The 2021 Drug Review Annual Report

Center for Drug Evaluation
National Medical Products Administration

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国家药品监督管理局
National Medical Products Administration

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Released on: June 1, 2022

2021 was a milestone in the history of both the Communist Party of China ("CPC" or the "Party") and our country. The CPC Central Committee under the leadership of Comrade Xi Jinping united and led the whole Party and Chinese people of all ethnic groups in accomplishing the following endeavors: We celebrated the centenary of the Communist Party of China. The 19th CPC Central Committee convened its sixth plenary session, in which a resolution on the Party's major achievements over the past century was adopted. We declared victory in the critical battle against poverty. We also achieved the first centenary goal of building a moderately prosperous society on schedule and began a new journey toward the second centenary goal of building a modern socialist country in all respects. In the opening year of the 14th Five-Year Plan, as the dedicated technical review institution responsible for drug registration and marketing in China, the Center for Drug Evaluation of the National Medical Products Administration of the PRC (NMPA) (hereinafter referred to as CDE) has always firmly implemented the spirit of important speeches by and important instructions from General Secretary Xi Jinping. It has fully implemented the requirements of "the most stringent standards, the strictest regulations, the most severe punishments and the most serious accountability" while remaining mindful of the original aspiration and mission of protecting and promoting public health. The CDE has held fast to the principles of "people first, life first and scientific review" and has actively contributed to the reform of the drug review and approval system. It has remained focused on strategic goals such as a healthy population, being at the forefront of science and technology and meeting major national needs. Additionally, it has accelerated the innovation and integration of systems and mechanism, technical standards, process management and team building.

Faced with the severe challenges of epidemic prevention and control as the already complicated task of drug review, the CDE, under the strong leadership of the Party Committee of the NMPA and guided by Xi Jinping Thought on Socialism with Chinese Characteristics for a New Era, has thoroughly studied and implemented the spirit of the fifth and sixth plenary sessions of the 19th Central Committee of the CPC and the spirit of the important speech delivered by General Secretary Xi Jinping on July 1, 2021. It has conscientiously implemented the decision-making and deployment of the CPC Central Committee and the State Council of the PRC, promoted the continuous development of comprehensive and strict Party governance, and conscientiously carried out learnings of the Party history while doing practical work for the masses. It spared no effort in advancing emergency review and approval of COVID-19 vaccines and drugs; promoted the continuous inclusion of two China-made COVID-19 vaccines into the World Health Organization's (WHO) Emergency Use Listing (EUL); finished emergency review and approval for the marketing of a set of COVID-19 neutralizing antibody drugs for combination therapy; focused efforts on building an open and transparent review mechanism; and took multiple measures to support the R&D of drugs for children's use. Ultimately the CDE has significantly contributed to happiness and security of the people.

In 2021, the CDE reviewed and approved 47 innovative drugs, hitting a record high. It continuously expedited the marketing of urgently needed new overseas drugs. Efficiency in priority review has been significantly improved. The CDE has steadfastly promoted the consistency evaluation for the quality and efficacy of generic drugs. It has raised the bar on clinical trial administration while streamlining the coordination mechanism for verification and inspection. The Electronic Common Technical Document (eCTD) for submitting drug applications was implemented. China Patent Information Registration Platform for Marketed Drugs was built up and made operational. The CDE also successfully transformed the "Three TCM Prescriptions" against COVID-19 while improving upon the technical standard system for review that meets the characteristics of TCMs. The CDE supported and promoted the development of inheritance and innovation in TCMs. It continued to deepen ICH-related work and ensured the successful re-election of the NMPA as a member of the ICH Management Committee. In 2021, the CDE issued 87 technical guidelines, which made the review standard system more complete and the process-oriented review system more scientific. CDE made continuous progress in the modernization of review systems and review capacity. This further enhanced the Chinese pharmaceutical industry's capacity for innovation and high-quality development.

Chapter 1: Drug registration application acceptances

(1) Overview

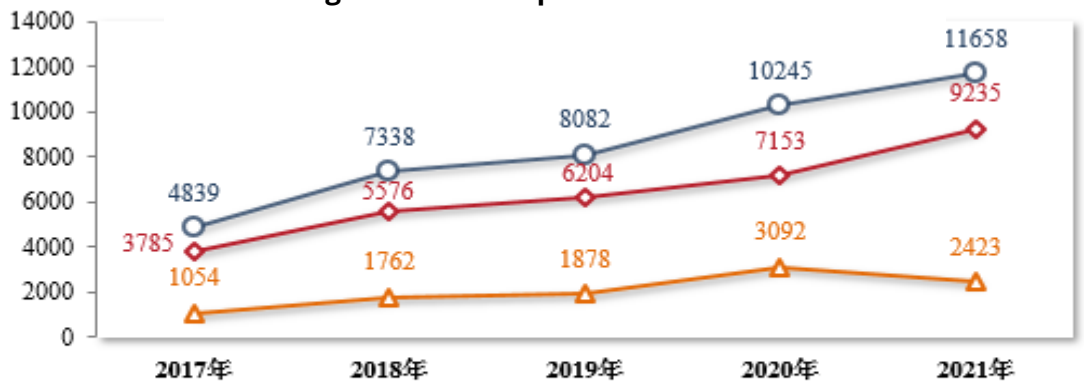
1. Annual acceptances

In 2021, the Center for Drug Evaluation of the NMPA (hereinafter referred to as CDE) accepted 11,658 registration applications (hereinafter referred to as "RAs"),[1] up 13.79% year-over-year (YoY).

In 2021, the CDE accepted 9,235 RAs requiring technical review, up 29.11% YoY, including: 2,180 RAs subject to technical review and then submission to the NMPA[2] for review and approval (hereinafter referred to as "technical review"); 7,051 RAs subject to technical review and then administrative review and approval in the name of NMPA[2] (hereinafter referred to as "review and approval"); and four RAs subject to technical review and then submission to the Center for Medical Device Evaluation of the NMPA ("CMDE") for technical review of drug-device combination (hereinafter referred to as "drug-device combination") products with primary effects of medical devices.

The CDE also accepted 2,423 RAs requiring no technical review but rather direct administrative review and approval in the name of the NMPA[3] (hereinafter referred to as "direct review and approval"). RA acceptances in 2017-2021 are shown in Figure 1.

Figure 1: RA acceptancesin 2017-2021



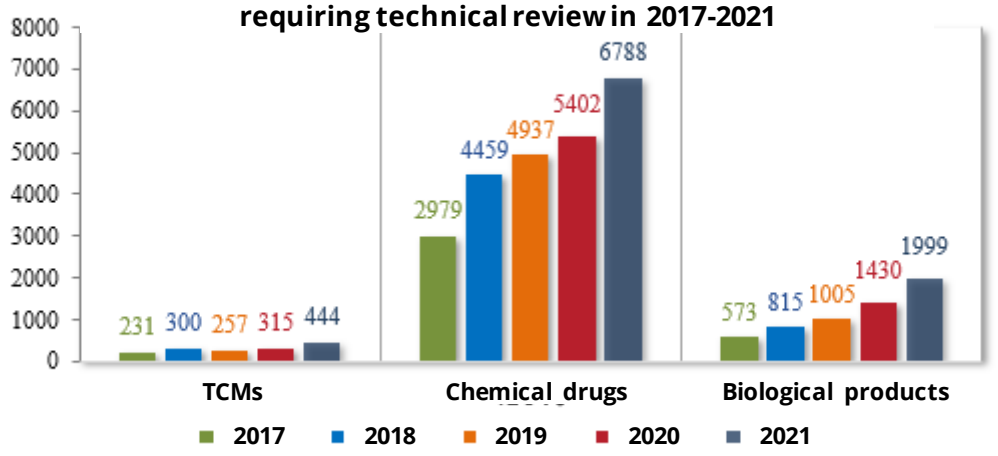
Notes: Since May 1, 2017, CDE has started to accept RAs subject to administrative approval in the name of NMPA in accordance with the Decision of NMPA on Adjusting Approval Procedures for Certain Administrative Examination and Approval Items of Drugs (NMPA Decree No. 31).

According to the requirements of the NMPA's Announcement on Issues Concerning the Further Improvement of Drug-related Associated Review & Approval and Supervision (2019 No. 56, hereinafter referred to as Announcement No. 56), 1,313 RAs of active pharmaceutical ingredients (APIs) were accepted in 2021, up 2.98% YoY.

2. Acceptance of various types of RAs requiring technical review

Among the 9,231 RAs[4] requiring technical review accepted in 2021, by drug class, 444 were for TCMs[5], up 40.95% YoY. 6,788 were for chemical drugs, up 25.66% YoY, accounting for 73.53% of the total number of accepted RAs requiring technical revie. 1,999 were for biological products, up 39.79% YoY. See Figure 2 for the acceptance of RAs for various classes of drugs requiring technical review in 2017-2021.

Figure 2: Acceptance of RAs for various classes of drugs requiring technical review in 2017-2021



When tabulated by RA category, the CDE accepted 2,412 Investigational New Drug applications (hereinafter referred to as INDs), up 55.81% YoY; 389 New Drug Applications (hereinafter referred to as NDAs), up 20.43% YoY; 1,791 marketing authorization applications for drugs of the same name and formula, generic drugs and biosimilars (hereinafter referred to as ANDAs), up 59.06% YoY; 908 RAs for consistency evaluation of quality and efficacy of generic drugs[6] (hereinafter referred to as consistency evaluation application); and 3,283 supplementary applications, up 16.13% YoY. See Figure 3 for the acceptance of RA categories requiring technical review in 2017-2021.

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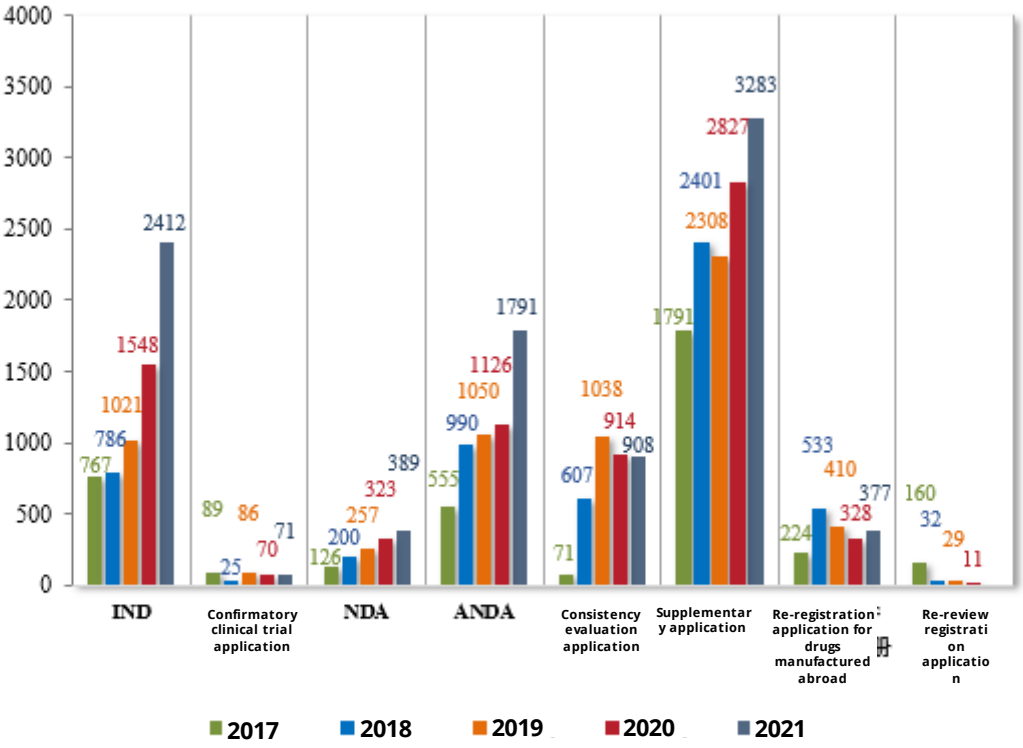
Figure 3: Acceptance of various categories of RAs requiring technical review in 2017-2021



Notes: Since July 1,2020, no registration application for "Re-review" is included in the current *Provisions for Drug Registration*, and such category of registration application is no longer accepted.

(2) Acceptance of innovative drugs RAs

The CDE accepted 1886 RAs for innovative drugs (involving 998 varieties[8]), up 76.10% YoY.

According to the statistics by drug type, 54 RAs (involving 51 varieties) were for innovative TCMs, up 134.78% YoY; 1,166 RAs (involving 508 varieties) for innovative chemical drugs, up 55.05% YoY; and 666 RAs (involving 439 varieties) for innovative biological products, up 125.00% YoY.

According to the statistics by RA category, the CDE accepted 1,821 INDs (involving 953 varieties), up 79.23% YoY and 65 NDAs (involving 45 varieties), up 18.18% YoY..

See Table 1 for the acceptance of RAs for innovative TCMs, innovative chemical drugs and innovative biological products in 2021; see Figure 4 for the acceptance of INDs for innovative drugs in 2017-2021; and see Figure 5 for the acceptance of NDAs for innovative drugs in 2017-2021.

Table 1: Acceptance of RAs for innovative TCMs, chemical drugs and biological products in 2021

Number of acceptances	Innovative TCMs		Innovative chemical drugs		Innovative biological products		Total	
	RA	Variety (N)	RAs	Variety (N)	RA	Variety (N)	RA	Variety (N)
IND	44	43	1134	487	643	423	1821	953
NDA	10	8	32	21	23	16	65	45
Total	54	51	1166	508	666	439	1886	998

Figure 4: Acceptance of INDs for innovative drugs in 2017-2021

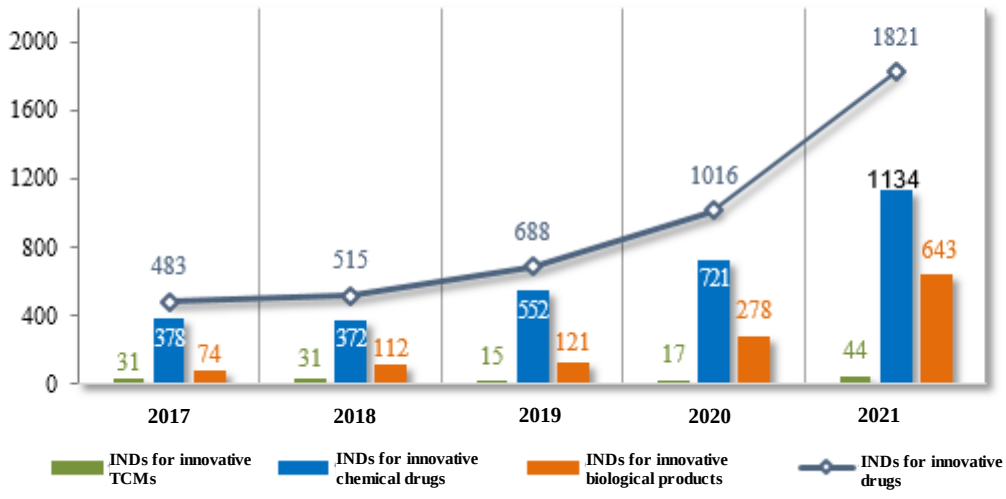
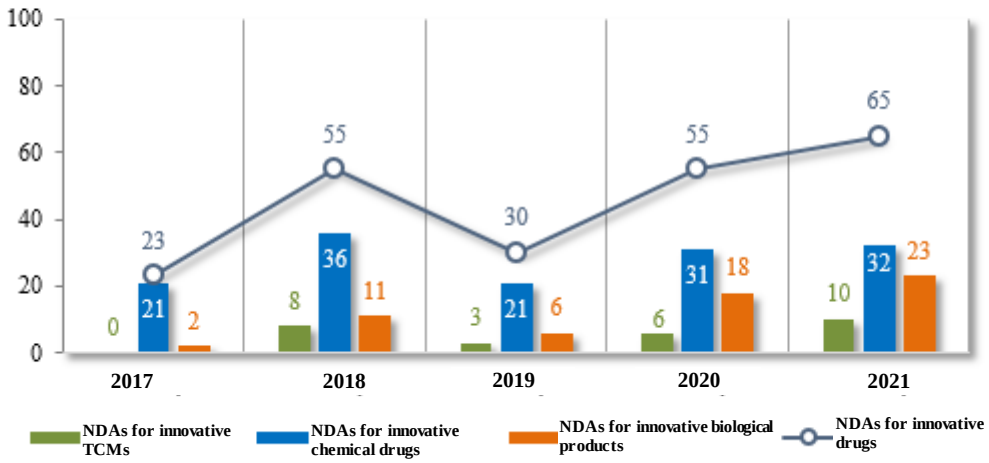


Figure 5: Acceptance of NDAs for innovative drugs in 2017-2021



According to the statistics by production site categories, 1,485 applications (involving 790 varieties) were for domestically produced innovative drugs and 401 (involving 208 varieties) for innovative drugs manufactured abroad. See Table 2 for the acceptance of RAs for innovative drugs manufactured in and outside China in 2021.

Table 2: Acceptance of RAs for innovative drugs manufactured in and outside China in 2021

RA category	Drugs manufactured in China		Drugs manufactured outside China		Total	
	RA	Variety (N)	RA	Variety (N)	RA	Variety (N)
IND	1428	750	393	203	1821	953
NDA	57	40	8	5	65	45
Total	1485	790	401	208	1886	998

(3) Acceptance of RAs for TCMs requiring technical review

A total of 444 RAs for TCMs requiring technical review were accepted in 2021. According to the statistics by RA category, 52 were for INDs, up 136.36% YoY, including 44 INDs (involving 43 varieties) for innovative TCMs, up 158.82% YoY. 14 were for NDAs, up 133.33% YoY, including 10 NDAs (involving 8 varieties) for innovative TCMs, up 66.67% YoY.

See Figure 6 for the acceptance of various categories of RAs for TCMs requiring technical review in 2021. See Figure 7 for the acceptance of various categories of RAs for TCMs requiring technical review in 2017- 2021.

