 7 targets were concentrated in the anti-tumor field.

Top Ten Targets of Drug Varieties and Indications Field Distribution

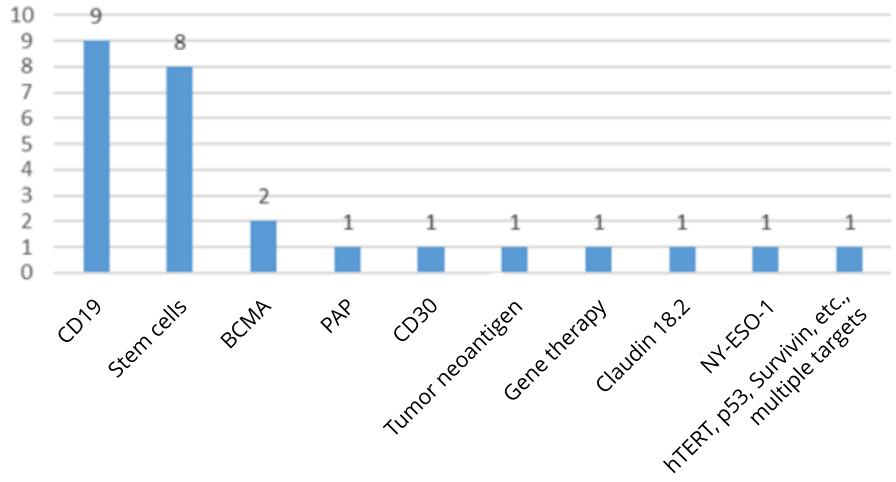


The top 10 targets with the largest number of clinical trials were also mainly concentrated in PD-1, VEGFR, etc. The PD-1, VEGFR and PD-L1 and other targets underwent more than 60 clinical trials, and PD-1 targets underwent nearly 100. In addition, the phase I clinical trials accounted for more than 40% of the drug clinical trials of 6 targets. Phase II clinical trials accounted for a low percentage in each target, and the number of phase III clinical trials of PD-1, VEGFR and PD-L1 and other targets reached 20.

Top Ten Targets and Trial Phases in Terms of Number of Clinical Trial Registrations

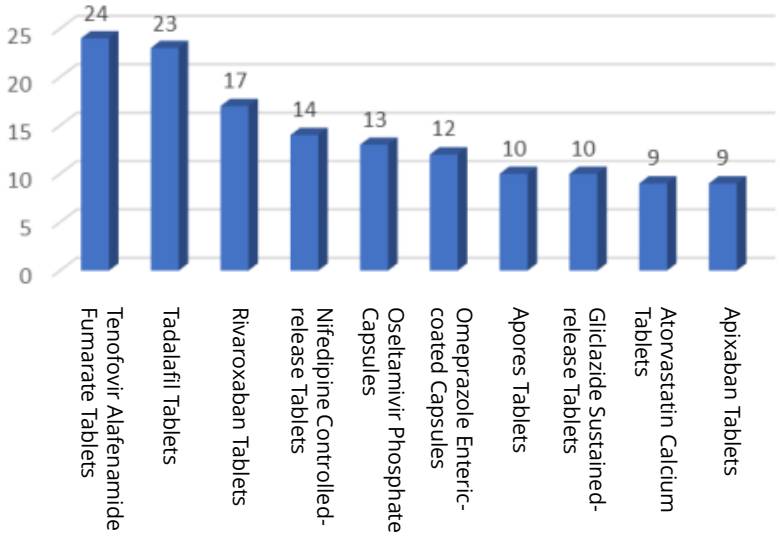


There were 26 (4.3%) cell/gene therapy clinical trials among 605 biological product trials, involving 22 varieties (in terms of acceptance number). These mainly comprise CD19 targets, followed by stem cell varieties, in addition to a type of gene therapy.



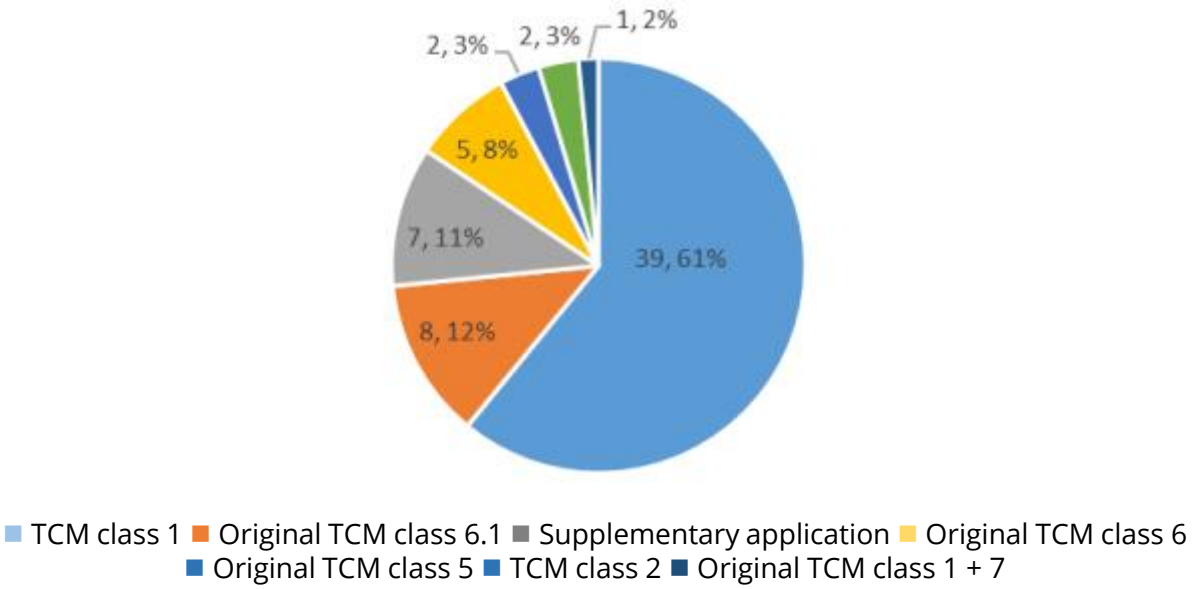
3. Drugs Involved in Bioequivalence Clinical Trial

The top 10 drugs involved in bioequivalence clinical trials were summarized by drug name, among which tenofovir alafenamide fumarate tablets and tadalafil tablets registered a higher number of trials — 24 and 23 respectively, as shown below.

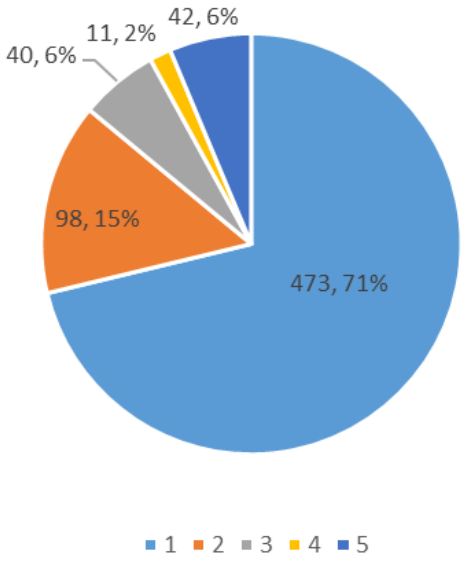


IV. Classification of Registration

The 67 TCM trials involved 64 acceptance numbers in total, of which the largest was for new drug class 1 (including the original registration classification), involving 40 (including one original TCM class 1+7) acceptance numbers, followed by original TMC class 6 and supplementary applications.

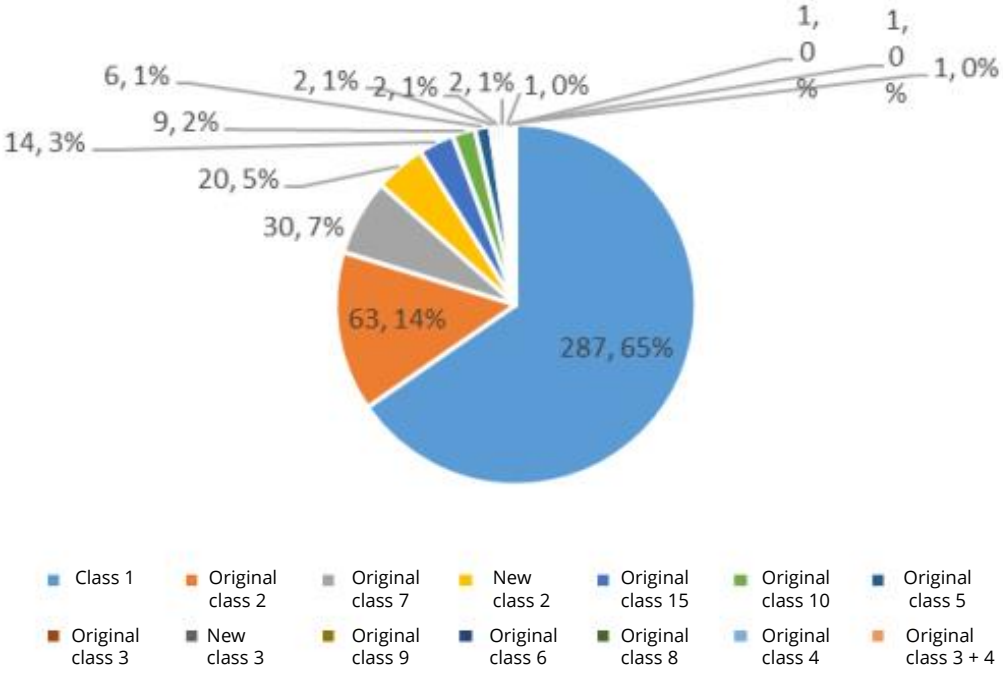


The 801 new chemical drug trials involved 664 acceptance numbers (an acceptance number of the same variety with multiple strengths or associated supplementary applications is deemed as one acceptance number) in total, of which import drugs involved 164 acceptance numbers (summarized by the acceptance number with the initials of J), and domestic drugs involved 500 acceptance numbers. Registration class 1 accounted for the highest percentage (71%), followed by class 2 (15%), 3 and 5 (6%), and class 4 (only 2%).

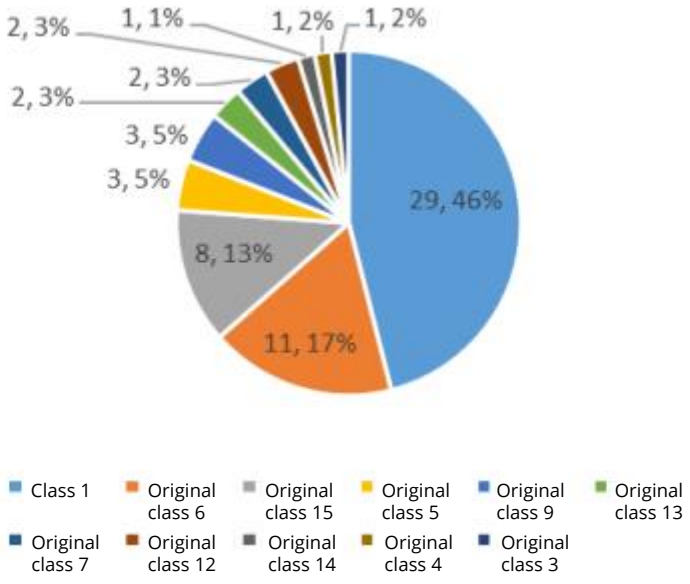


A total of 502 acceptance numbers were involved in the 605 biological product trials (an acceptance number of the same variety with multiple strengths or associated supplementary applications is deemed as one acceptance number), among which, acceptance numbers for therapeutic biological products were notably higher than those for preventive biological products (n = 439 versus 63). Registration class 1 accounted for the largest percentage, therapeutic biological products 65.4% (287 acceptance numbers), and preventive biological products 46.0% (29 acceptance numbers); secondly, the percentages of original registration class 2 therapeutic biological products (14.4%), original registration class 6 (17.5%) and class 15 (12.7%) preventive biological products were higher than that of other registration classifications. The registration classification is as follows:

Registration Classification of Therapeutic Biological Products

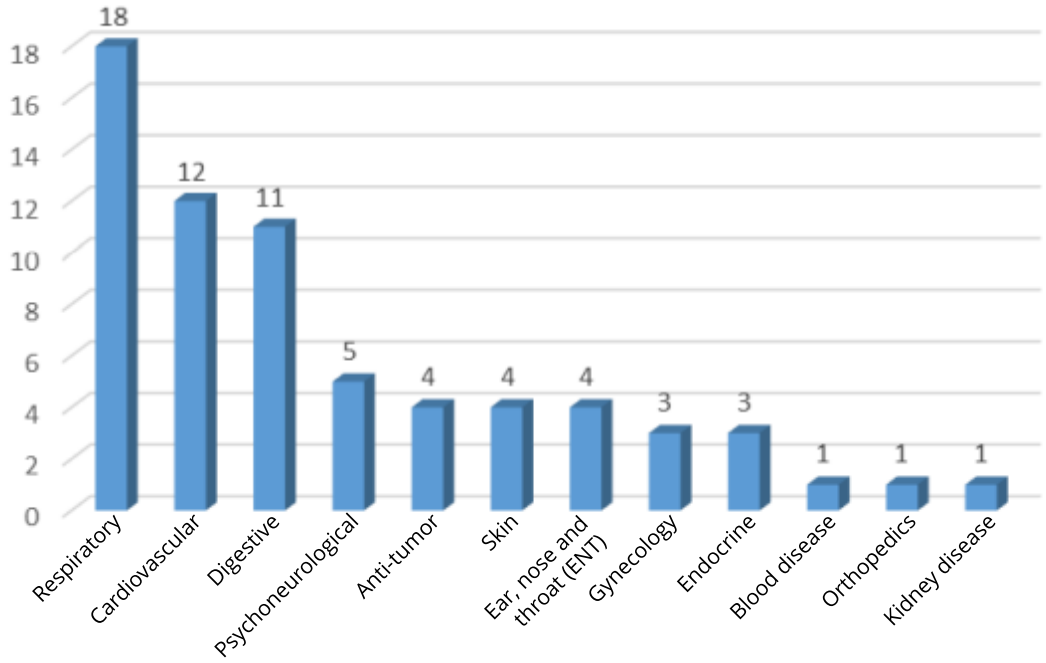


Registration Classification of Preventive Biological Products

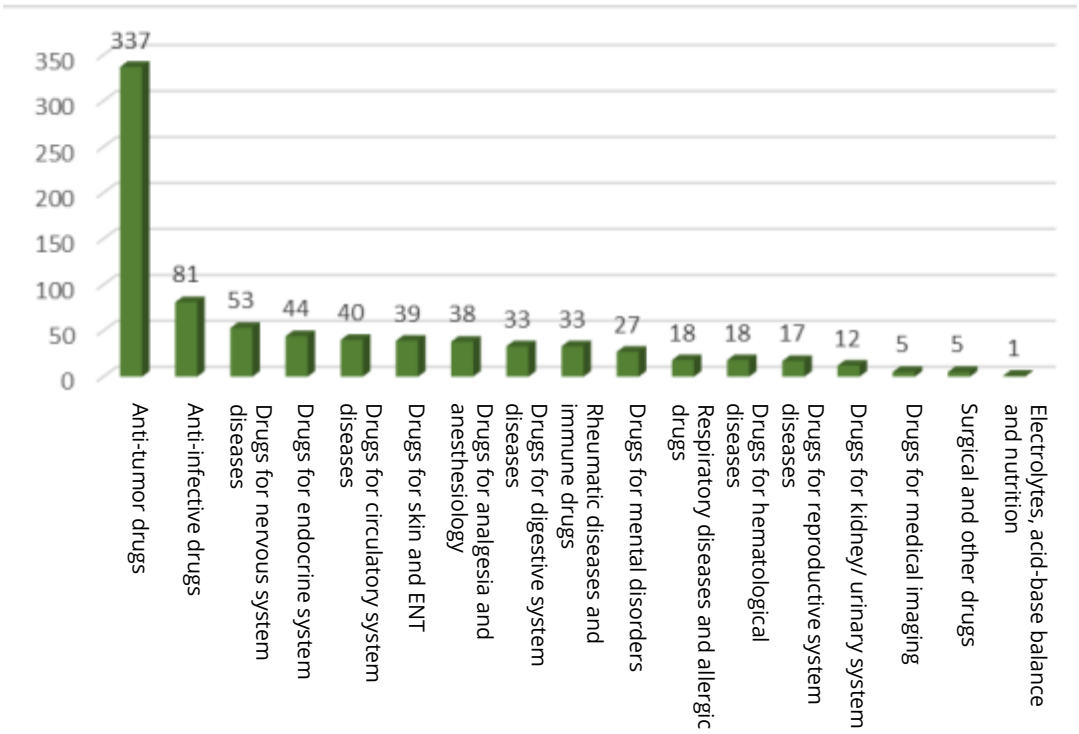


V. Indications

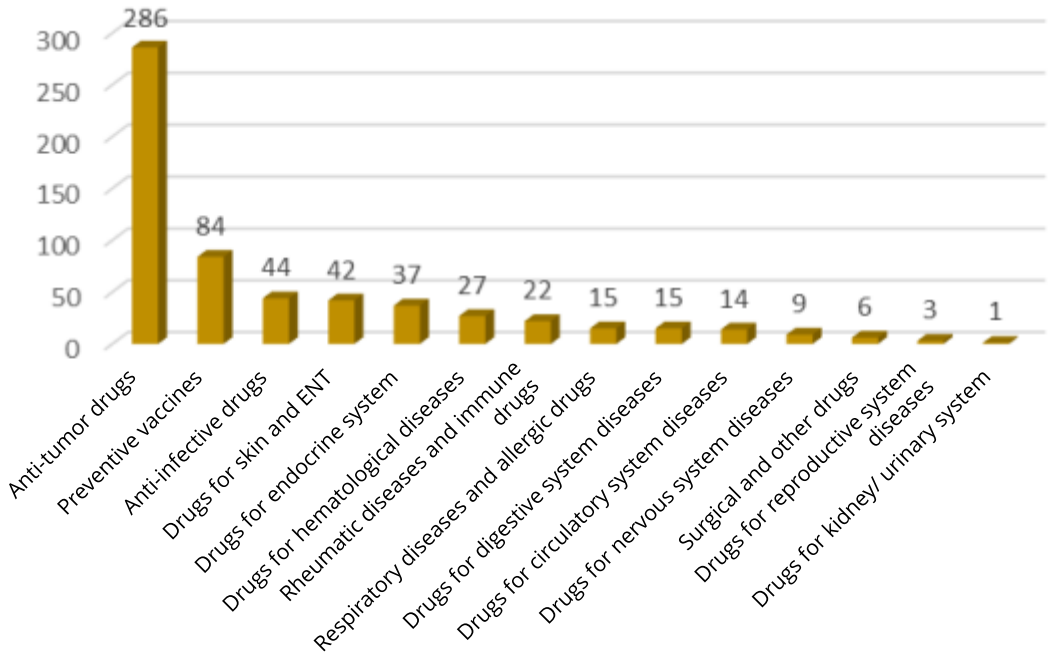
Trials for TCM mainly focused on three indications, i.e., respiratory, cardiovascular and digestive indications, accounting for approximately 61.2% of the overall clinical trials of TCM.



Chemical drug indications were mainly concentrated in anti-tumor drugs, accounting for 42.1% of all trials, followed by anti-infective drugs (10.1%), drugs for nervous system diseases (6.6%), drugs for endocrine system (5.5%), drugs for circulatory system diseases (5.0%), and drugs for skin and ENT (4.9%), respectively.

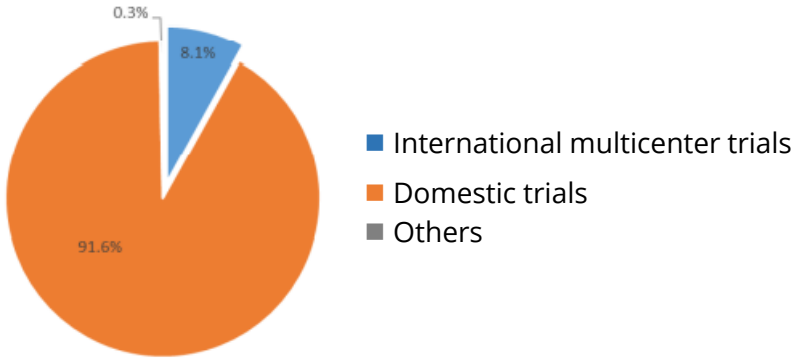


Biological product indications were also concentrated in anti-tumor drugs, accounting for 47.3% of all biological product trials, followed by preventive vaccines (13.9%), anti-infective drugs (7.3%), drugs for skin and ENT (6.9%) and drugs for endocrine system (6.1%).