Figure 6: Acceptance of various categories of RAs for TCMs requiring technical review in 2021

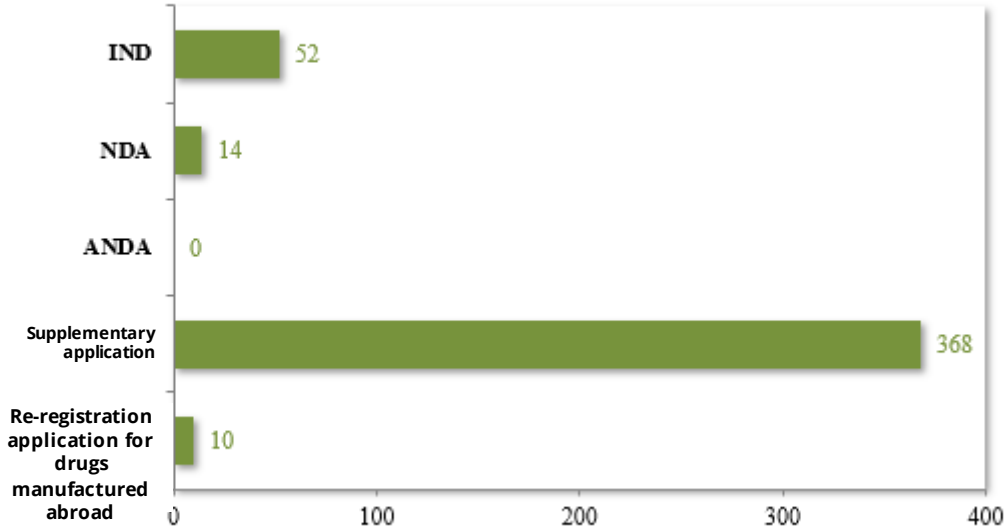
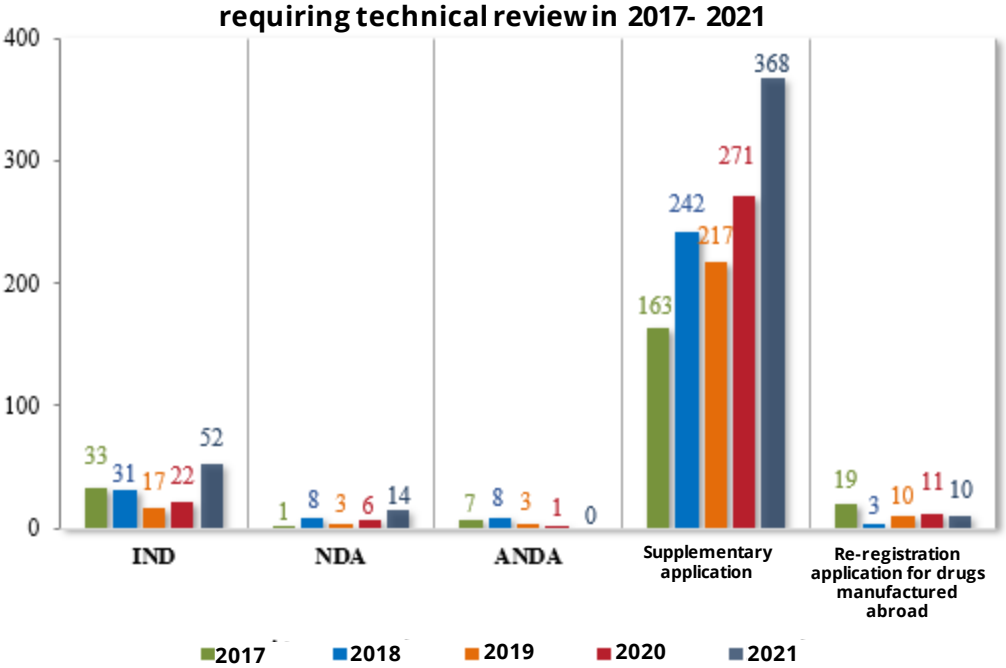


Figure 7: Acceptance of various categories of RAs for TCMs requiring technical review in 2017- 2021



(4) Acceptance of RAs for chemical drugs requiring technical review

In 2021, 6,788 RAs for chemical drugs requiring technical review were accepted. According to the statistics by RA category, 1,500 applications were for INDs, up 58.56% YoY, including 1,134 INDs (involving 487 varieties) for innovative chemical drugs, up 57.28% YoY. 197 were for NDAs, up 3.14% YoY, including 32 NDAs (involving 21 varieties) for innovative chemical drugs, up 3.23% YoY. 169 RAs were for Class 5.1 chemical drugs[9], up 5.63% YoY, including 44 applications for clinical trial application[10] and 125 NDAs; 1,791 ANDAs, up 59.20% YoY; and 908 RAs for consistency evaluation.

See Figure 8 for the acceptance of various categories of RAs for chemical drugs requiring technical review in 2021. See Figure 9 for the acceptance of INDs for chemical drugs, applications for confirmatory clinical trials, NDAs, ANDAs and applications for consistency evaluation in 2017-2021.

Figure 8: Acceptance of various categories of RAs for chemical drugs requiring technical review in 2021

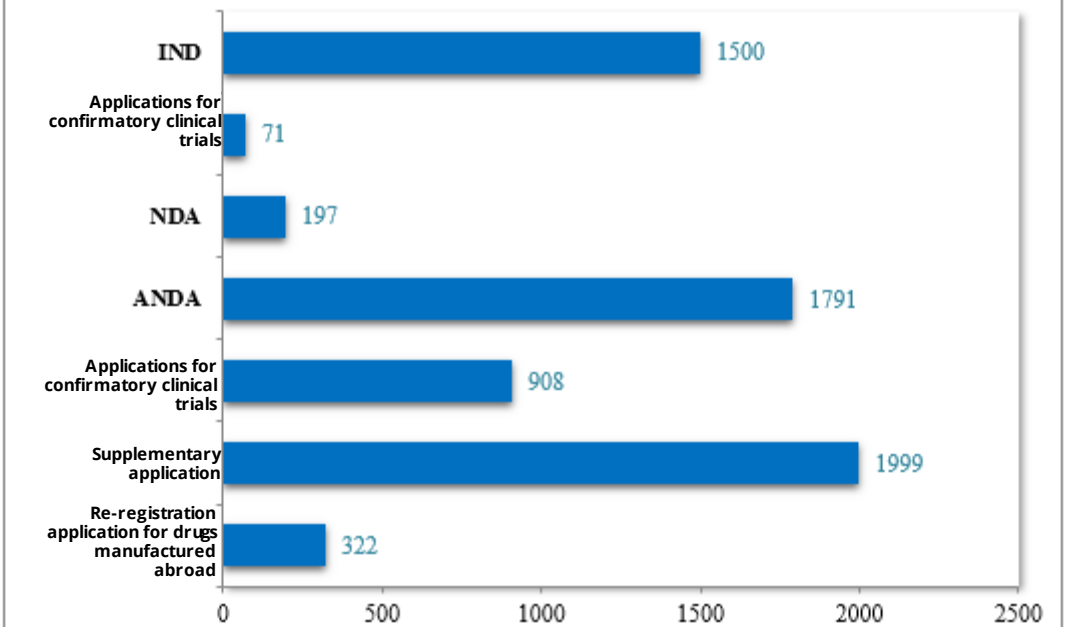
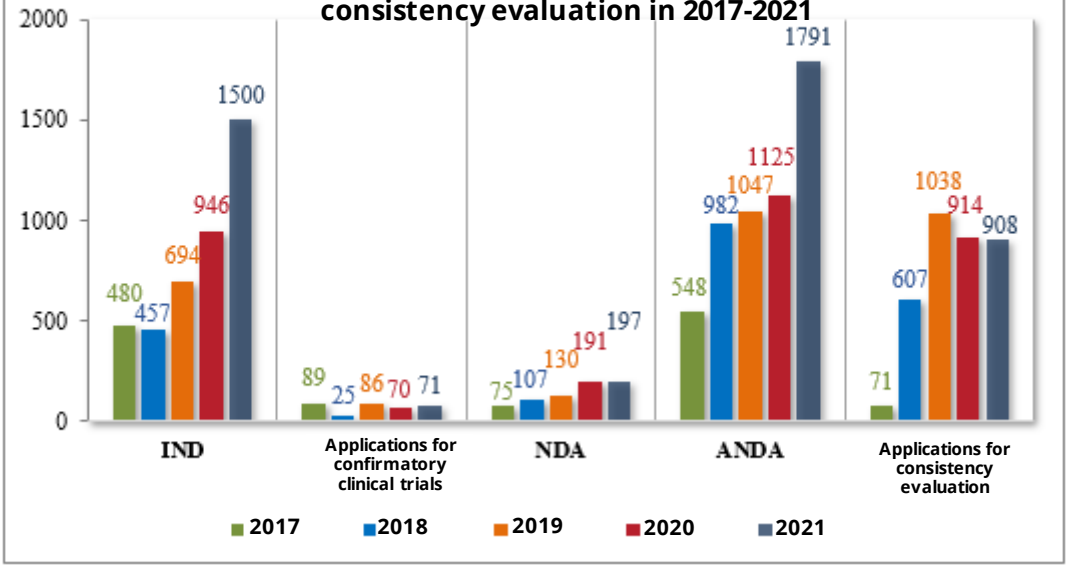
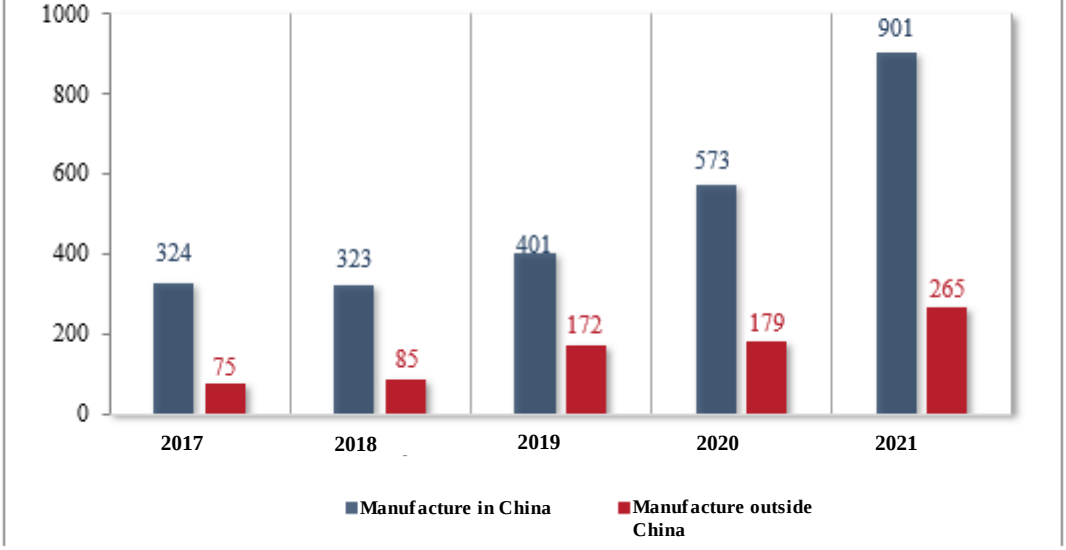


Figure 9: Acceptance of INDs for chemical drugs, applications for confirmatory clinical trials, NDAs, ANDAs and applications for consistency evaluation in 2017-2021



Among the 1,166 RAs (involving 508 varieties)[11] for innovative chemical drugs requiring technical review, according to production site, 901 RAs (involving 385 varieties) were for manufacture in China while 265 RAs (involving 123 varieties) were for manufacture outside China. See Figure 10 for the acceptance of RAs of innovative chemical drugs for manufacture in China and overseas in 2017-2021.

Figure 10: Acceptance of RAs of innovative chemical drugs for manufacture in and outside China in 2017-2021



(5) Acceptance of RAs for biological products requiring technical review

1,999 RAs were accepted for biological products requiring technical review, including 229 RAs for prophylactic biological products, 1,755 RAs for therapeutic biological products and 15 RAs for in vitro diagnostic reagents. According to the statistics by RA category:

860 applications were for INDs, up 48.28% YoY, including 643 INDs (involving 423 varieties) for innovative biological products, up 131.29% YoY. Among them, 45 INDs were for prophylactic biological products, covering 26 INDs (involving 16 varieties) for innovative prophylactic biological products. 815 INDs were for therapeutic biological products, covering 617 INDs (involving 407 varieties) for innovative therapeutic biological products.

178 applications were for NDAs, up 41.27% YoY, covering 23 NDAs (involving 16 varieties) for innovative biological products, up 27.78% YoY. Among them, 13 NDAs were for prophylactic biological products, covering 5 NDAs (involving two varieties) for innovative prophylactic biological products. 156 NDAs were for therapeutic biological products, covering 18 NDAs (involving 14 varieties) for innovative therapeutic biological products; and nine NDAs for in vitro diagnostic (IVD) reagents.

916 cases were for supplementary applications. 45 cases were for re-registration applications for drugs manufactured abroad.

See Table 3 for the acceptance of INDs and NDAs for biological products and innovative biological products in 2021. See Figure 11 for the acceptance of various categories of RAs for biological products requiring technical review in 2021. See Figure 12 for the acceptance of INDs and NDAs for biological products in 2017-2021.

Table 3: Acceptance of INDs and NDAs for biological products and innovative biological products in 2021

Drug type	IND		NDA	
	Total quantity of biological products	Innovative biological products	Total quantity of biological products	Innovative biological products
Prophylactic biological products	45	26	13	5
Therapeutic biological products	815	617	156	18
In vitro diagnostic reagents	—	—	9	—
Total	860	643	178	23

Figure 11: The acceptance of various categories of RAs for biological products requiring technical review in 2021

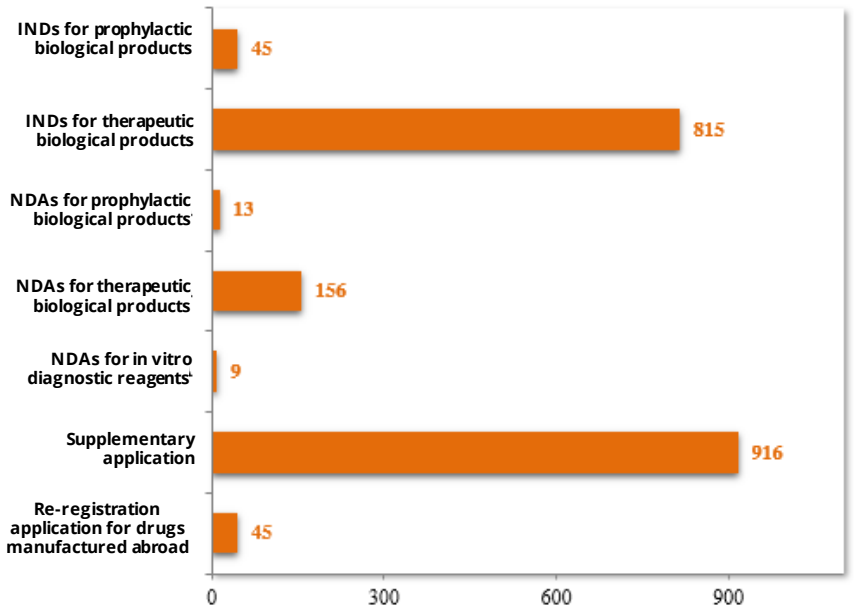
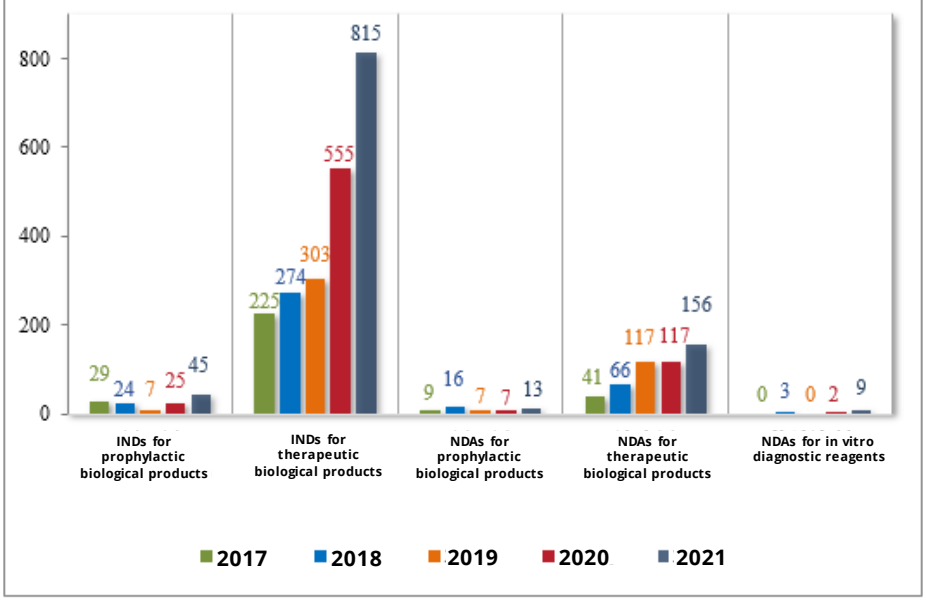
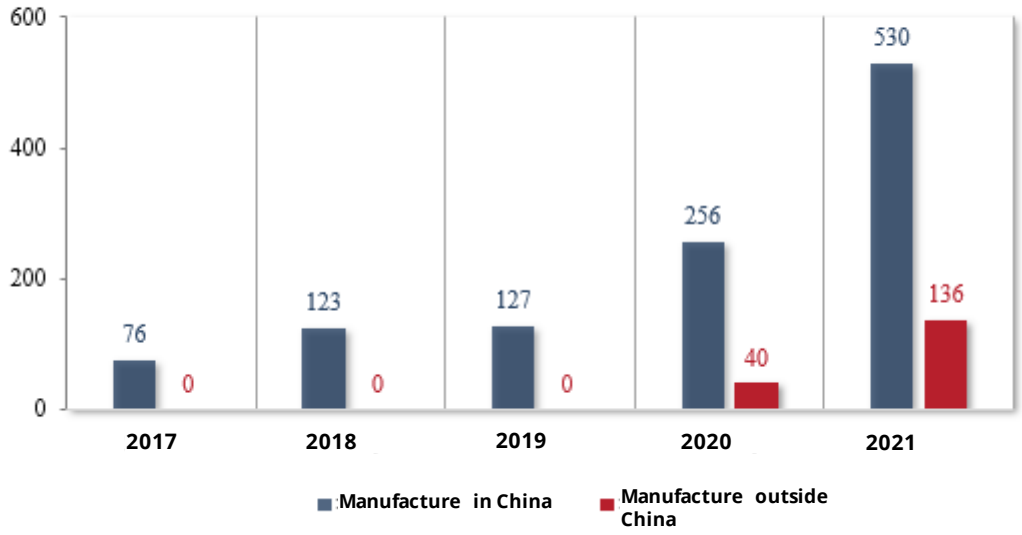


Figure 12: Acceptance of INDs and NDAs of biological products in 2017 -2021



Among the 666 RAs (involving 439 varieties[12]) for innovative biological products requiring technical review, according to the statistics by production site, 530 RAs (involving 354 varieties) were for innovative biological products manufactured in China, and 136 RAs (involving 85 varieties) were for innovative biological products manufactured outside China. See Figure 13 for the acceptance of RAs for innovative biological products for manufacture in and outside China in 2017-2021.