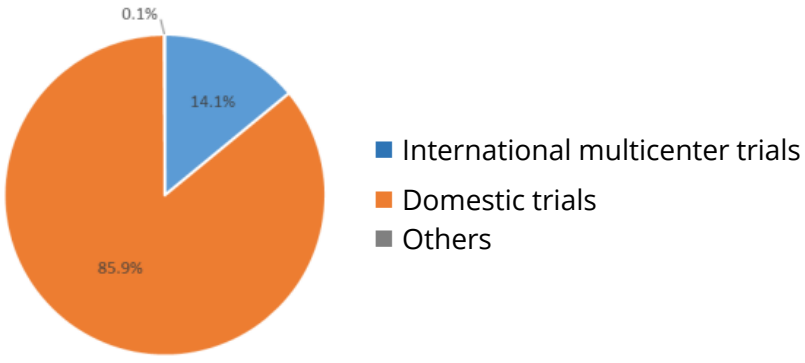


VI. Participating Countries

Domestic clinical trials accounted for up to 91.6% (n = 2384), and the international multicenter trials accounted for only 8.1% (n = 210). Single-center clinical trials not recruiting subjects in China or only performed abroad were summarized by Others, accounting for 0.3% (n = 8).

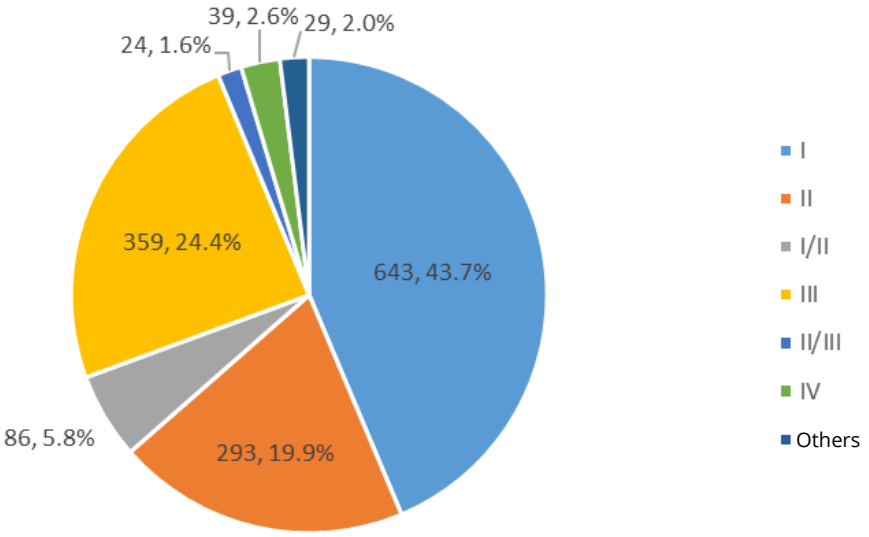


International multicenter trials accounted for a relatively high percentage of 14.1% (n = 208, including one international multicenter trial not recruiting subjects in China), and domestic trials at 85.9% (n = 1265).

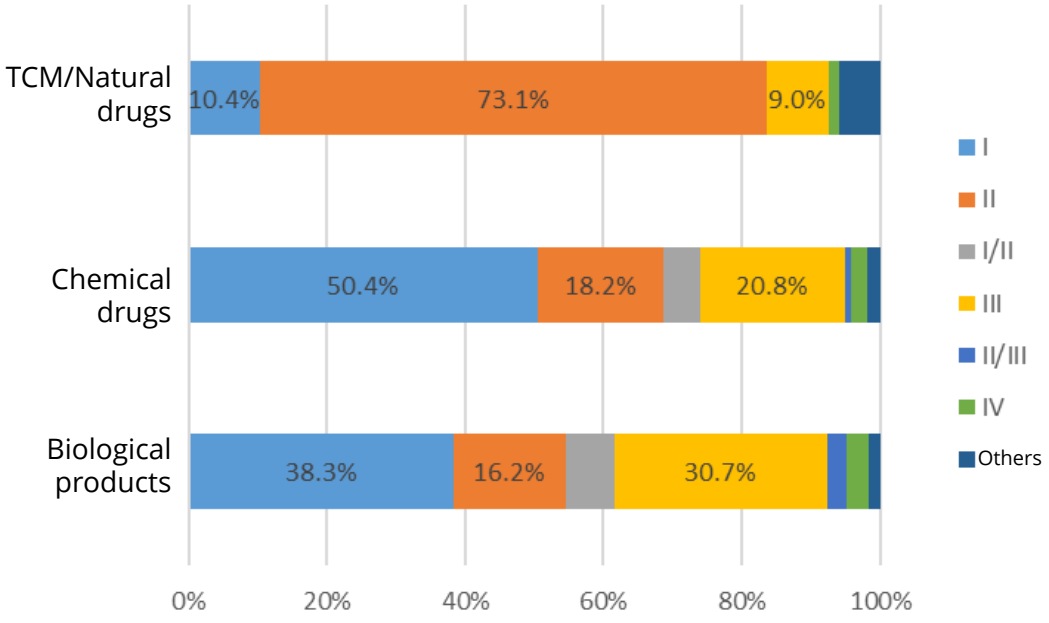


VII. Trial Phases

Phase I clinical trials accounted for the highest percentage at 43.7% (n = 643), followed by phase III and II clinical trials, accounting for 24.4% (n = 359) and 19.9% (n = 293), respectively. Four of the 39 Phase IV clinical trials were real-world studies.



Phase I chemical drug and biological products trials accounted for 50.4% and 38.3%, respectively. TCM trials were mainly concentrated in phase II, accounting for 73.1%. The percentage of phase III biological trials (30.7%) was higher than that of chemical drugs (20.8%) and TCM (9.0%).



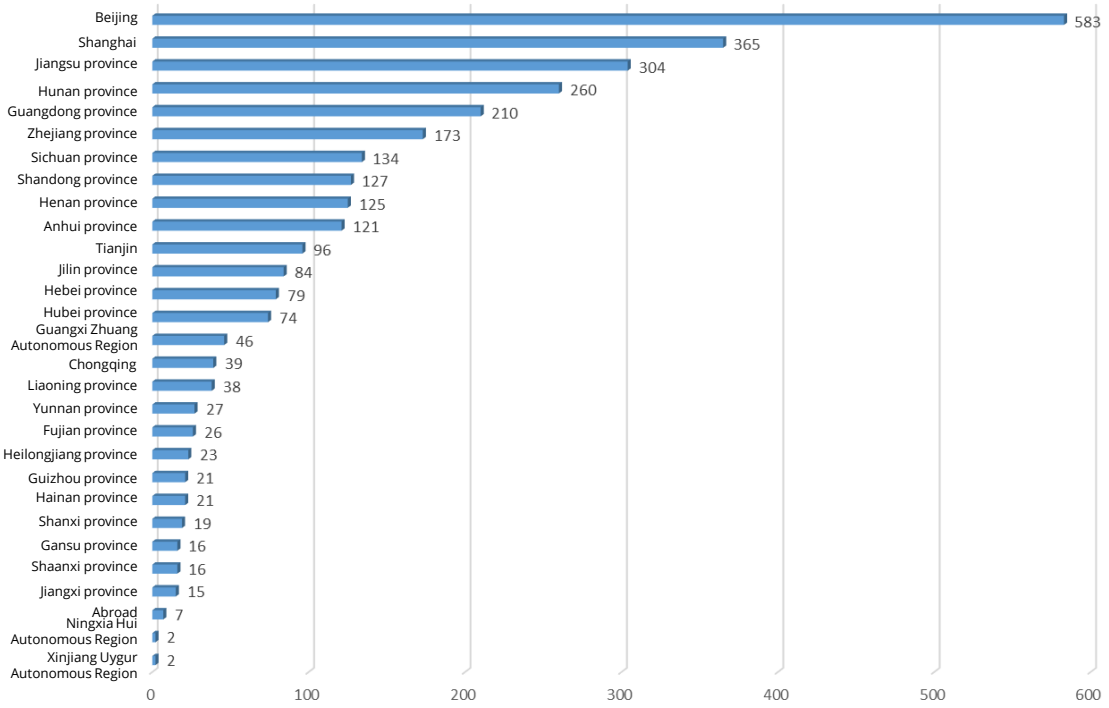
VIII. Sample Size Distribution

In 2020 there were 320 target enrollments on average (international multicenter clinical trials in terms of domestic target enrollments) for clinical trials, with 53.2% (783) of the clinical trials having target enrolments ≤ 100.