Figure 13: Acceptance of RAs for innovative biological products for manufacture in and outside China in 2017-2021



(6) Acceptance of RAs subject to administrative approval

1. Overview

9,474 RAs for administrative approval were accepted, up 7.82% YoY. Among them, 2,423 RAs were for direct review and approval. 137,051 RAs for review and approval, up 23.81% YoY, including 2,483 applications for clinical trials, up 53.46% YoY.

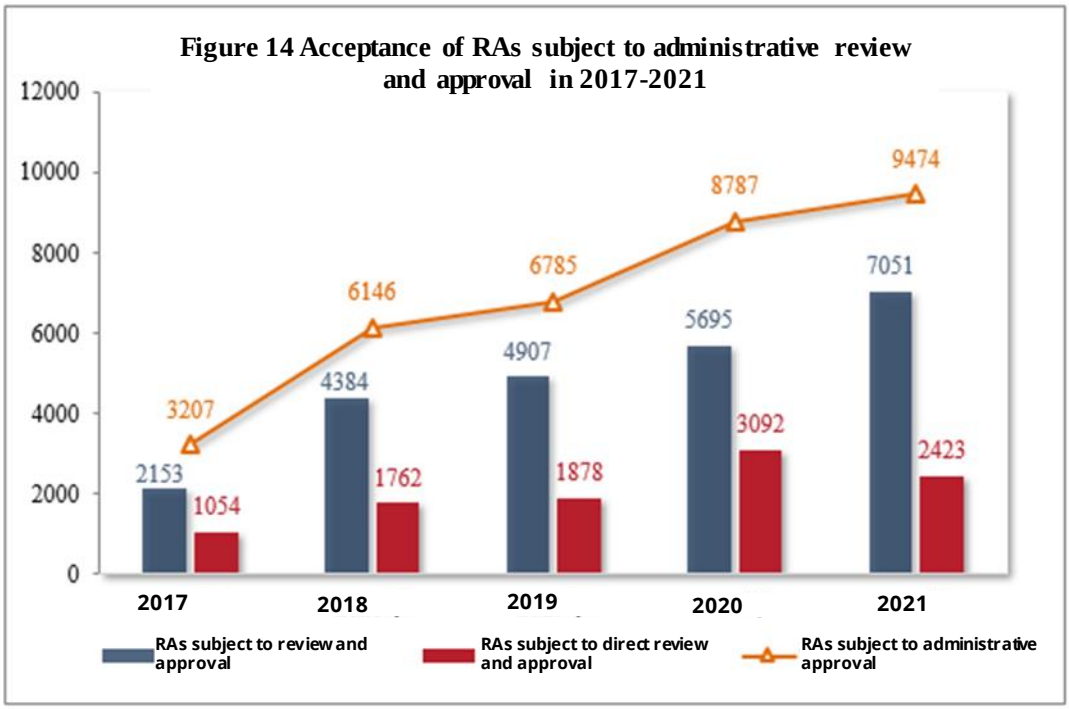
See Table 4 for the acceptance of RAs for administrative review and approval in 2021. See Figure 14 for the acceptance of RAs subject to administrative review and approval in 2017[14]-2021.

Table 4: Acceptance of (cases of) RAs subject to administrative review and approval in 2021

RA type		TCMs	Chemical drugs	Biological products	Total
RAs subject to review and approval	Clinical trial application	52	1571	860	2483
	Consistency evaluation application	—	908	—	908
	Supplementary application	368	1999	916	3283
	Re-registration application for drugs manufactured abroad	10	322	45	377

	Total	430	4800	1821	7051
RAs subject to direct review and approval	Supplementary applications not requiring technical review	930	1038	34	2002
	RA for temporary import	1	340	80	421
	Total	931	1378	114	2423
Total		1361	6178	1935	9474

Note: According to the current Provisions for Drug Registration, an administrative review and approval decision shall be made within twenty (20) working days.



2. Acceptance of RAs subject to review and approval

In 2021, 7,051 RAs for review and approval were accepted. According to statistics by drug type, 430 RAs were for TCMs, up 40.07% YoY. 4,800 RAs were for chemical drugs, up 17.50% YoY, accounting for 68.08% of all RAs up for review and approval. Additionally, 1,821 RAs were for biological products, up 39.75% YoY.

According to the statistics by RA category, 2,483 RAs were for clinical trial applications, up 53.46% YoY; 908 RAs for consistency evaluation; 3,283 for supplementary applications, up 16.13% YoY; and 3,377 for re-registration for drugs manufactured outside China, up 14.94% YoY.

3. Acceptance of RAs subject to direct approval

2,423 RAs subject to direct approval were accepted, according to the statistics by drug type, covering 931 RAs for TCMs, 1,378 RAs for chemical drugs and 114 RAs for biological products. According to the statistics by RA category, 2,002 RAs were supplementary applications, and 421 RAs were for temporary import.

Chapter 2: RA review and approval

(1) Overview

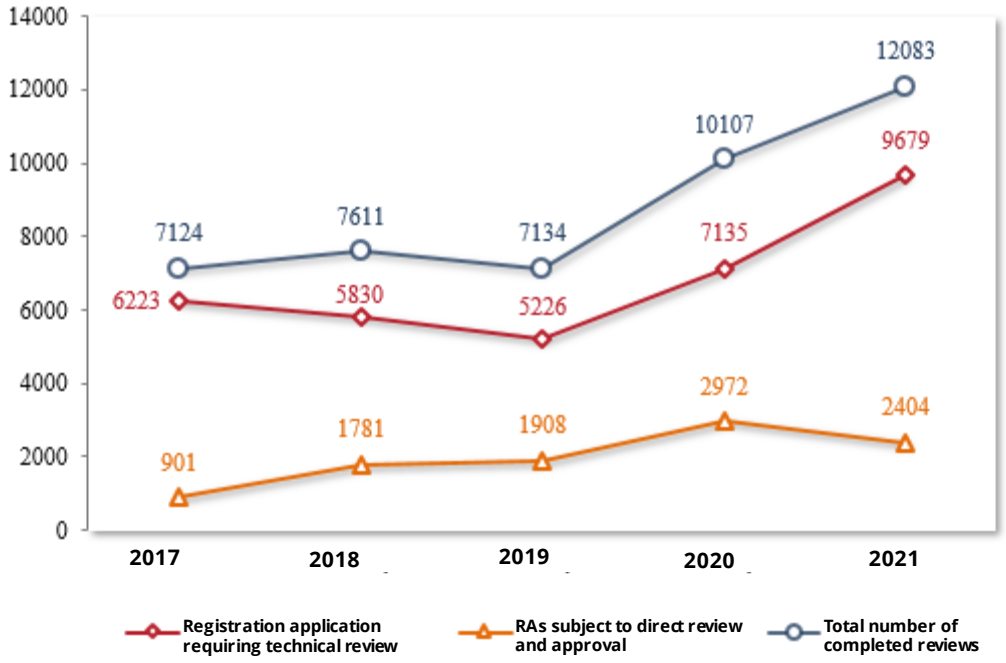
1. Annual review and approval status

12,083 RAs[16] were completed[15] in 2021, up 19.55% YoY.

A total of 9,679 RAs requiring technical review were reviewed and completed, up 35.66% YoY. These included 2,632 RAs for technical review, 7,039 RAs for review and approval and eight RAs for drug-device combinations.

2,404 RAs subject to direct review and approval were reviewed and completed. See Figure 15 for the completed RA reviews in 2017-2021.

Figure 15: Completed reviews of RAs in 2017-2021



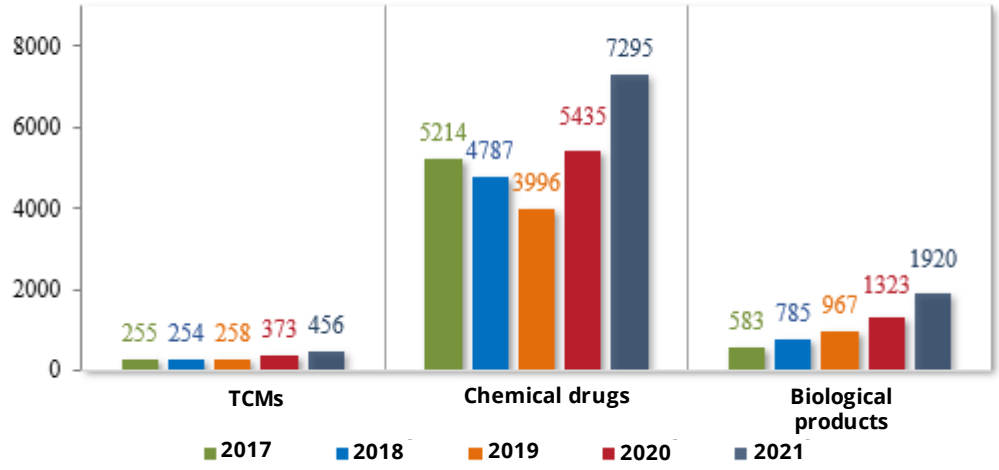
As of the end of 2021, 5,652 RAs were under review and approval. 1,353 RAs were pending for the applicant's supplementary dossiers. According to Announcement No.56, 494 RAs for active pharmaceutical ingredients (APIs) were reviewed and completed in 2021. 1,302 RAs for APIs were also under review and approval as of the end of the year. 582 RAs for APIs were pending for the Applicant's supplementary dossiers as well.

2. Review of various types of RAs requiring technical review

Counted by drug type, 9,671 RAs[17] requiring technical review were reviewed and completed, including 456 RAs for TCMs, up 22.25% YoY; 7,295 RAs for chemical drugs, up 34.22% YoY, accounting for 75.43% of all reviewed RAs requiring technical review; and 1,920 RAs for biological products, up 45.12% YoY.

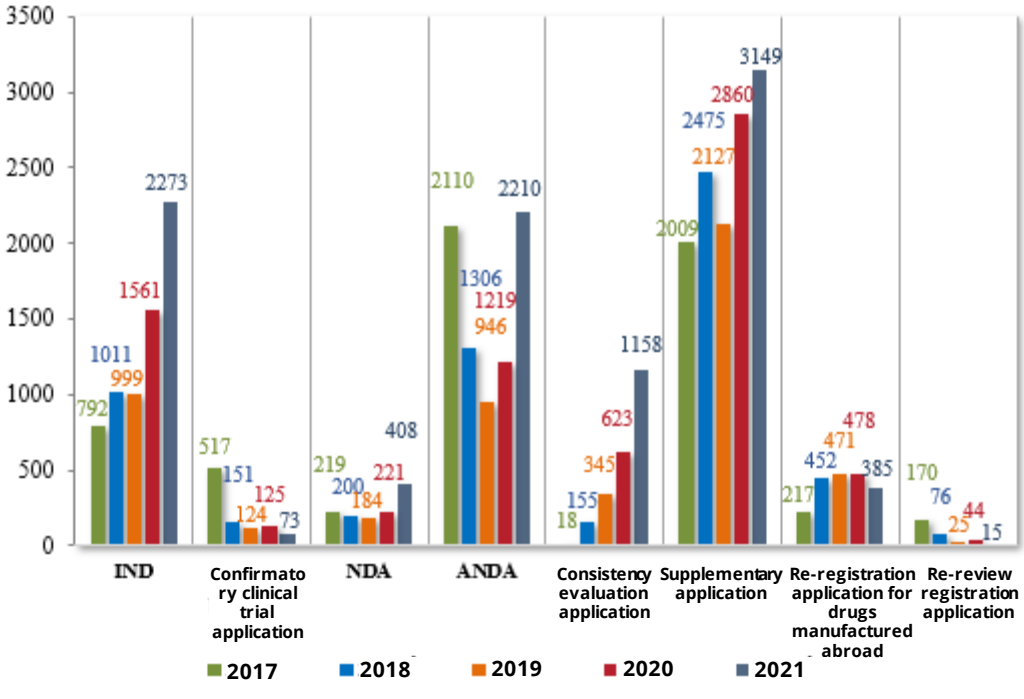
See Figure 16 for the review of RAs for various classes of drugs requiring technical review in 2017-2021.

Figure 16: Review of RAs for various classes of drugs requiring technical review in 2017-2021



According to RA figures, there were 2,273 IND applications, up 45.61% YoY; 408 NDA applications, up 84.62% YoY; 2210 ANDAs, up 81.30% YoY; 1158 consistency evaluation applications, up 85.87% YoY; and 3149 supplementary applications, up 10.10% YoY. See Figure 17 for the review of various categories of RAs requiring technical review in 2017-2021.

Figure 17: Review of various categories of RAs requiring technical review in 2017-2021



3. Approval/Recommended Approval

2,108 INDs were approved, up 46.90% YoY; 323 NDAs were recommended for approval (see Annex 1), up 55.29% YoY; 1,003 ANDAs were recommended for approval, up 9.26% YoY; 1,080 RAs for consistency evaluation were approved, up 87.18% YoY. See Table 5 for the approval/recommended approval of various categories of RAs.

Table 5: Approval/recommended approval of various categories of RAs.

RA Category	Approval/recommended approval
IND	2108
Confirmatory clinical trial application	59
NDA	323
ANDA	1003
Consistency evaluation application	1080
Supplementary application	2751
Re-registration application for drugs manufactured abroad	372
RAs subject to direct review and approval	2362
Re-review registration application	1
Total	10059

A total of 76 varieties of brand -name drugs[18] manufactured outside China (including varieties with newly-added indications, see Annex 2) were recommended for approval.

Among the 81 varieties[19] in the List of Overseas New Drugs Urgently Needed in Clinical Settings, RAs had been submitted for 54 varieties; 51 varieties were approved for marketing in China; and the rate of review completion as per review time limit (hereinafter referred to as the "rate of review completion as per time limit") was 100%. See Annex 3 for the review and approval of Overseas New Drugs Urgently Needed in Clinical Settings.

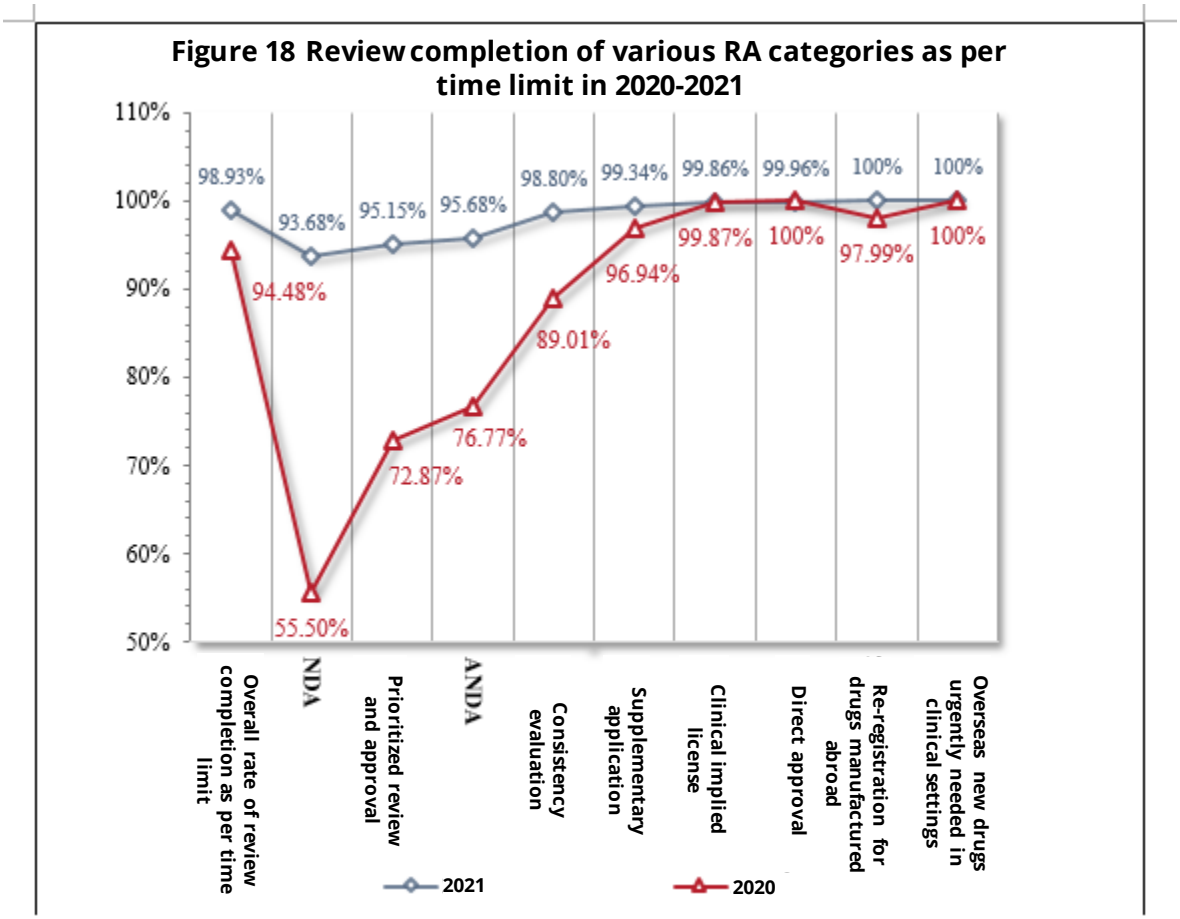
4. Review completion of various RA categories according to time limit

The CDE continued to optimize its review process in 2021. It strictly managed the review time limit, accelerated its speed and enhanced project supervision, reaching an annual rate of review completion of 98.93%. NDAs, ANDAs and RAs included in the Priority Review and Approval Procedure ("PRAP") saw a rate of review completion exceeding 90%, a new record high. See Table 6 for details on review completion of various RA categories as per time limit in 2021. See Figure 18 for details about review completion of various RA categories as per time limit in 2020-2021.

Table 6: Review completion of various RA categories as per time limit in 2021

RA category	Rate of review completion as per time limit
Overseas new drugs urgently needed in clinical settings	100.00%
Re-registration for drugs manufactured abroad	100.00%
Direct approval	99.96%
Clinical implied license	99.86%
Supplementary application	99.34%
Consistency evaluation	98.80%
ANDA	95.68%
Priority review and approval	95.15%
NDA	93.68%
Overall rate of review completion as per time limit	98.93%

Figure 18 Review completion of various RA categories as per time limit in 2020-2021



(2) Completion of review for innovative drug RAs

1. Overview

The CDE reviewed and completed 1,744 RAs (involving 943 varieties) for innovative drugs[20], up 67.85% YoY.

According to drug type, 55 RAs (involving 55 varieties) were for innovative TCMs, up 52.78% YoY. 1085 RAs (involving 484 varieties) were or innovative chemical drugs, up 45.44% YoY. 604 RAs (involving 404 varieties) were for innovative biological products, up 135.02% YoY.

1663 (involving 885 varieties) were for INDs, up 67.14% YoY. 81 (involving 58 varieties) were for NDAs, up 84.09% YoY.

2. Approval/Recommended Approval

1,628 RAs (involving 878 varieties) for innovative drugs were approved/recommended for approval, up 67.32% YoY.

39 RAs (involving 39 varieties) were for innovative TCMs, up 39.29% YoY. 1029 RAs (involving 463 varieties) were for innovative chemical drugs, up 44.32% YoY. 560 RAs (involving 376 varieties) were for innovative biological products, up 141.38% YoY.

1,559 (involving 831 varieties) were for INDs, up 65.32% YoY. 69 were for NDAs (involving 47 varieties, see Annex 4), up 130.00% YoY.

1,261 RAs (involving 684 varieties) were for innovative drugs manufactured in China, up 60.84% YoY. 367 RAs (involving 194 varieties) were for innovative drugs manufactured outside China, up 94.18% YoY. See Table 7 for the number of approvals/recommended approvals of RAs for various innovative drugs in 2021. See Table 8 for the number of approvals/recommended approvals of RAs for various innovative drugs manufactured in and outside China in 2021. See Figure 19 for the number of approvals of INDs for innovative drugs in 2017-2021. See Figure 20 for the number of recommended approvals of NDAs for innovative drugs in 2017-2021.

Table 7: Number of approvals/recommended approvals of RAs for various innovative drugs in 2021

RA category	Innovative TCMs		Innovative chemical drugs		Innovative biological products		Total	
	RA (N)	Variety (N)	RA (N)	Variety (N)	RA (N)	Variety (N)	RA (N)	Variety (N)
IND	28	28	994	439	537	364	1559	831
NDA	11	11	35	24	23	12	69	47
Total	39	39	1029	463	560	376	1628	878

Table 8: Number of approvals/recommended approvals of RAs for innovative drugs manufactured in and outside China in 2021

RA Category	Domestic production		Overseas production		Total	
	RA (N)	Variety (N)	RA (N)	Variety (N)	RA (N)	Variety (N)
IND	1194	639	365	192	1559	831
NDA	67	45	2	2	69	47
Total	1261	684	367	194	1628	878

Figure 19: Number of approvals of INDs for innovative drugs in 2017-2021

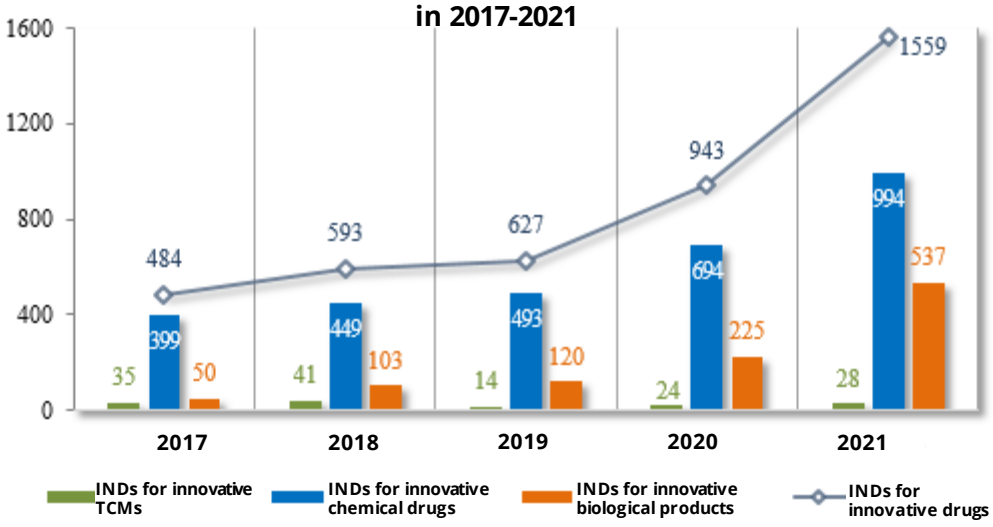
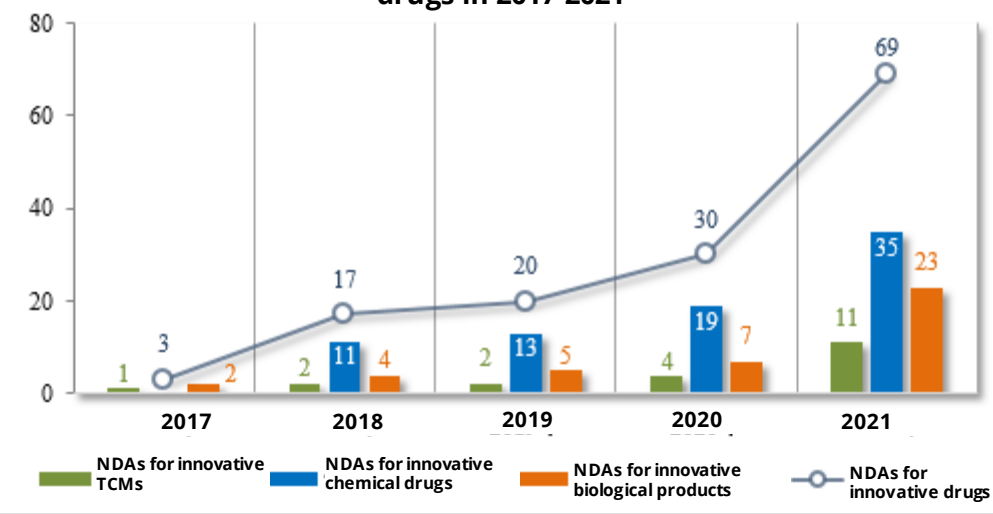


Figure 20: Number of recommended approvals of NDAs for innovative drugs in 2017-2021

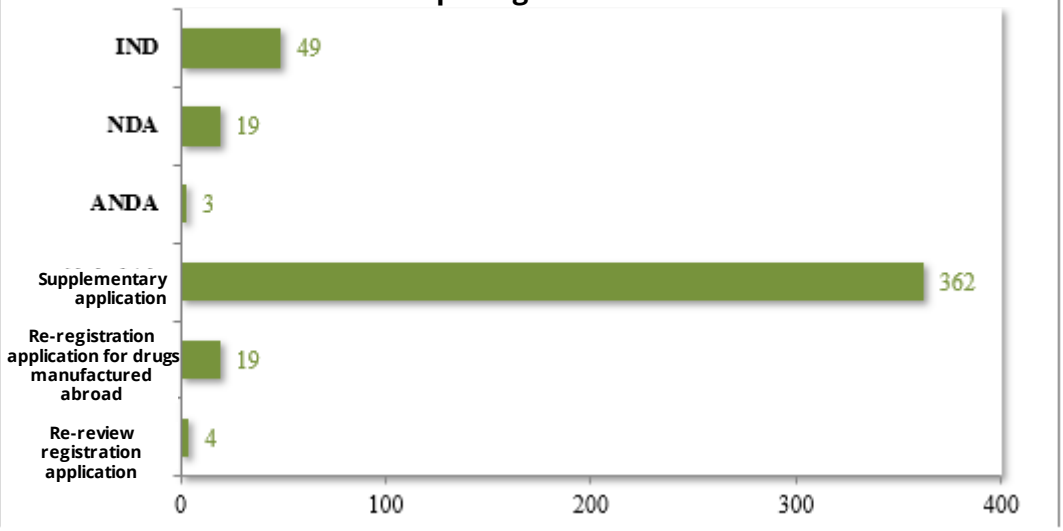


(3) Review completion of RAs for TCMs requiring technical review

1. Overview

456 RAs for TCMs requiring technical review were reviewed and completed in 2021, up 22.25% YoY. 49 RAs were INDs, up 32.43% YoY. 19 were NDAs, up 216.67% YoY. Three RAs were ANDAs. See Figure 21 for the review completion of various RA categories for TCMs requiring technical review.

Figure 21 Review completion of various RA categories for TCMs requiring technical review in 2021



2. Approval/Recommended Approval

Among the TCM INDs reviewed in 2021, 34 were approved and nine were not approved. Among TCM NDAs reviewed, 14 were recommended for approval, and three were recommended for rejection. See Figure 9 for the review completion of RAs for TCMs requiring technical review in 2021.

Table 9 Review completion of RAs for TCMs requiring technical review in 2021

RA category	Number of review completion			
	Approval/recommended approval	Rejection/recommended rejection	Other	Total
IND	34	9	6	49
NDA	14	3	2	19
ANDA	0	1	2	3
Supplementary application	291	7	64	362
Re-registration application for drugs manufactured abroad	19	0	0	19
Re-review RA	0	3	1	4
Total	358	23	75	456

Note: "Other" refers to the circumstances in which review and approval were terminated due to applicants' failure to pay fees, application withdrawal and other reasons.

34 TCM INDs were approved in 2021, up 21.43% YoY, including 28 INDs (involving 28 varieties) for innovative TCMs, up 16.67% YoY. 14 TCM NDAs were recommended for approval, up 250.00% YoY, a five-year high. This included 11 NDAs (involving 11 varieties) for innovative TCMs, up 175.00% YoY. See Figure 22 for the number of IND approvals for TCMs and INDs for innovative TCMs in 2017-2021. See Figure 23 for the number of recommended NDA approvals for TCMs and NDAs for innovative TCMs in 2017-2021.

Figure 22 Number of IND approvals for TCMs and INDs for innovative TCMs in 2017-2021

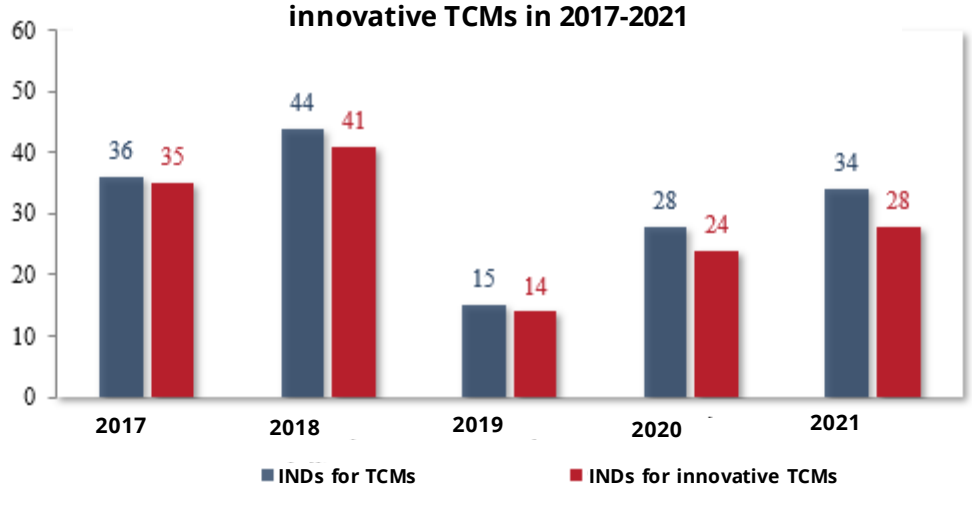
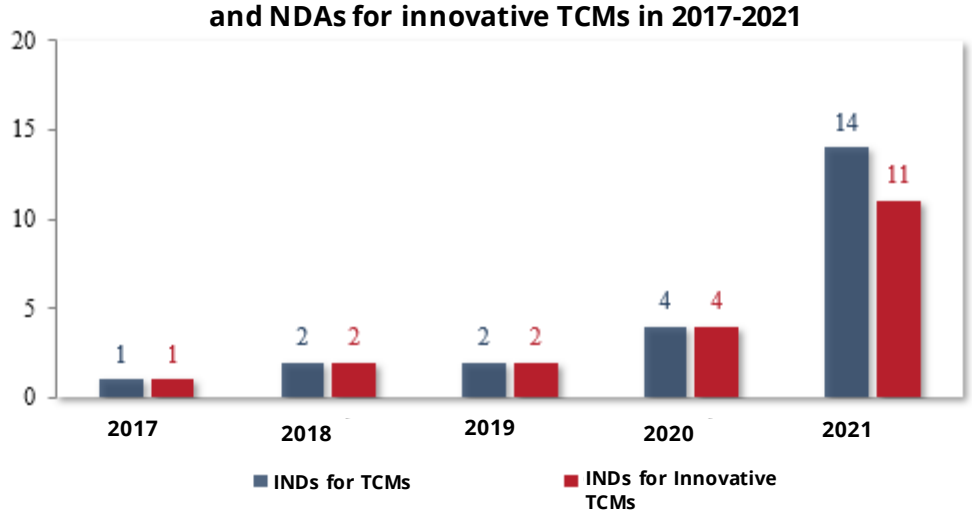
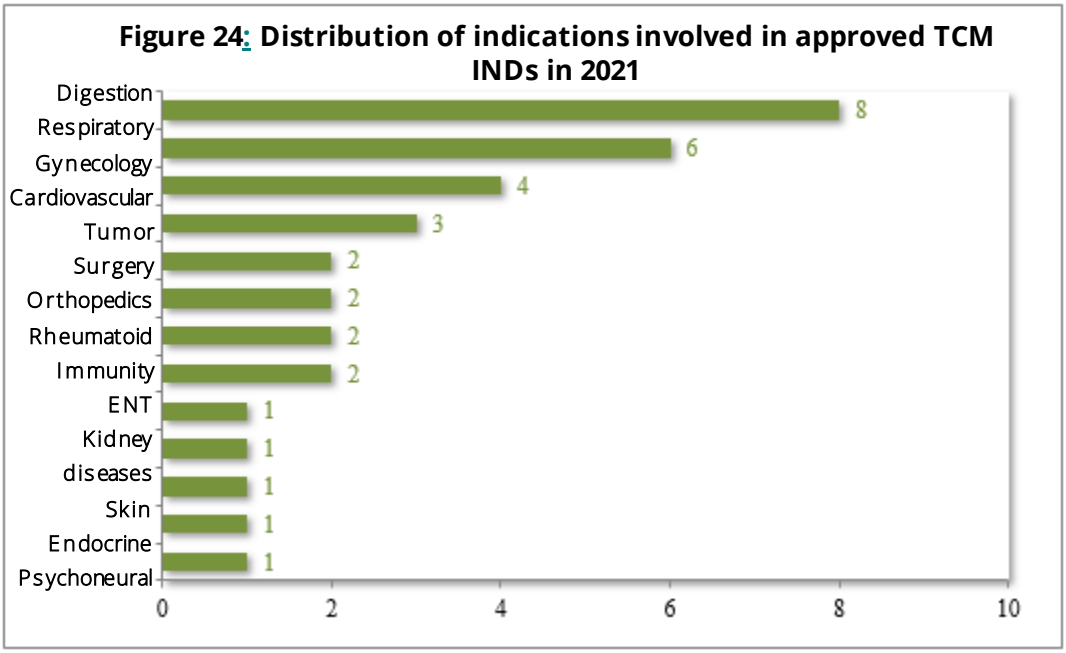


Figure 23: Number of recommended NDA approvals for TCMs and NDAs for innovative TCMs in 2017-2021

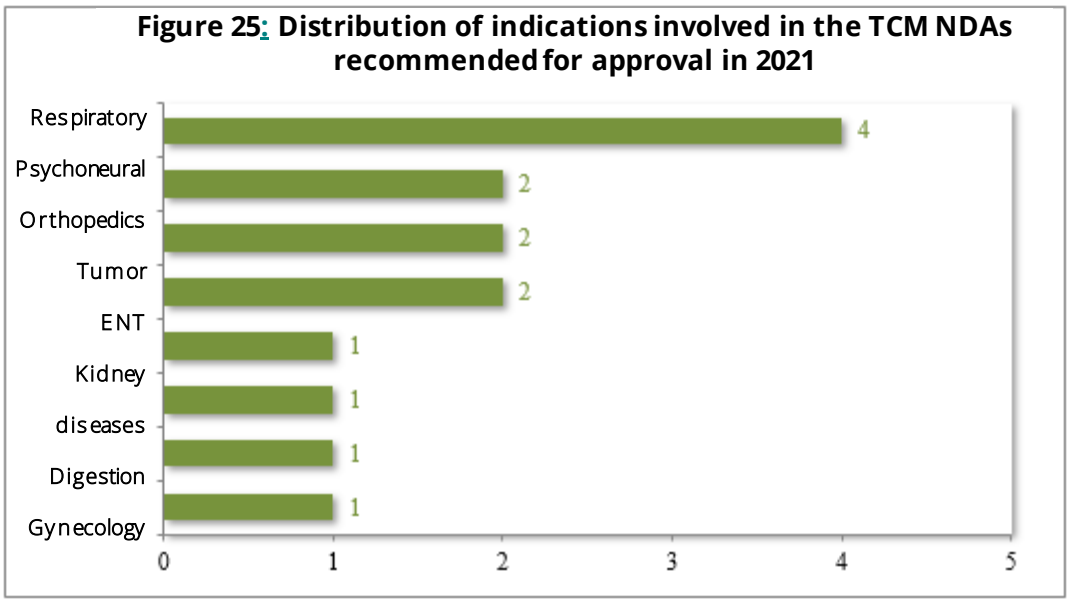


A total of 34 TCM INDs were approved. These involved 13 indications, covering eight for digestion, six for respiration and four for gynecology, accounting for 52.94% of all TCM INDs. See Figure 24 for the distribution of indications involved in approved TCM INDs.