Range of Number of Target Enrollment	Number of Trials (total number 1473)	Proportion
Number of target enrollments ≤ 100	783	53.2%
100 < number of target enrollments ≤ 200	209	14.2%
200 < number of target enrollments ≤400	148	10.0%
400 < number of target enrollments ≤1000	208	14.1%
Number of target enrollments > 1000	61	4.1%
Others	64	4.3%

IX. Leading Institutions

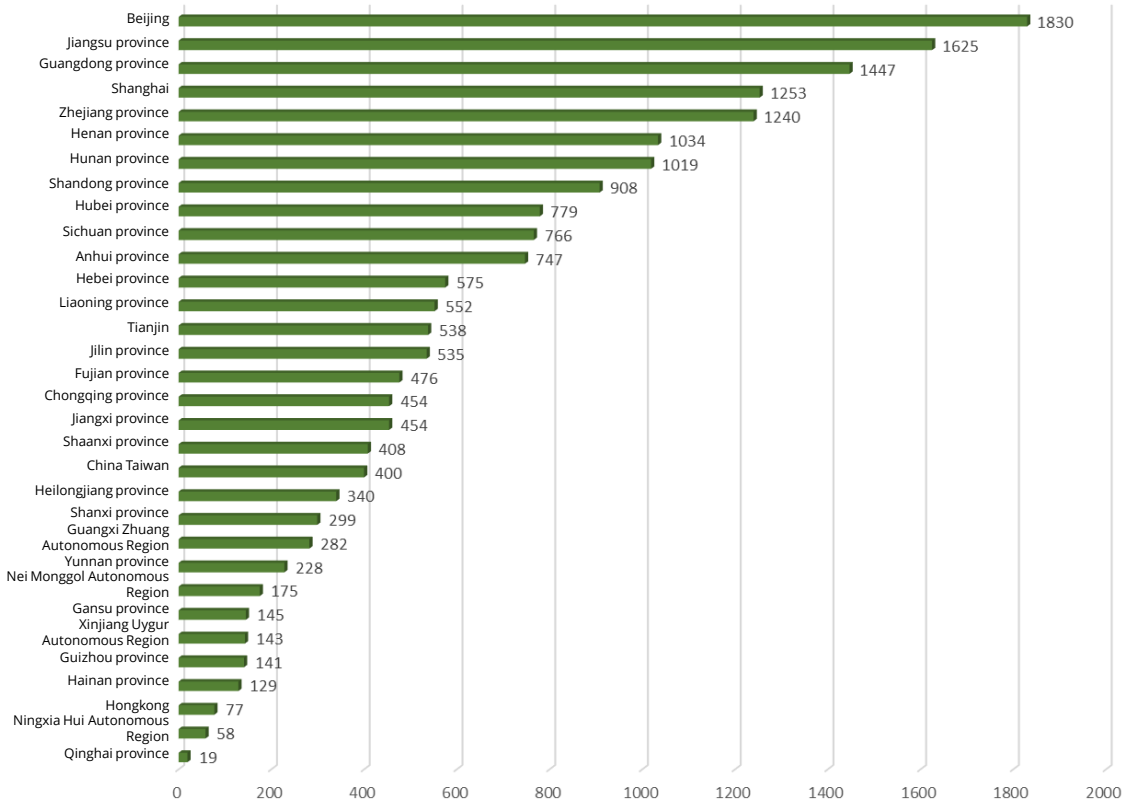
The clinical trial institutions in Beijing, Shanghai and Jiangsu Province participated in more clinical trials as leading institutions (if a clinical trial institution participated in multiple clinical trials as a leading institution at the same time, it was counted separately), accounting for approximately 41.0%. Among them, the clinical trial institutions in Beijing participated in the most as leading institutions, up to 583 times, accounting for 19.1% of the total.



X. Participating Institutions

In aggregate, clinical trial institutions participated in trials 33,680 times in China and abroad (if a clinical trial institution participated in multiple clinical trials at the same time, it was counted separately in), and 19,076 times in Greater China alone.

Clinical trial institutions in Beijing, Shanghai, and Jiangsu Province participated most frequently in clinical trials, each more than 1200 times. Clinical trial institutions in Guangdong Province, however, did participate in clinical trials more often than their counterparts in Shanghai. In addition, the times (400 times) of participation in the clinical trials for Taiwan clinical trial institutions were significantly higher than those of clinical trial institutions in individual provinces/autonomous regions in China's mainland, such as Heilongjiang, Shanxi and Yunnan provinces, etc.