Among the 14 TCM NDAs recommended for approval, the majority covered respiratory, oncological, psychoneural and orthopedic indications, all of which together accounted for 71.43% of the total.

See Figure 25 for the distribution of indications involved in the TCM NDAs recommended for approval in 2021.

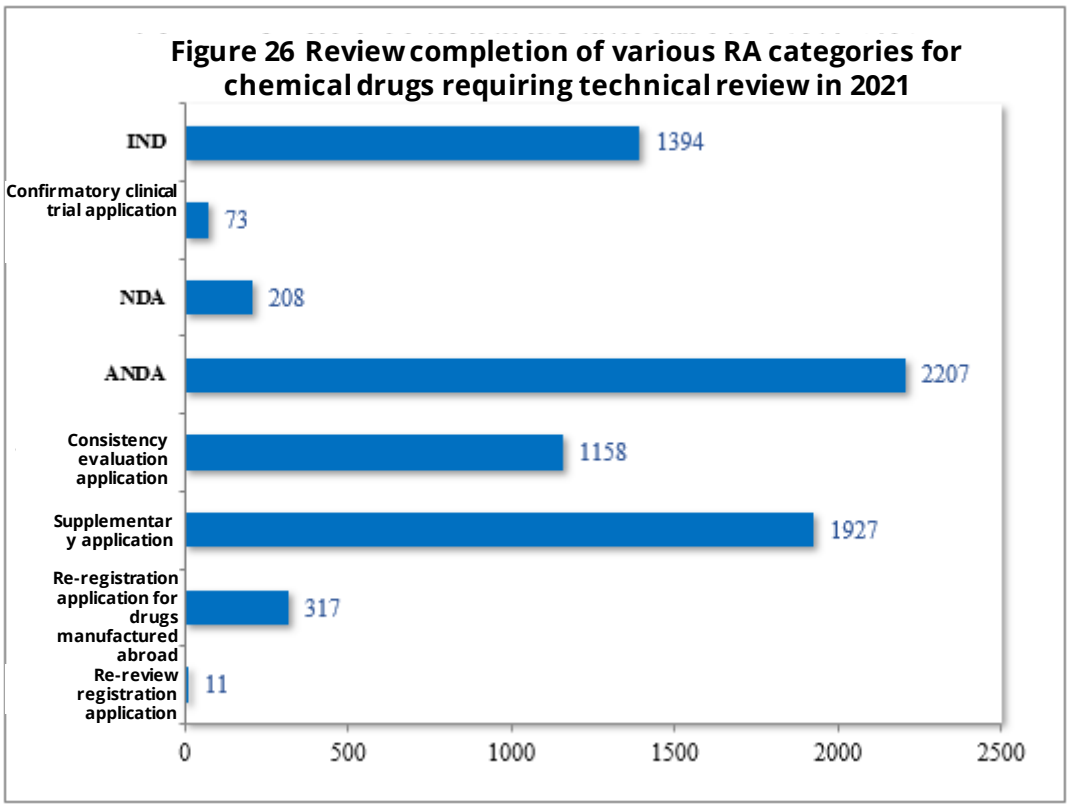


(4) RA review completion for chemical drugs requiring technical review

1. Overview

In 2021, 7,295 RAs for chemical drugs requiring technical review were reviewed and completed. 1,467 RAs for clinical trial applications for chemical drugs, up 35.21% YoY. 208 were NDAs for chemical drugs, up 67.74% YoY. 2,207 were ANDAs for chemical drugs, up 81.50% YoY. 1,158 were for consistency evaluation of chemical drugs, up 85.87% YoY. See Figure 26 for the review completion of various RA categories for chemical drugs requiring technical review in 2021.

Figure 26 Review completion of various RA categories for chemical drugs requiring technical review in 2021



2. Approval/Recommended Approval

Among the reviewed INDs for chemical drugs, 1,310 were approved and 26 were not approved. 160 NDAs for chemical drugs were recommended for approval. Eight were not recommended for approval. 1,003 ANDAs for chemical drugs were recommended for approval, and 394 were not recommended for approval. See Table 10 for the review completion of RAs for chemical drugs requiring technical review in 2021.

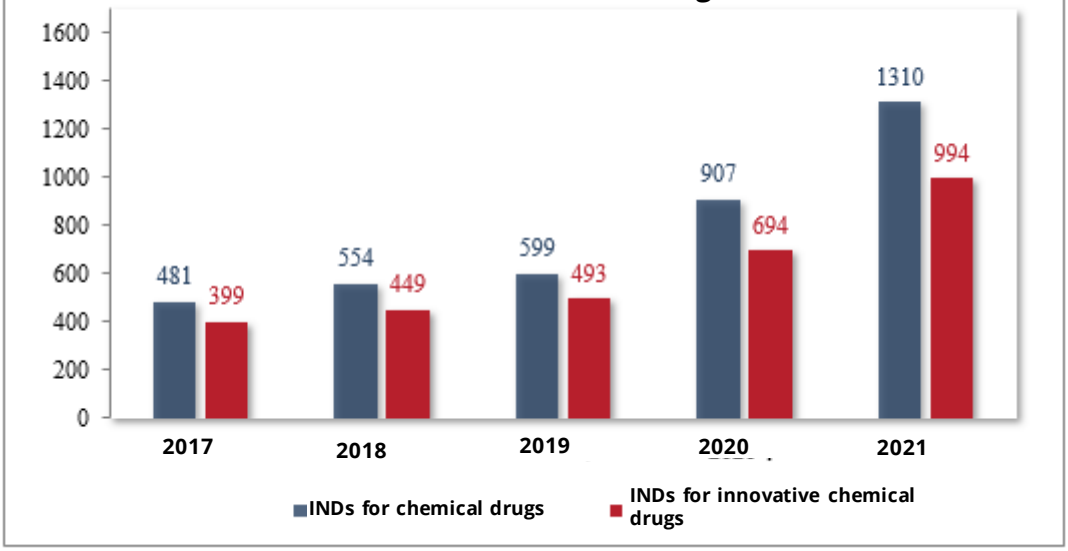
Table 10 Review completion of RAs for chemical drugs requiring technical review in 2021

RA category	Number of review completion			
	Approval/recommended approval	Rejection/recommended rejection	Other	Total
IND	1310	26	58	1394
Confirmatory clinical trial application	59	1	13	73
NDA	160	8	40	208
ANDA	1003	394	810	2207
Consistency evaluation application	1080	16	62	1158
Supplementary application	1673	23	231	1927
Re-registration application for drugs manufactured abroad	305	0	12	317
Re-review RA	1	7	3	11
Total	5591	475	1229	7295

Note: "Other" refers to the circumstances in which review and approval were terminated due to applicants' failure to pay fees, application withdrawal and other reasons.

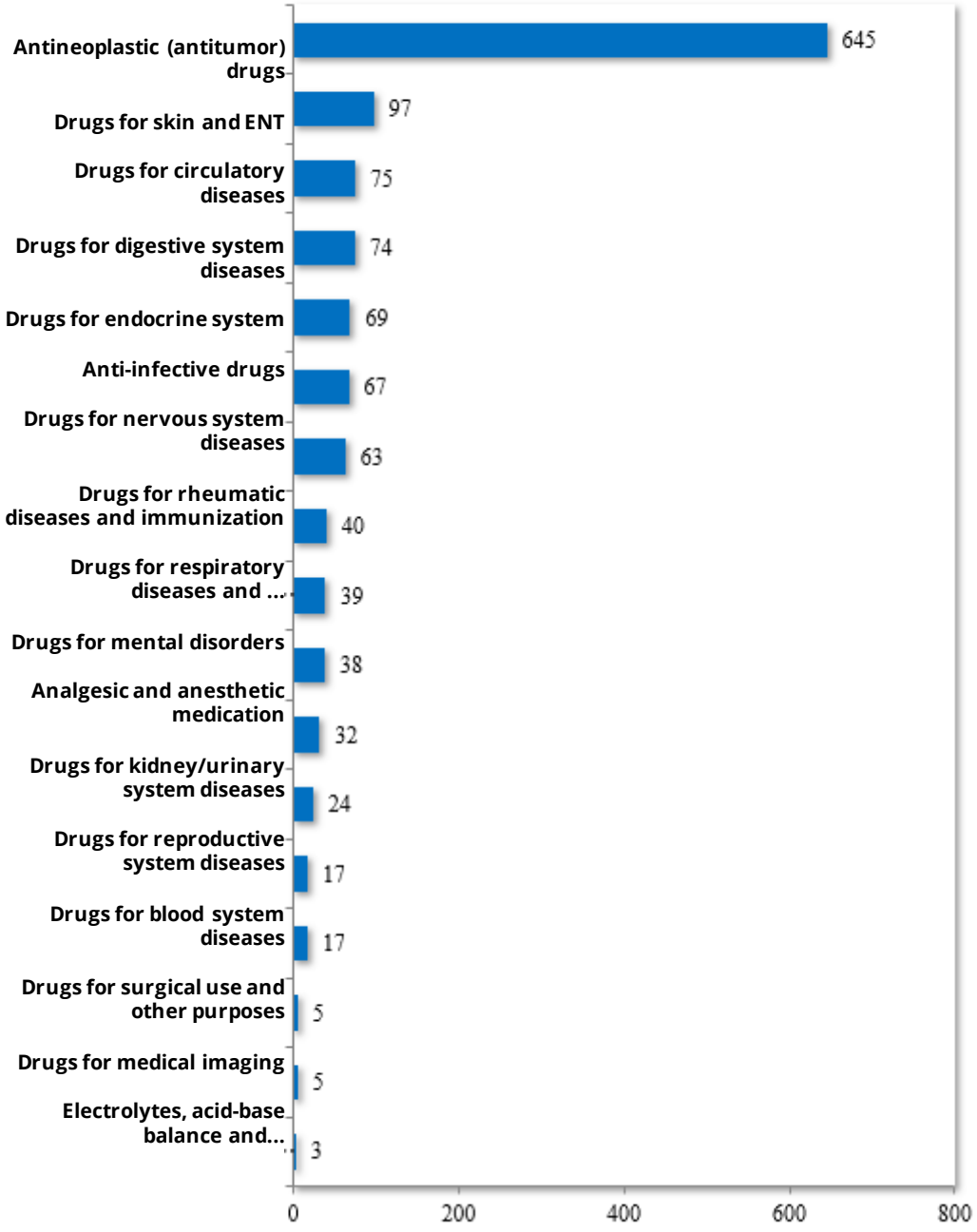
1,310 INDs for chemical drugs were approved in 2021, up 44.43% YoY, including 994 INDs (involving 439 varieties) for innovative chemical drugs, up 43.23% YoY. See Figure 27 for the number of approved INDs for chemical drugs and INDs for innovative chemical drugs in 2017-2021.

Figure 27 Number of approved INDs for chemical drugs and INDs for innovative chemical drugs in 2017-2021



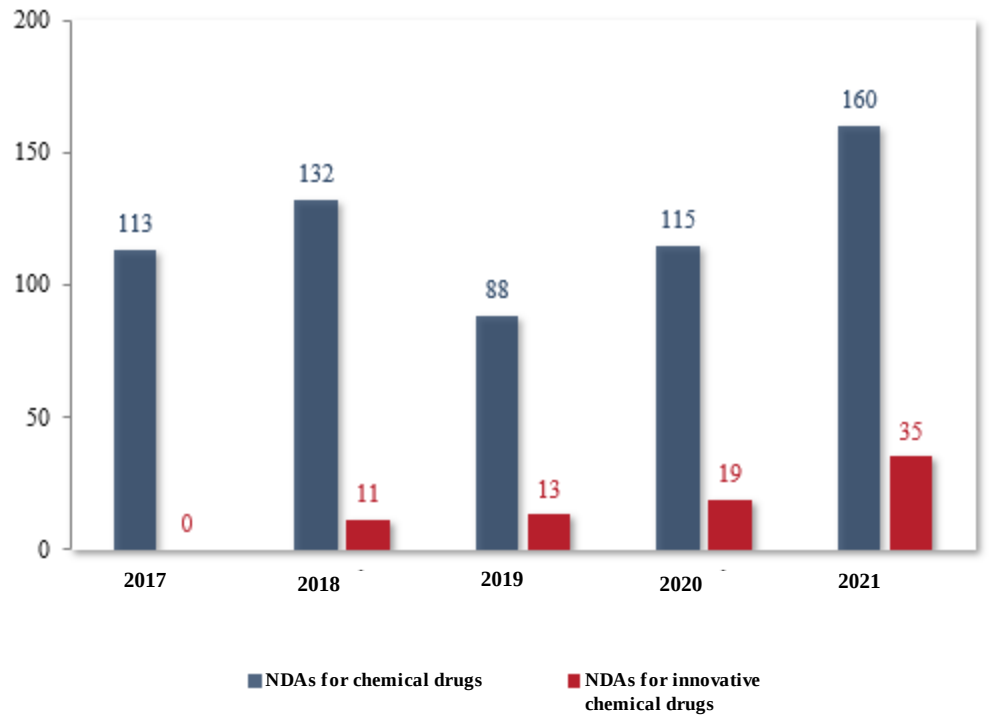
Among the approved 1,310 INDs for chemical drugs, most covered anti-tumor drugs as well as drugs for skin and ENT, circulatory diseases, digestive system diseases, the endocrine system, nervous system diseases and anti-infectives, all of which accounted for 83.21% of all approved INDs for chemical drugs. See Figure 28 for the distribution of indications involved in the approved INDs for chemical drugs in 2021.

Figure 28: Distribution of indications involved in approved INDs for chemical drugs in 2021



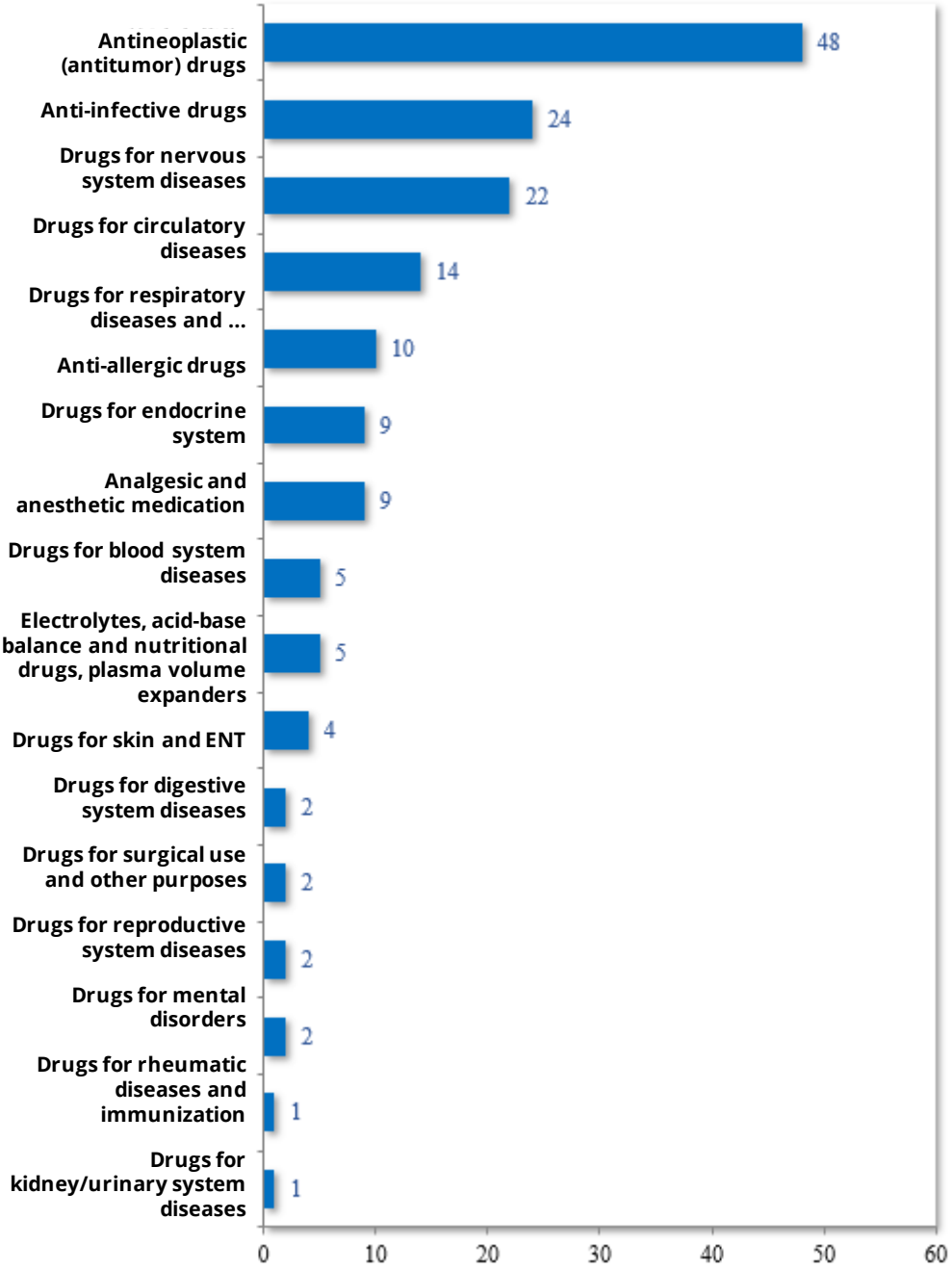
A total of 160 NDAs for chemical drugs were recommended for approval, up 39.13% YoY, including 35 NDAs (involving 24 varieties) for innovative chemical drugs, up 84.21% YoY. 1,003 ANDAs for chemical drugs were recommended for approval, up 9.26% YoY. See Figure 29 for the number of the recommended approvals of NDAs for chemical drugs and NDAs for innovative chemical drugs in 2017-2021.