Chapter III Other Characteristics of Clinical Trials

I. Clinical Trials in Special Populations

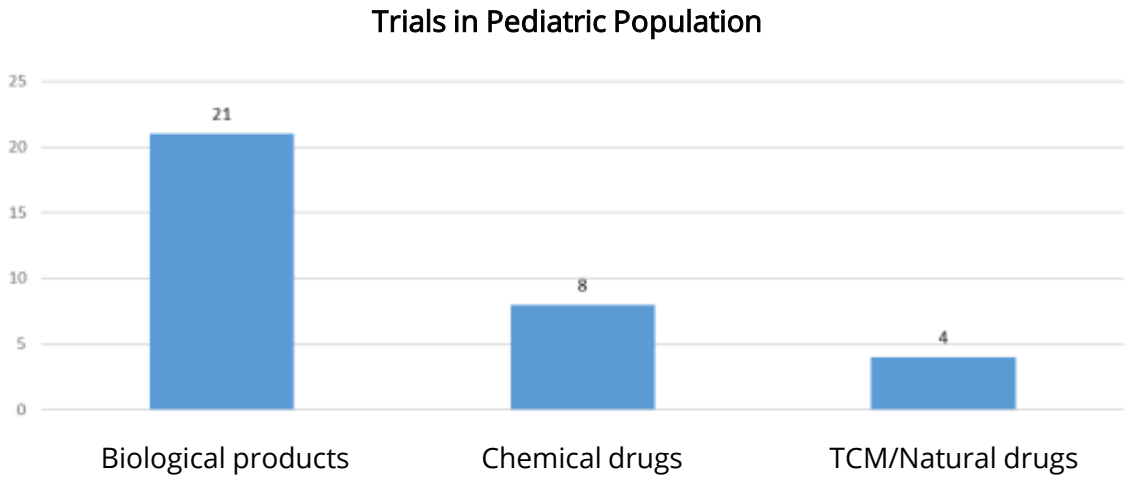
1. Geriatric Population

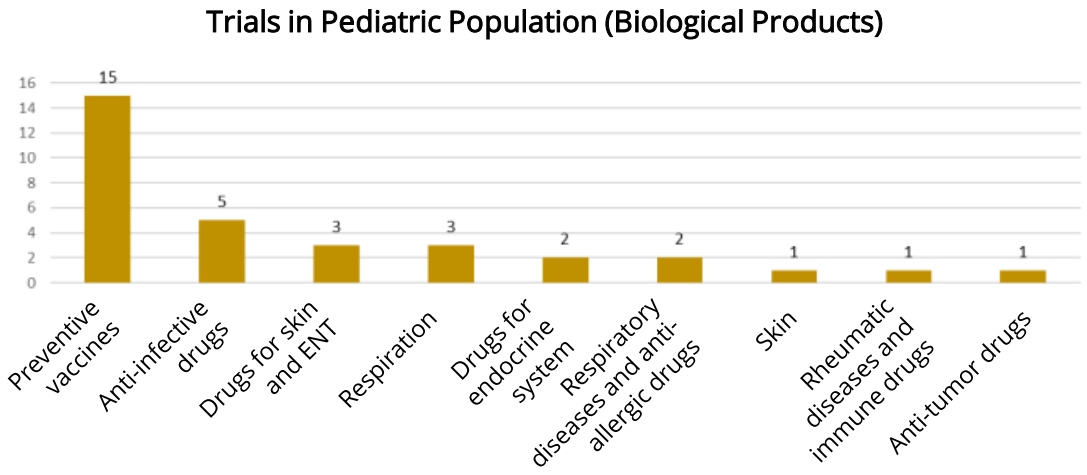
1038 trials in 2020 involved geriatric subjects, accounting for 70.5% of all new drug clinical trials. Only three were carried out in the geriatric population, accounting for 0.2%. All three were for chemical drugs, including anti-tumor drugs (n = 2) and drugs for reproductive system diseases (n = 1).

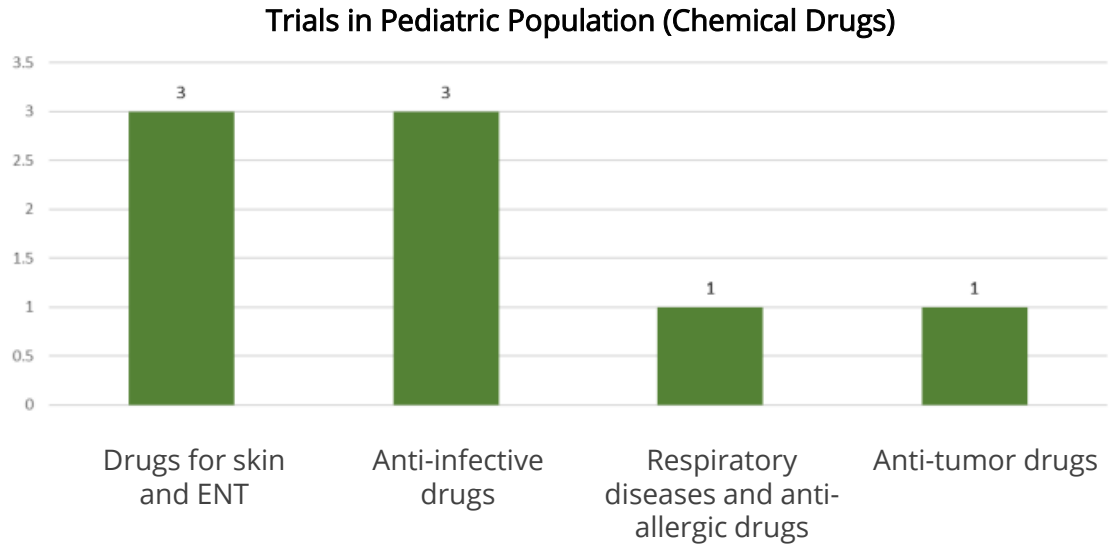
2. Pediatric Population

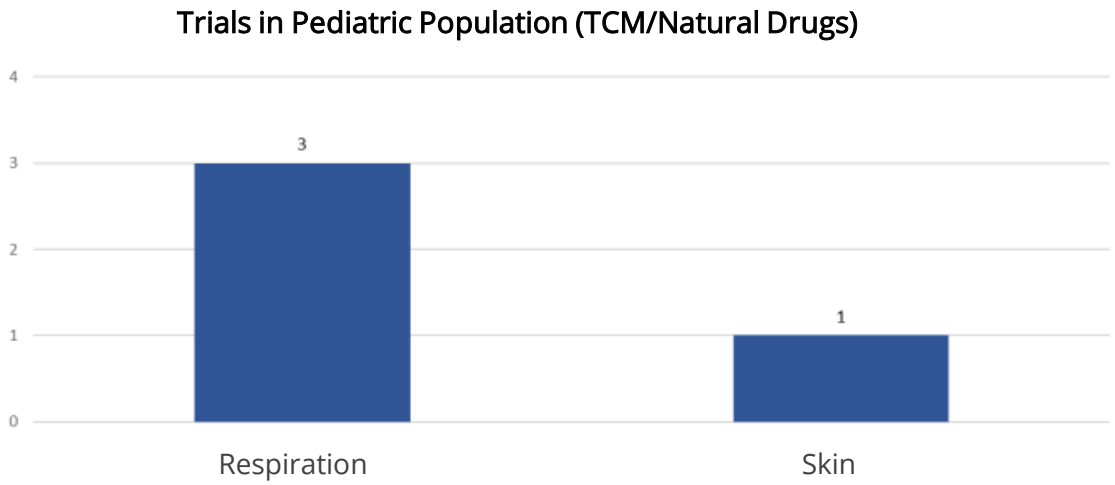
There were 129 clinical trials involving pediatric subjects, accounting for 8.8%. 70 trials were registered for biological products, the largest amount, followed by chemical drugs and TCM. Major indications were distributed as anti-tumor drugs, preventive vaccines, skin and ENT, etc. The distribution of biological products and chemical drugs was roughly the same, and TCM was mainly concentrated in respiratory drugs.

A total of 33 new drug clinical trials were registered for the pediatric population, accounting for 2.2% of all new drug clinical trials. 21trials for biological products were registered, the largest amount, followed by eight chemical drug trials and four TCM trials. According to the analysis by indications, the biological products were mainly preventive vaccines, accounting for 39.4%; chemical drugs were mainly drugs for skin and ENT and anti-infective drugs; TCM/natural drugs were respiratory and skin drugs.


Trials in Pediatric Population
25
20
15
10
5
0
21
8
4
Biological products
Chemical drugs
TCM/Natural drugs

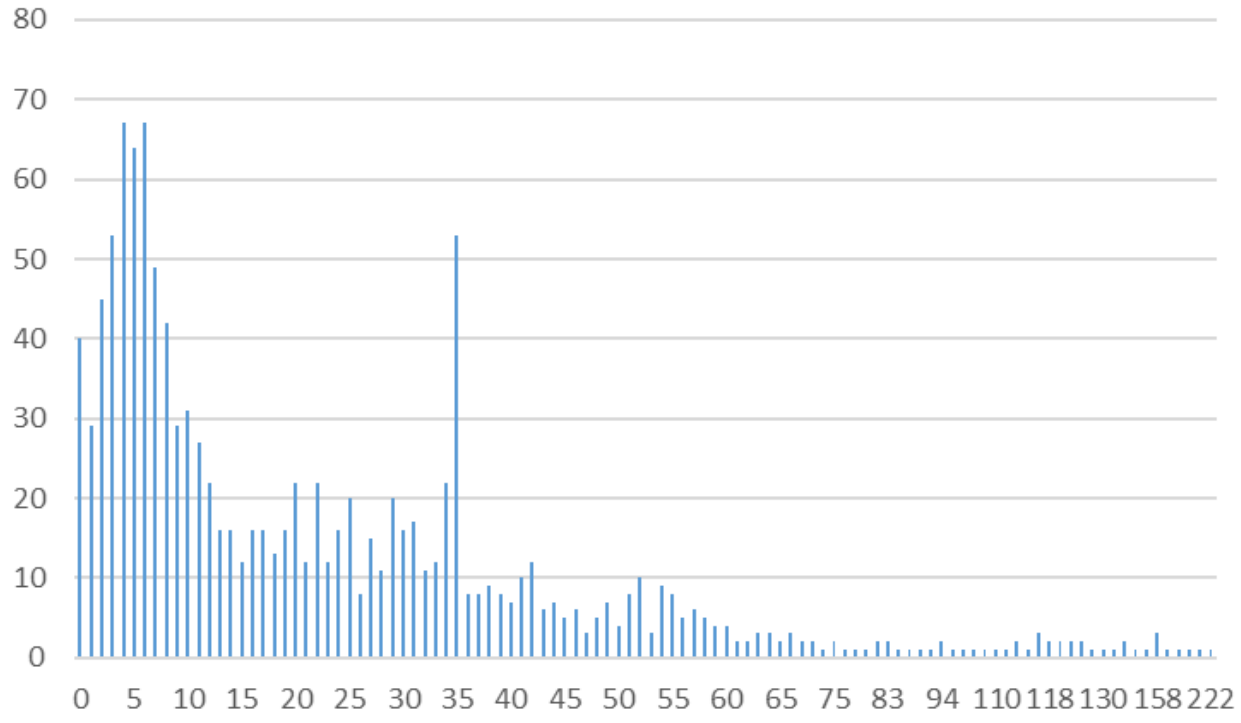

Trials in Pediatric Population (Biological Products)
16
14
12
10
8
6
4
2
0
15
5
3
3
2
2
1
1
1
Preventive vaccines
Anti-infective drugs
Drugs for skin and ENT
Respiration
Drugs for endocrine system
Respiratory diseases and anti-allergic drugs
Skin
Rheumatic diseases and immune drugs
Anti-tumor drugs


Trials in Pediatric Population (Chemical Drugs)
3.5
3
2.5
2
1.5
1
0.5
0
3
3
1
1
Drugs for skin and ENT
Anti-infective drugs
Respiratory diseases and anti-allergic drugs
Anti-tumor drugs

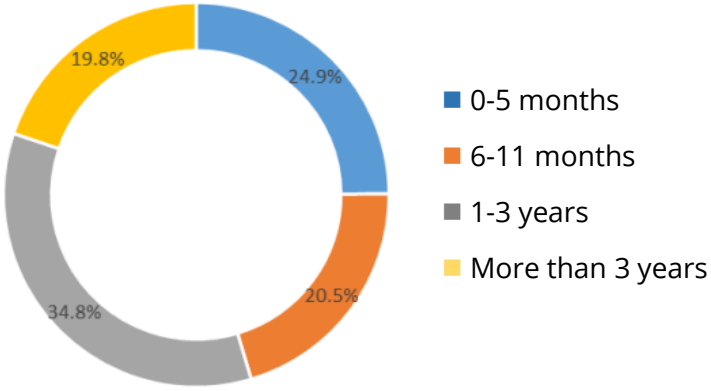


II. Startup Time of Clinical Trials

Among the 1473 new drug clinical trials, 1203 (81.7%) had registered the first ICF (Informed Consent Form) date in China. The time taken to initiate clinical trials was analyzed according to the clinical trial approval date (i.e., the first ICF date in China - the clinical trial approval date, calculated in natural months). The elapsed time for clinical trial initiation ranged from 0 to 222 months, with an average of 23.4 months.

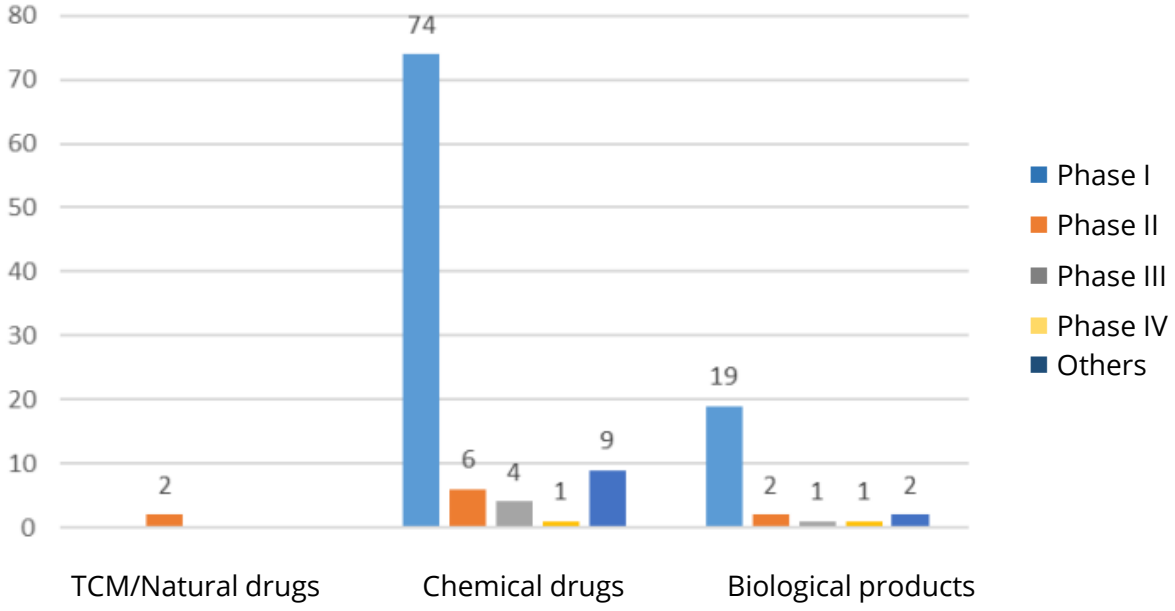


The percentage of clinical trials initiating subject recruitment within 6 months (<6 months) after approval was 24.9%; within 1 year (<12 months), 45.4%. If calculated on the basis of a three-year (< 36 months) approval validity period, approximately 80.2% of the clinical trials initiated subject recruitment within the validity period of the approval.