Figure 29: Number of the recommended approvals of NDAs for chemical drugs and NDAs for innovative chemical drugs in 2017-2021



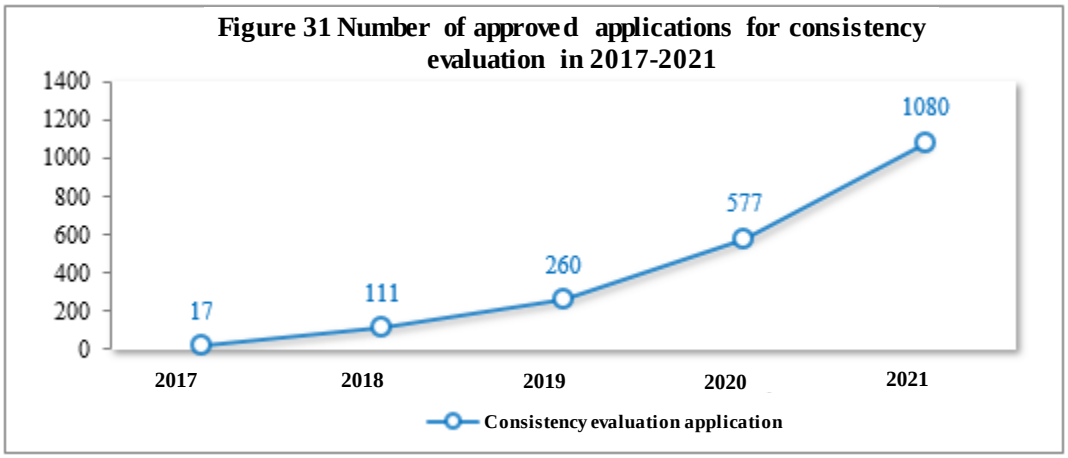
Among the 160 NDAs for chemical drugs recommended for approval, most covered anti-tumor drugs, anti-allergics and anti-infectives as well as drugs for nervous system diseases, circulatory system diseases, respiratory diseases, all of which accounted for 73.75% of all approved chemical drug NDAs. See Figure 30 for the distribution of indications involved in the NDAs for chemical drugs recommended for approval in 2021.

Figure 30: Distribution of indications involved in the NDAs for chemical drugs recommended for approval in 2021



A total of 1,158 applications for consistency evaluation were reviewed and completed. 1,080 were approved. 391 were for consistency evaluation of oral solid preparations, 689 were for injections. See Figure 31 for the number of approved applications for consistency evaluation in 2017-2021. See Annex 5 for the varieties approved for consistency evaluation in 2021.

Figure 31 Number of approved applications for consistency evaluation in 2017-2021

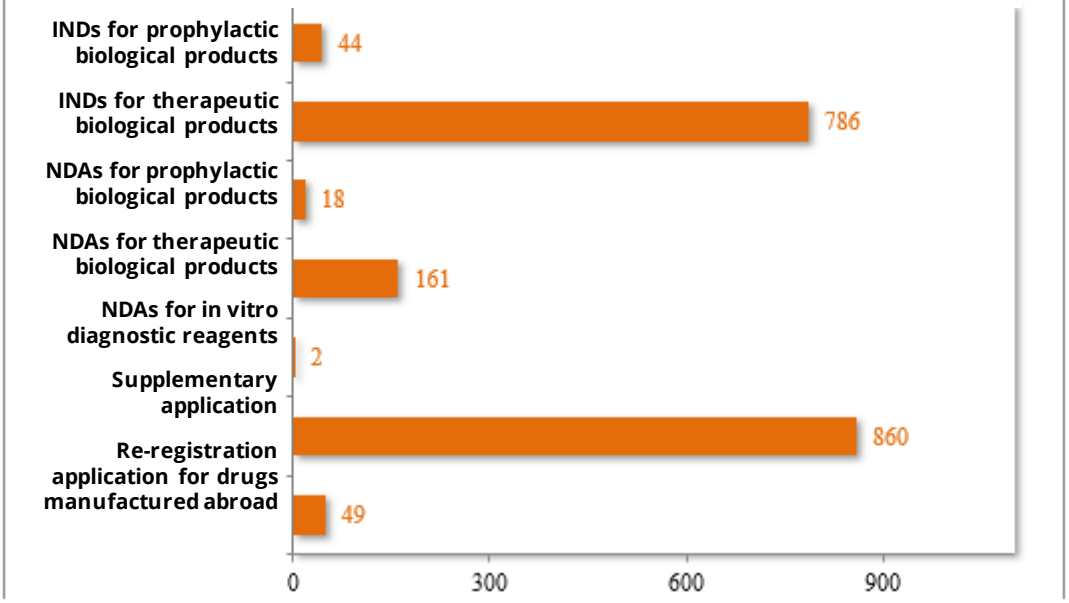


(5) Review completion of RAs for biological products requiring technical review

1. Overview

1,920 RAs for biological products requiring technical review were reviewed and completed, including 234 for prophylactic biological products, 1,676 for therapeutic biological products, and 10 for in vitro diagnostic (IVD) reagents. 830 were for INDs, up 47.16% YoY. 181 were for NDAs, up 98.90% YoY. 860 were for supplementary applications. 49 were for re-registration applications for drugs manufactured abroad. See Figure 32 for the review completion of various RA categories for biological products requiring technical review.

Figure 32: Review completion of various categories of RAs for biological products requiring technical review in 2021



2. Approval/Recommended Approval

764 INDs for biological products were approved, and 34 were not approved. 149 NDAs were recommended for approval, and four were recommended for rejection. See Figure 11 for the review completion of RAs for biological products requiring technical review in 2021.

Figure 11: Review completion of RAs for biological products requiring technical review in 2021

RA category	Number of review completion			
	Approval/recommended approval	Rejection/recommended rejection	Other	Total
INDs for prophylactic biological products	44	0	0	44
INDs for therapeutic biological products	720	34	32	786
NDAs for prophylactic biological products	15	0	3	18
NDAs for therapeutic biological products	134	2	25	161
NDAs for in vitro diagnostic reagents	0	2	0	2
Supplementary application	787	6	67	860
Re-registration application for drugs manufactured abroad	48	0	1	49
Total	1748	44	128	1920

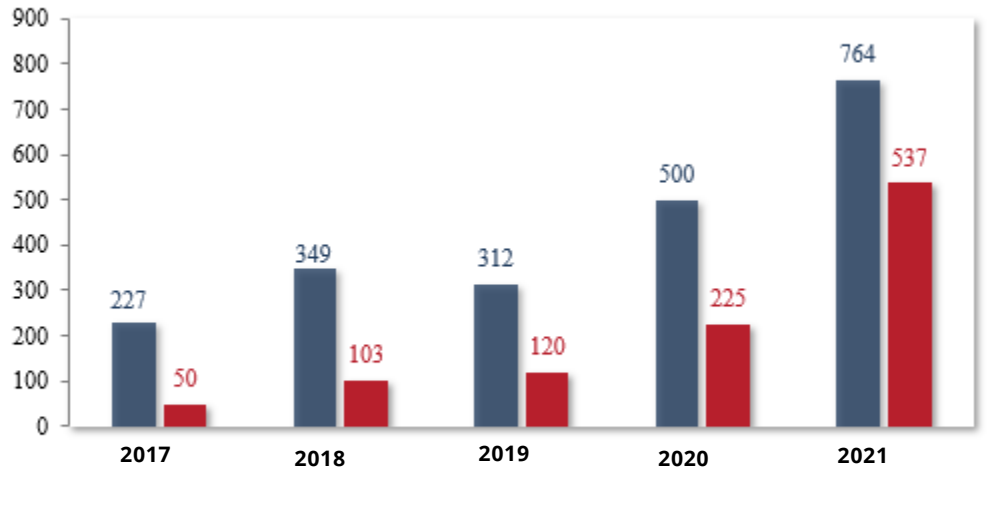
Note: "Other" refers to the circumstances in which review and approval were terminated due to applicants' failure to pay fees, application withdrawal and other reasons.

A total of 764 INDs for biological products were approved in 2021, up 52.80% YoY, including 537 INDs (involving 364 varieties) for innovative biological products, up 138.67% YoY. 44 INDs were for prophylactic biological products, up 131.58% YoY, including 24 INDs (involving 16 varieties) for innovative prophylactic biological products, up 800% YoY. 720 INDs were for therapeutic biological products, up 49.69% YoY, including 513 INDs (involving 348 varieties) for innovative therapeutic biological products, up 131.08% YoY. See Table 12 for the number of the approved INDs for biological and innovative biological products in 2021. See Figure 33 for the number of the approved INDs for biological and innovative biological products in 2017-2021.

Table 12: Number of the approved INDs for biological and innovative biological products in 2021

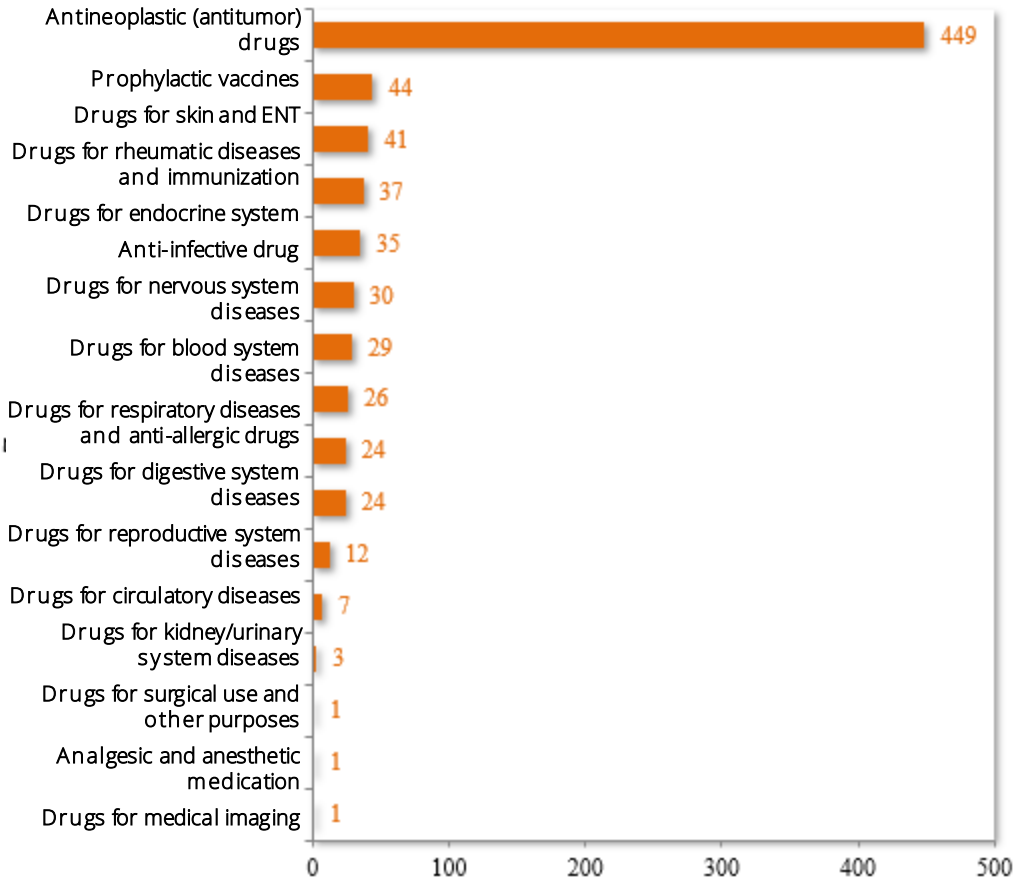
Drug type	IND	
	Total quantity	Innovative drugs
Prophylactic biological products	44	24
Therapeutic biological products	720	513
Total	764	537

Figure 33: Number of the approved INDs for biological and innovative biological products in 2017-2021



Among the approved 764 INDs for biological products, most were for anti-tumor drugs, accounting for 58.77%. See Figure 34 for the distribution of indications.

Figure 34 Distribution of indications of INDs for biological products approved in 2021



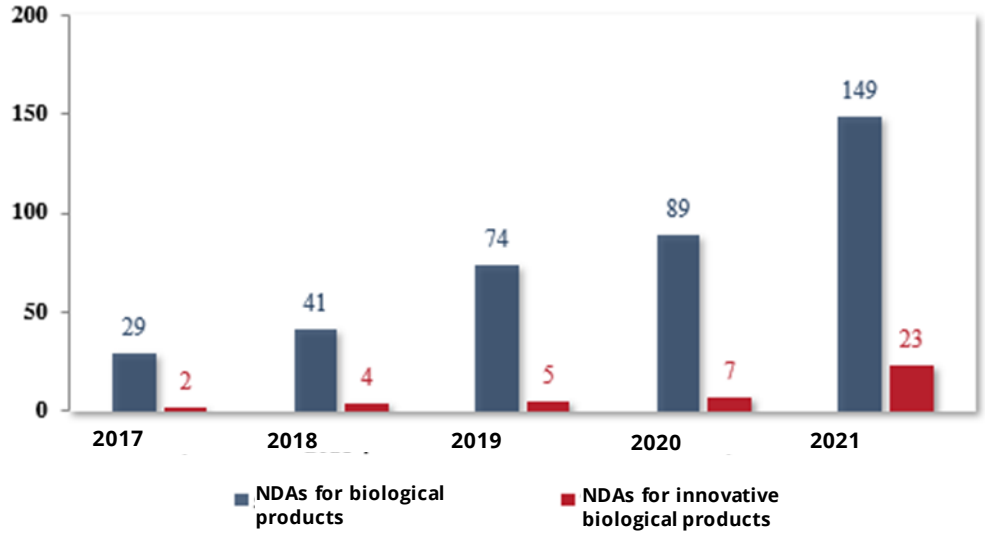
Note: Prophylactic vaccines are counted as a broad category and are not subdivided into indications.

A total of 149 NDAs for biological products were recommended for approval, up 67.42% YoY, including 23 NDAs (involving 12 varieties) for innovative biological products, up 228.57% YoY. 15 NDAs were for prophylactic biological products, up 114.29% YoY, including six NDAs (involving 3 varieties) for innovative prophylactic biological products. 134 NDAs were for therapeutic biological products, up 65.43% YoY, including 17 NDAs (involving nine varieties) for innovative therapeutic biological products, up 142.86% YoY. See Table 13 for the number of the recommended approvals of NDAs for biological and innovative biological products in 2021. See Figure 35 for the number of the recommended approvals of NDAs for biological products and NDAs for innovative biological products in 2017-2021.

Table 13: Number of recommended approvals of NDAs for biological and innovative biological products in 2021

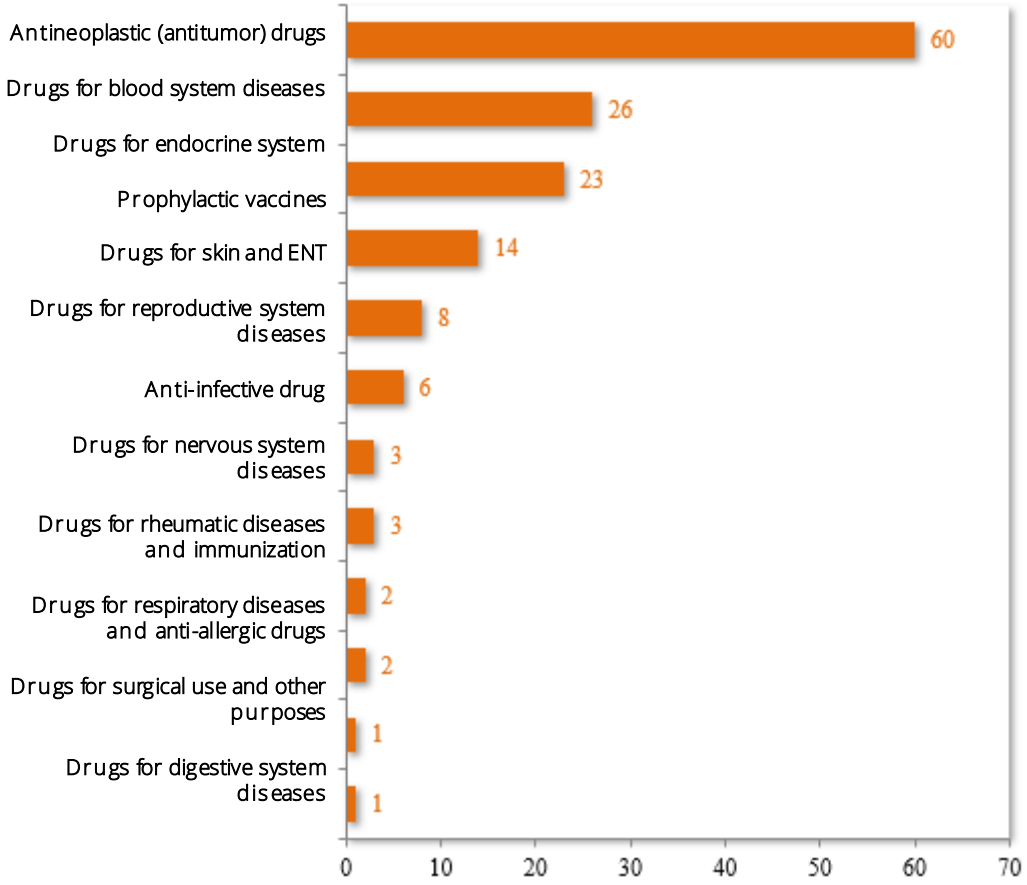
Drug type	NDA	
	Total quantity	Innovative drugs
Prophylactic biological products	15	6
Therapeutic biological products	134	17
In vitro diagnostic reagents	0	—
Total	149	23

Figure 35 Number of the recommended approvals of NDAs for biological and innovative biological products in 2017-2021



Among the 149 NDAs for biological products recommended for approval, the majority covered anti-tumor drugs as well as drugs for blood system diseases, endocrine system diseases and vaccines, accounting for 82.55% of all approved NDAs for biological products. See Figure 36 for the distribution of indications involved in NDAs for biological products recommended for approval.