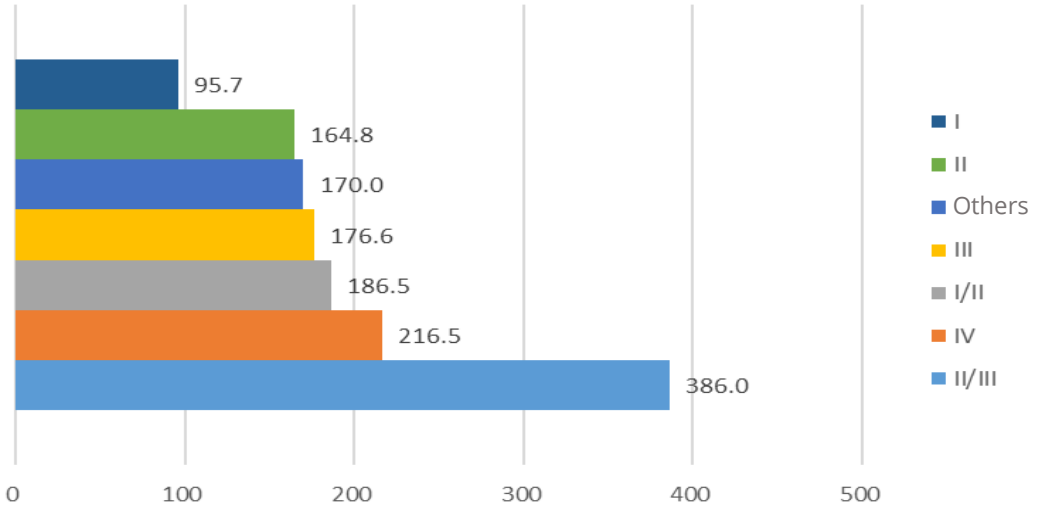


III. Completion of Clinical Trials

Among the 1473 clinical trials of new drugs, 121 were completed in 2020 (i.e., the completion date in China was between January 1, 2020 and December 31, 2020, and the first ICF date in China was not left blank), including 2 trials of TCM, 94 of chemical drugs, and 25 of biological products. By trial phases, the number of phase I clinical trials completed — 93 in total — was the largest, followed by 11 others, 10 phase II, 5 phase III and 2 phase IV trials.



The clinical trial completion time was analyzed based on the completion date of the domestic trial and the date of the first ICF in China. Completion time ranged from 6 to 735 days (natural days), with an average of 115.6 days. Completion time was analyzed by trial phases. The average phase I clinical trial complete time was the shortest at 95.7 days. Phase II/III trials were the longest at 386 days.



Among the above-mentioned 121 clinical trials, there were two voluntary suspensions and seven voluntary terminations. These included one voluntarily terminated phase III chemical drug trial, one voluntarily terminated phase III biological products trial, and one voluntarily suspended phase I biological product clinical trial. The drug types and reasons for suspension/termination are as follows:

Type of Drugs	Voluntary Suspension	Voluntary Termination	Type of Reasons (Number of Clinical Trials)
TCM/Natural drugs	-	1	Adjustment of R&D strategy and protocol design
Chemical drugs	-	4	1) Limited clinical benefits (2); 2) Limited subject recruitment due to epidemic factors (1); 3) Protocol design issues (1)
Biological products	2	2	1) Adjustment of R&D strategy and termination of trial (2) 2) Limited subject recruitment due to epidemic factors (1); 3) Adjustment of supplier of reagents for trails (1);
Total	2	7	

Chapter IV How New Drug Clinical Trials are Progressing in China

I. Obvious Lack of Diversity for New Drug Clinical Trials

Both the number of new drug clinical trials and that of the drug varieties in China have increased remarkably. The percentage of new therapies in biological products has reached 4.3%, indicating that the clinical trial reform in China has effectively promoted the development of clinical drug trials in China.

The drug clinical trials registered in 2020 mainly focused on anti-tumor, endocrine and cardiovascular indications, and the majority of lung cancer indications was concentrated in non-small cell cancers. At present, most of the biological innovative drugs under development are antibody drugs and targets are lack of diversity, resulting in cut-throat competition.

II. Inefficient Implementation of Clinical Trials after Approval

Less than half (45.4%) of the clinical trials registered in 2020 initiated subject recruitment within one year after approval. Only 93 of the 643 newly registered phase I clinical trials were completed in 2020, and even fewer phase II and III clinical trials were completed.

III. Low Proportion of Clinical Trials in Pediatrics

There were fewer pediatric drug clinical trials, mainly for biological products, chemical drugs, and even fewer for TCM. Meanwhile, the indications were mainly concentrated in anti-tumor drugs and vaccines. Applicants' low enthusiasm for pediatric drug R&D was possibly related to the long period of clinical trials for pediatric drugs, difficulties in subject recruitment and high safety risks.

IV. Unbalanced Geographical Distribution of Clinical Trials

Although more medical institutions are encouraged to participate in clinical trials after the qualification of clinical trial institutions in China is changed from a certification system to a filing system, the geographical distribution of the clinical trials is still unbalanced. In the new drug clinical trials in China, the institutions in Beijing, Shanghai and Jiangsu Province still participate in the most clinical trials.

Appendix: Instructions for Compilation

1. This report is statistically described and analyzed with the clinical trial registration (CTR) number by searching the clinical trial registration information first published from January 1, 2020 to December 31, 2020 in the Drug Clinical Trial Registration and Information Disclosure Platform database (hereinafter referred to as the "registration platform"), as well as by referring to the public database retrieval information in the industry. Due to a system upgrade, there may be cases such as applicants deleting duplicated registration information. As a result, the number of clinical trials published in the report is slightly different from the real-time data published on the Center for Drug Evaluation's website.
2. This report mainly focuses on the summary analysis of the registration information of new drug clinical trials (excluding bioequivalence trials). The registration information of bioequivalence trials (including the consistency evaluation of quality and efficacy of generic drugs) is only a general analysis and description.
3. In this report, the clinical trial registration information is classified and analyzed mainly by drug classification (TCM, chemical drugs and biological products), registration classification (including the original registration classification information), indications, drug targets, clinical trial phases and trial progress. The annual drug review report of the Center for Drug Evaluation is referenced to maintain consistency in the classification of indications.
4. The pediatric population is defined as subjects aged ≤ 14, and the geriatric population is defined as the subjects aged ≥ 65.

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Website: https://www.tigermedgrp. com/
Email: marketing@tigermedgrp.com

About Yaxincheng

Beijing Yaxincheng Medical InfoTech Co., Ltd., founded in July 2000 in Beijing and a wholly-owned subsidiary of Tigermed, is a leading language service provider in China specializing in medical translation for over 20 years. Yaxincheng now has a strong network of linguists, project managers, DTP professionals and engineers with over 350 full-time employees and over 650 freelancers, and is providing services to over 600 global clients.

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(EN) https://yaxincheng.com/en-us
Email: marketing@yaxincheng.com

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Website: http://eng.pharmadj.com
Email: Support@PharmaDJ.com
Author: Elise Mak, Justin Fischer