Figure 36: Distribution of indications involved in NDAs for biological products recommended for approval in 2021



Note: Prophylactic vaccines are counted as a broad category and are not subdivided into indications.

(6) Review completion of RAs for administrative review and approval

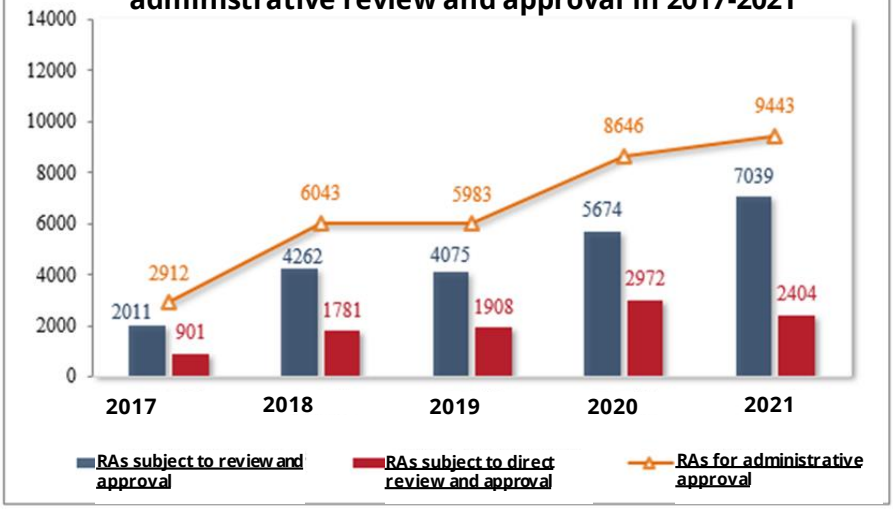
1. Overview

In 2021, 9443 RAs subject to administrative review and approval were reviewed and completed, up 9.22% YoY. 7,039 of them[21] were subject to review and approval process, up 24.06% YoY. 2,404[22] were subject to direct review and approval process. See Table 14 for the review completion of RAs for TCMs, chemical drugs and biological products subject to administrative review and approval of in 2021. See Figure 37 for the review completion of RAs requiring administrative review and approval in 2017-2021.

Table 14: Review completion of RAs for TCMs, chemical drugs and biological products subject to administrative review and approval ofin 2021

RA category		TCM	Chemical drugs	Biological products	Total
RAs subject to review and approval	Clinical trial application	49	1467	830	2346
	Consistency evaluation application	0	1158	0	1158
	Supplementary application	362	1927	860	3149
	Re-registration application for drugs manufactured abroad	19	317	49	385
	Re-review RA	1	0	0	1
	Total	431	4869	1739	7039
RAs subject to direct review and approval	Supplementary applications requiring no technical review	897	1028	57	1982
	RA for temporary import	1	344	77	422
	Total	898	1372	134	2404
Total		1329	6241	1873	9443

Figure 37: Review completion of RAs subject to administrative review and approval in 2017-2021



2. Review completion of RAs subject to review and approval

Among the 7,039 RAs subject to review and approval, 431 were for TCMs, up 20.73% YoY. 4,869 were for chemical drugs, up 19.16% YoY, accounting for 69.17% of the total. 1,739 were for biological products, up 41.27% YoY. 2,346 were for clinical trial applications, up 39.15% YoY. 1,158 were for consistency evaluations, up 85.87% YoY. 3,149 were for supplementary applications, up 10.10% YoY. 385 were for re-registration applications for drugs manufactured abroad. One was for a re-review registration.

3. Review completion of RAs subject to direct review and approval

Among the 2,404 RAs subject to direct review and approval, 898 were for TCMs, 1,372 were for chemical drugs and 134 were for biological products. 1982 were for supplementary applications, and 422 RAs were for temporary import.

(7) Verification of drug registration

8,526 RAs were for compliance review. 617 were for NDAs. 2,375 were for ANDAs. 1,687 were RAs for consistency evaluation, 2,423 were Ras for supplementary applications and 1,424 Ras were for APIs.

The CDE initiated 1,067 registration verification tasks[23] based on risks, including 684 on production sites (hereinafter referred to as "production site") and 383 on drug clinical trial sites (hereinafter referred to as "clinical trial sites"). 285 tasks were for NDA verification, 619 for ANDA verification, 101 for consistency evaluation applications and 62 were for supplementary applications. See Table 15 for registration verification tasks initiated based on risks.

Additionally, 34 on-site/causal inspections were initiated for COVID-19 therapeutic drugs vaccines.

The NMPA's Center for Food and Drug Inspection has returned a total of 1,165 CDE inspection reports.

Table 15: Registration verification tasks initiated based on risks

Type of Verification Task	High risk		Medium risk		Low risk	
	Manufacture site	Clinical trial sites	Manufacture site	Clinical trial sites	Manufacture site	Clinical trial sites
NDA	104	181	0	0	0	0
ANDA	407	93	29	25	52	13
Consistency evaluation application	8	34	31	13	13	2
Supplementary application	6	20	28	1	6	1
Subtotal	525	328	88	39	71	16
Sub-total	853		127		87	
Total	1067					

Chapter 3: Registration procedure for expedited drug marketing and communication

(1) Registration procedures for expedited drug marketing

1. Breakthrough therapy designation

Among the RAs accepted in 2021, 263 were to register for a Breakthrough Therapy Designation. 53 RAs (involving 41 varieties) were approved, covering such indications as diseases caused by COVID-19, non-small cell lung cancer and ovarian cancer. See Annex 6 for Breakthrough Therapy Designations in 2021. Among those the CDE approved for Breakthrough Therapy Designations, five were approved for expedited marketing.

2. Conditional approval

Among the 323 NDAs recommended for approval, 60 (involving 38 varieties) were marketed after conditional approval, accounting for 18.58%. See Annex 1 for the conditional approvals for marketing authorization of new drugs in 2021.

3. Priority review and approval

According to the current Provisions for Drug Registration, 115 RAs (involving 69 varieties) were included in the Priority Review and Approval Procedure ("PRAP") in 2021. 41 RAs for drugs received conditional approval, accounting for 35.65%. 34 RAs were for new varieties, dosage forms and strengths of pediatric drugs, accounting for 29.57%. The CDE's priority review resources were increasingly focused on RAs for new drugs, pediatric drugs, and drugs for rare diseases (RDs) with clinical advantages.

See Table 16 for the RAs included in the Priority Review and Approval Procedure ("PRAP") in accordance with the current Provisions for Drug Registration in 2020-2021.

Table 16: RAs (cases) included in the Priority Review and Approval Procedure ("PRAP") according to the current Provisions for Drug Registration in 2020-2021

Included after issuance of Provisions for Drug Registration	2020		2021	
	RA	Percentage (%)	RA	Percentage (%)
Shortly supplied drugs meeting urgent clinical needs, innovative drugs and modified new drugs for the prevention of major infectious diseases and rare diseases	14	18.67%	5	4.35%
New varieties, dosage forms and strengths of pediatric drugs complying with the physiological characteristics of children	7	9.33%	34	29.57%
General and innovative vaccines urgently needed for disease prevention and control	4	5.33%	3	2.61%
Drugs included in breakthrough therapy designation	—	—	11	9.57%
Drugs meeting the requirements for conditional approval	27	36.00%	41	35.65%
Other circumstances of prioritized review and approval stipulated by the NMPA.	23	30.67%	21	18.26%
Total	75	100%	115	100%

Among the RAs that have been included in the Priority Review and Approval Procedure ("PRAP"), 219 (involving 131 varieties) were recommended for approval for marketing in 2021. According to the scope of inclusion before the issuance of the current Provisions for Drug Registration, 130 have been included in the PRAP. 56 of which were synchronous applications, accounting for 43.08%. 22 were for new drugs with apparent clinical value, accounting for 19.92%. 89 have been included in the PRAP, including 31 for drugs qualifying for conditional approval, accounting for 34.83%. Nine RAs were for new varieties, dosage forms and strengths of pediatric drugs complying with the physiological characteristics of children, accounting for 10.11%. See Table 17 for the RAs recommended for approval through the Priority Review and Approval Procedure (PRAP) in 2021.

Table 17: RAs recommended for approval through the Priority Review and Approval Procedure (PRAP) in 2021

Included after issuance of Provisions for Drug Registration	RA	Percentage (%)	Included after issuance of Provisions for Drug Registration	RA	Percentage (%)
Shortly supplied drugs catering to urgent clinical needs, innovative drugs and modified new drugs for the prevention of major infectious diseases and rare diseases	9	10.11%	New drugs with significant clinical value	22	16.92%
New varieties, dosage forms and strengths of pediatric drugs complying with the physiological characteristics of children	9	10.11%	Synchronous application	56	43.08%
General and innovative vaccines urgently needed for disease prevention and control	2	2.25%	Orphan diseases	13	10.00%
Drugs included in breakthrough therapy designation	5	5.62%	Pediatric drug	9	6.92%
Drugs meeting the requirements for conditional approval	31	34.83%	Re-apply after improvement according to standards consistent with the quality and efficacy of brand-name drugs	16	12.31%
			Major project	3	2.31%
Other circumstances of prioritized review and approval stipulated by the NMPA	33	37.08%	Patent expiration	8	6.15%
			Drugs with urgent needs in clinical and shortage in market	3	2.31%
Total	89	100%	Total	130	100%

4. Special approval procedure

The CDE reviewed 81 RAs (for COVID-19 vaccines and therapeutic drugs) included in the Special Review and Approval Procedure ("SRAP"). 12 INDs for COVID-19 vaccines were approved, and five NDAs for COVID-19 vaccines (all conditionally approved for marketing) were recommended for approval, including four inactivated COVID-19 vaccines (Vero cell) and 1 recombinant COVID-19 vaccine (adenovirus Type-5 [Ad5] vector). 15 INDs for COVID-19 therapeutic drugs were approved, including 4 INDs for small molecule antiviral drugs, nine INDs for neutralizing antibodies and two INDs for other drugs. Five NDAs for COVID-19 therapeutic drugs were recommended for approval, including Lung Cleansing and Detoxifying Granules, Huashibaidu Granules, Xuanfeibaidu Granules, Amubarvimab Injection (BRII-196) (a SARS-CoV-2 virus-neutralizing monoclonal antibody combination therapy) and Romlusevimab (BRII-198) (a SARS-CoV-2 virus-neutralizing monoclonal antibody combination therapy). 44 supplementary applications related to SARS-CoV-2/COVID-19 were also approved.

(2) Communication with applicants

The CDE constantly adjusts its communication and consultation methods to meet the needs of epidemic prevention and control and increasing communication with applicants. Currently, the CDE communicates with applicants via communication meetings (CMs), via the official CDE website (Window for Applicants) and telephone and email consultations.

The CDE received 4,450 applications for CMs, up 37.81% YoY. It processed 3,946 applications for CMs, up 61.00% YoY. It received 18,867 consultations on general technical issues, and processed 18,423 consultations. The CDE also processed over 10,000 telephone consultations and received nearly 10,000 consultations via eight contact mailboxes.[24] See Figure 38 for the received and processed applications for CMs in 2017-2021. See Figure 39 for the received consultations on general technical issues in 2021.

Figure 38: Number of CDE-received and CDE-processed applications for communication meetings in 2017-2021

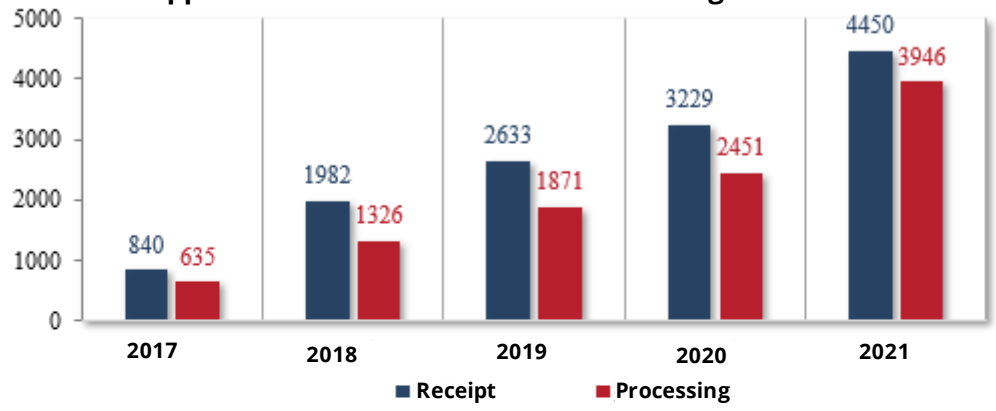
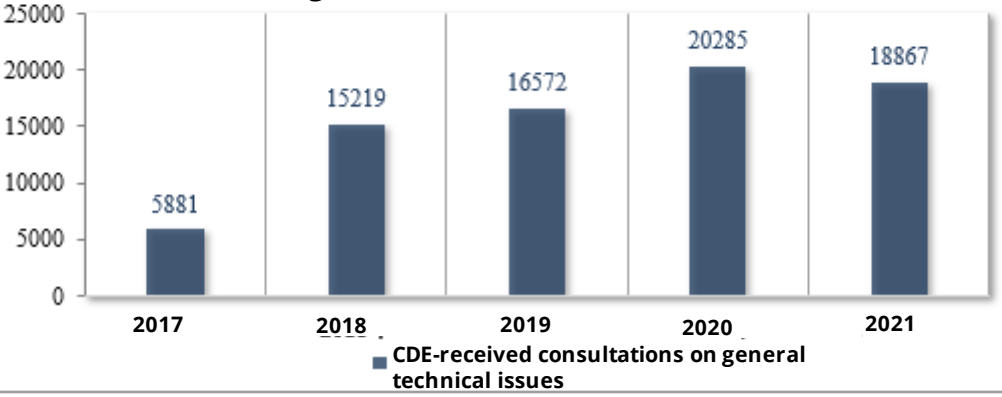


Figure 39: Number of CDE-received consultations on general technical issues in 2021



2. Processing CMs

The CDE received 4,450 applications for CMs (CMs). After comprehensive evaluation, if an application meets the conditions for convening a CM, the CDE contacts the applicant to discuss the details. If it is unnecessary to convene a CM, the CDE replies to the applicant in writing as soon as possible. In 2021, CDE processed 3,946 CM applications. Class II meetings in critical stages of drug R&D accounted for 69.23% of all CDE-held CMs. 32.84% of all applications were for Pre-IND CMs. The CDE processed 11.05% of these applications. See Table 18 for a breakdown of applications for CMs in 2021.

Table 18: Number of applications for CMs received and processed by the CDE in 2021

Type of communication meeting applied for		Amount	Percentage	Amount	Percentage
Class I meeting		589	13.24%	538	13.63%
Class II meeting	Pre-investigational new drug (Pre-IND) application	1418	31.87%	1296	32.84%
	Investigational new drug (IND) application	279	6.27%	271	6.87%
	Application after end of phase I	245	5.51%	236	5.98%
	Application after end of phase II	364	8.18%	308	7.81%
	Pre-new drug application (Pre-NDA)	478	10.74%	436	11.05%
	New drug application (NDA)	172	3.87%	156	3.95%
	Application for consistency evaluation	9	0.20%	6	0.15%
	Complex generic drug application	30	0.67%	23	0.58%
Class III meeting		866	19.46%	676	17.13%
Total		4450	100%	3946	100%

In 2021, CDE held 425 CMs (face-to-face meetings, video conferences and teleconferences), up 58.58% YoY. CDE-held Class II CMs accounted for 70.35%, wherein, CDE-held Pre-IND CMs accounted for 21.65%, and CDE-held Pre-NDA CMs accounted for 18.12%. See Table 19 for CDE-held applications for CMs in 2018-2021.

Table 19: Number of CDE-held applications for CMs in 2018-2021

Type of CM applied for		2018		2019		2019		2020	
		Meeting held	Percentage (%)	Meeting held	Percentage (%)	Meeting held	Percentage (%)	Meeting held	Percentage (%)
Class I conference		—	—	20	4.75%	26	9.70%	72	16.94%
Class II conference	Pre-investigational new drug (Pre-IND) application	120	37.27%	134	31.83%	77	28.73%	92	21.65%
	Investigational new drug (IND) application	31	9.63%	33	7.84%	14	5.22%	37	8.71%
	Application after end of phase I	37	11.49%	33	7.84%	22	8.21%	31	7.29%
	Application after end of phase II	47	14.60%	42	9.98%	33	12.31%	43	10.12%
	Pre-new drug application (Pre-NDA)	87	27.02%	71	16.86%	47	17.54%	77	18.12%
	New drug application (NDA)	—	—	6	1.43%	10	3.73%	17	4.00%
	Application for consistency evaluation	—	—	1	0.24%	0	0.00%	0	0%
	Complex generic drug application	—	—	2	0.48%	1	0.37%	2	0.47%
Class III meeting		—	—	79	18.76%	38	14.18%	54	12.71%
Total		322	100%	421	100%	268	100%	425	100%

Chapter 4: Main Issues with Drug RAs and an Analysis thereof

542 drug RAs were not approved or recommended for rejection after technical review. 359 were because the applicant failed to provide supplement materials on time. These accounted for 66.3% of all RAs that were not approved. They included nine RAs for TCMs, 349 RAs for chemical drugs and one RA for a biological product. 183 were rejected because their application dossier failed to prove the safety, efficacy or quality controllability of the drug. These included 14 RAs for TCMs, 126 RAs for chemical drugs and 43 RAs for biological products.

(1) Main issues

1. Establishment of R&D projects

Issues in this aspect existed mainly in the stage of project establishment for the development of early-developed varieties (in IND stage), some generic drugs and supplementary applications. Specifically, these issues included: unclear clinical positioning of drug R&D; unreasonable selection of indications; unreasonable selection of dosage form or route of administration; existing study data was suggestive of unobvious efficacy, unclear target and mechanism of action, and high risk in drugability; combined medication violated the principles of clinical diagnosis, treatment and medication or lacked support from efficacy and safety study data; existing study data failed to support development of marketed varieties; the reference preparation developed for a generic drug was withdrawn from the market due to safety and efficacy issues; or change item(s) in a supplementary application lacked scientificity and rationality.

2. Efficacy

Issues in this aspect were common in RAs for marketing. Specifically, these issues included: existing clinical study data failing to prove the efficacy of the variety concerned; the efficacy of the test variety could not be evaluated due to trial protocol or study quality control problems with the clinical study already conducted; human bioequivalence (BE) test results for a generic drug failed to show an equivalence to the reference product; and domestic (China-based) clinical data of efficacy lacked the RA for marketing of a Class 3 chemical drug.

3. Safety

Drug safety issues/concerns were present at various stages of drug development. Specifically, these issues/concerns included: early (IND stage) study results that were suggestive of obvious toxicity or too narrow a safety window, making it difficult to enter clinical development or suggest that the comprehensive benefit may be very limited from clinical use; issues/concerns in preclinical safety study methods or study quality control, or insufficient study data were too serious to support subsequent clinical development; existing clinical study data showed serious adverse reactions, and the benefit-risk ratio of clinical use was unreasonable; and domestic (China-based) clinical safety data lacked an application for marketing registration of a Class 3 chemical drug.

4. Quality controllability

Issues in this aspect were common in the development of generic drugs. Specifically, these issues included: serious defects present in the pharmaceutical study, which failed to prove quality controllability; the submission dossier could not prove consistency of quality between generic drug and the reference product; study trial samples at different stages of drug development were inconsistent; sample stability study results and API starting materials failed to meet the technical requirements for marketing generic drugs; the drug manufacturer failed to use APIs with required legitimate sources; the sample review inspection failed to meet applicable requirements; or a serious defect was identified in the testing methods.

5. Compliance

Issues in this aspect were common in RAs subject to registration verification and inspection. Specifically, these issues included: authenticity issues with study data were identified during registration verification; other major defects affecting product quality were identified during registration verification; or sampling inspection during registration verification yielded an unqualified result.

6. Other aspects

Issues in this aspect included: failure to provide study data or supplement and improve the study project according to the requirements and standards raised by the regulatory authority; missing items in study content identified during the review could not support an RA; supplementary application package insert (PI) revision failed to meet PI preparation requirements and management specifications; existing literature supported a supplementary application for change; or support for study data was insufficient.

(2) Comparison with previous years

Overall, the main issues/problems with 2021 RAs were like those in previous years in terms of classification and specific performance. However, some changes have also occurred, including:

1. Newly occurring problems

Some applicants failed to submit the required study data. As a result some IND study contents were missing during the review process. As a result, the review failed. According to Article 88 of the current Provisions for Drug Registration, an applicant may not supplement new technical materials while an application is being reviewed for a drug clinical trial.

The paragraph that follows this one, said almost the exact same thing, so I deleted it.

2. New trends in rejections

No RAs were rejected because of a lack of communication in 2021. The number of RAs for Class 3 chemical drugs were rejected because of a lack of domestic (China-based) clinical data on efficacy and safety. Fewer RAs were rejected due to compliance problems compared with previous years. There was a significant increase in RAs that were rejected due to problems related to the rationality for drug development project.

The above circumstances are the related to changes in communication requirements while the RA is being processed and changes to requirements for the marketing of Class 3 chemical drugs.

(3) Recommendations and suggestions

Analysis of recent issues with RAs has yielded several helpful suggestions for all parties involved in the R&D, registration and regulation of drugs.

1. Place more emphasis on the importance on clinical needs in drugs development

Drug development should be based on clinical needs. Sufficient attention should be paid to solving unmet clinical needs. Drug development should be clinical value-oriented, paying full attention to the advantages of developing similar innovative drugs. Low-level and repetitive innovations should be avoided. Efforts should be made to fully evaluate the clinical values and advantages of modified new drugs. The principles of necessity and rationality should be followed for supplementary applications for changes.

2. Use communication mechanisms effectively

In addition to submitting an application for communication at each key step in the drug development process, an applicant may also strengthen communication via other R&D channels and the Review & Approval process. Communication should aim to solve issues/problems/concerns (“problems”), reach a consensus and eliminate inconsistencies. Equating communication with Administrative Review & Approval procedures is not advised.

3. Strengthen preliminary research for innovative drug development

Adequate evaluation of drugability should be made for some new mechanisms and new targets. Proof-of-concept (PoC) studies should be conducted as often as possible to reduce the risks in subsequent development and avoid wasting research resources. Commercial development strategies for innovative drugs should be based on scientificity and emphasize the integrity of drugability evidence chains. Follow the scientific logic of drug development step by step is essential. This minimizes the interference from non-scientific factors in the development process.

Chapter 5: Varieties in Key Therapeutic Areas

COVID-19 vaccines and COVID-19 therapeutic drugs:

1-2. The Inactivated COVID-19 Vaccine (Vero Cell) (Sinovac Biotech Co., Ltd.) and Inactivated COVID-19 Vaccine (Vero Cell) (Sinopharm Wuhan Institute of Biological Products Co., Ltd.) are indicated for the prevention of diseases caused by novel coronavirus infection ("COVID-19").

3. Recombinant COVID-19 Vaccine (adenovirus Type-5 [Ad5] vector), the first approved adenovirus vector COVID-19 vaccine made in China, is indicated for the prevention of diseases caused by COVID-19.

4-6. Lung Cleansing and Detoxifying Granule, Huashibaidu Granules and Xuanfeibaidu Granules, i.e., the varieties in the "Three TCM Prescriptions", are recommended drugs in the Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 9). Lung Cleansing and Detoxifying Granules are used to treat epidemic diseases caused by cold and wet epidemic virus es. Huashibaidu Granules are used for treating epidemic diseases caused by wet viral infection of the lungs . Xuanfeibaidu Granules treat epidemic diseases caused by wet viral depression in the lung s. These "Three TCM Prescriptions" are adapted from ancient TCM formulas, which were screened by a group of academicians and experts fighting on the front line against COVID-19 in Wuhan since the initial outbreak. They were reviewed and approved for the first time according to "TCM Registration Classification Class 3.2: Other TCM compound preparations derived from famous ancient classic TCM recipes" after the NMPA issued the requirements for Traditional Chinese Medicine registration classification and application dossiers (No.[2020]68). The approved marketing of these "Three TCM Prescriptions" provides more options for the treatment of COVID-19, giving full play to the role of TCM in epidemic prevention and control.

7-8. Amubarvimab Injection (BRII-196) and Romlusevimab (BRII-198) are the first SARS-CoV-2 virus-neutralizing monoclonal antibody combination therapy drugs approved in China with independent intellectual property rights (IPRs). These two drugs can treat COVID-19, and are used in combination to treat adult and adolescent (aged 12-17, weight≥40kg) patients diagnosed with CoVID-19 of light and common type with high risk factors of progression to severe type (including hospitalization or death). Wherein, the indication for adolescents (aged 12-17, weight≥40 kg) was approved conditionally. Its approval for marketing provides more options for the treatment of COVID-19.

New TCMs:

9. Yiqi Tongqiao Pills tonify qi while securing exterior as well as dispelling wind and opening orifices. The medicine is indicated for the treatment of seasonal allergic rhinitis with TCM differentiations of lung and spleen deficiency patterns. It is classified as an original Class 6 New TCM compound preparation, composed of 14 kinds of raw herbal ingredients (e.g., Astragalus membranaceus and Saposhnikovia divaricate, etc.). It is based on TCM clinical prescriptions and a randomized, double-blind, placebo-controlled, parallel-group, multicenter clinical trial has been conducted for it.

10. Yishen Yangxin Anshen Tablets tonifying the kidneys, nourish the heart and calm the mind. The drug is indicated for the treatment of heart and kidney deficiencies exhibiting symptoms like insomnia, excessive dreaming, palpitations, fatigue, forgetfulness, dizziness, soreness and weakness of waist and knees. It is also indicated for treatment of conditions like a light red tongue with a thin coating, a deep and thready pulse, or a thready and weak pulse. It is classified as original Class 6 New TCM compound preparation, composed of 10 kinds of raw herbal ingredients (e.g., fried sour jujube kernels, Radix polygoni multiflori preparata, etc.). It is developed based on TCM clinical experience prescriptions and a randomized, double-blind, placebo-controlled, parallel-group, multicenter clinical trial has been conducted for it. Its approval for marketing provides a new treatment option for patients with insomnia.

Unclear. Is this normal TCM terminology?

11. Yinqiao Qingre Tablets release the exterior with pungent-cool and clearing heat while removing toxins. The drug is indicated for the treatment of common cold due to external contraction of wind heat, with symptoms of fever, sore throat, aversion to wind, nasal congestion, runny nose, headache, systemic soreness, sweating, cough, dry mouth, red tongue and rapid pulse. This variety is a Class 1.1 innovative TCM composed of nine kinds of raw herbal ingredients (e.g., honeysuckle and pueraria). It is developed based on TCM clinical experience prescriptions, and a randomized, double-blind, placebo/positive drug-controlled, parallel-group, multicenter clinical trial has been conducted for it.

12. Xuanqi Jiangu Tablets help to circulate blood, relax tendons, unblock the pulse, relieve pain, tonifying the kidneys and strengthen the bones. The medicine is indicated for the treatment of mild to moderate osteoarthritis of the knee with TCM differentiation patterns of stasis and stagnation in the tendon and pulse. It is a Class 1.1 innovative TCM composed of 11 kinds of raw herbal ingredients (e.g., Corydalis Rhizoma and Scorpio, etc.). It is developed based on TCM clinical experience prescriptions. Evidence of safety and efficacy has been obtained through a randomized, double-blind, placebo-controlled, parallel-group, multicenter clinical trial.

13. Qizhi Yishen Capsules supplement qi, nourish yin, transform stasis and unblock collaterals. The drug is indicated for the treatment of qi and yin deficiency patterns in early diabetic nephropathy. It is a Class 1.1 innovative TCM composed of 10 kinds of raw herbal ingredients (e.g., Astragalus membranaceus and Rehmannia glutinosa, etc.). It is developed based on TCM clinical experience prescriptions. Evidence of safety and efficacy has been obtained through a randomized, double-blind, placebo-controlled, parallel-group, multicenter clinical trial.

14. Kunxinning Granules have the function of warming yang, nourishing yin, tonifying the kidneys and soothing the liver. They are indicated for the treatment of female climacteric syndrome with TCM differentiation of yin and yang deficiency patterns. It is a Class 1.1 innovative TCM composed of seven kinds of raw herbal ingredients (e.g., Rehmannia glutinosa and abalone shell, etc.). It is developed based on TCM clinical experience prescription. Evidence of safety and efficacy has been obtained through a randomized, double-blind, placebo-controlled, parallel-group, multicenter clinical trial.

15. Huzhen Qingfeng Capsules clear heat and transform dampness, stasis and turbidity. They nourish and supplement the liver and kidneys, and are indicated for the treatment of mild to moderate acute gouty arthritis with TCM differentiations of damp heat accumulation patterns. This drug is a Class 1.1 innovative TCM composed of four kinds of raw herbal ingredients (e.g., Reynoutria japonica and Plantago asiatica, etc.). It is developed based on TCM clinical experience prescriptions. Evidence of safety and efficacy has been obtained through a randomized, double-blind, placebo-controlled, parallel-group, multicenter clinical trial.

16. Jieyu Chufan Capsules relieve depression, transform phlegm, clear heat and alleviate vexation. They are indicated for the treatment of mild and moderate depression with TCM differentiations of qi stagnation with phlegm retention patterns and internal stagnant heat disturbance patterns. This is a Class 1.1 innovative TCM composed of eight kinds of raw herbal ingredients (e.g., Gardenia jasminoides and officinal magnolia bark, etc.). It is developed based on TCM clinical experience prescription. The prescription is derived from a Banxia Houpu decoction recorded in the classic TCM work *Synopsis of the Golden Chamber [Jinguiyaolue]* and a Banxia Houpu decoction recorded in *Treatise on Cold Damage Diseases [Shanghanlun]*. Evidence of safety and efficacy has been obtained through a randomized, double-blind, positive drug (chemical drug)-controlled, placebo-controlled, parallel-group, multicenter clinical trial.

17. Qirui Weishu Capsules circulate blood, transform stasis, dry dampness and alleviate pain. They are indicated for the treatment of stomach pain caused by mild-to-moderate chronic non-atrophic gastritis accompanied by ulceration and damp heat accumulation patterns. They are a Class 1.1 innovative TCM composed of four kinds of raw herbal ingredients (e.g., Panax notoginseng and Alumen exsiccatum). It is developed based on a preparation from medical institutions. A randomized, double-blind, positive drug-controlled, parallel-group, multi-center clinical trial has been conducted for it. Its approval for marketing provides a new treatment option for patients with chronic gastritis.

18. Icaritin Soft Capsules are indicated for the treatment of unresectable hepatocellular carcinoma (HCC) in patients who are not eligible for or are refusing standard therapy or have not received systemic treatment in the past, and have peripheral blood composite markers meeting at least two of the following test indicators: AFP≥400ng/mL; TNF-α<2.5pg/mL; IFN-γ≥7.0pg/mL. This drug is a Class 1.2 innovative TCM extracted and made from the Chinese herbal medicinal material Epimedii Folium.

Orphan drugs:

19. Brosuumab Injection is indicated for the treatment of X-linked hypophosphatemia (XLH) in adult patients and pediatric patients aged over 1 year. XLH is a rare disease. Currently no effective therapeutic drug is available for to treat XLH. This product is included in the CDE's List of Overseas New Drugs Urgently Needed in Clinical Settings. It is a recombinant fully human IgG1 monoclonal antibody targeting fibroblast growth factor 23 (FGF23) antigen, which can bind to and inhibit FGF23 activity and thus increase serum phosphorus levels. Its approval for marketing provides a new treatment option for patients.

20. Icatibant Acetate Injection is indicated for the treatment of acute attacks of hereditary angioedema (HAE) in adults, adolescents and children aged at or over 2 years. HAE is a rare disease. Nearly half of all HAE patients will experience mucosal edema in the upper respiratory tract, causing life threatening asphyxia. HAE has been included on the List of Rare Diseases (First Batch) jointly released by the National Health Commission of the PRC and other four authorities of the PRC. This product is included in the CDE's List of Overseas New Drugs Urgently Needed in Clinical Settings. It is a competitive antagonist of bradykinin B2 receptors. Its approval for marketing provides a safe and effective drug for its prevention in Chinese patients with HAE.

21. Eftrenonacog Alfa for Injection is indicated for the treatment of adults and children with hemophilia B (congenital factor IX deficiency) for the following options: on-demand treatment and control of bleeding episodes; perioperative management of bleeding; and routine prophylaxis to reduce the frequency of bleeding episodes. Hemophilia B is a rare genetic and hemorrhagic disease. Currently, there is no long-acting recombinant human coagulation factor IX imported to or marketed in China. This product is on the List of Overseas New Drugs Urgently Needed in Clinical Settings. It is also the first long-acting recombinant human coagulation factor IX product under application for import to China.

22. Silximab for Injection is indicated for the treatment of adult patients with multicentric Castleman Disease (MCD) who are negative for human immunodeficiency virus (HIV) and human herpesvirus-8 (HHV-8). MCD is a rare disease characterized by lymphoid tissue growth. Most MCD patients suffer from multi-organ damage and poor prognosis. In some patients, MCD may evolve into malignant lymphoma. MCD has been included in the List of Rare Diseases (First Batch) jointly released by the National Health Commission of the PRC and four other authorities of the PRC. This product is included in the List of Overseas New Drugs Urgently Needed in Clinical Settings.

23. Ofatumumab Injection is indicated for the treatment of relapsing multiple sclerosis (RMS) in adults, including clinically isolated syndromes (CIS), relapsing-remitting multiple sclerosis (RRMS), and active secondary-progressive multiple sclerosis (SPMS). Multiple sclerosis (MS), an immune-mediated chronic diseases of the central nervous system (CNS) and has been included in the List of Rare Diseases (First Batch) jointly released by the National Health Commission of the PRC and other four authorities of the PRC. This is a fully human immunoglobulin G1 monoclonal antibody against human CD20.

Pediatric use:

24. Risdiplam Powder for Oral Solution is indicated for the treatment of spinal muscular atrophy (SMA) in patients aged 2 months and above. SMA is a hereditary neuromuscular disease caused by functional deficiency of SMN protein due to mutation of survival motor neuron gene 1 (SMN1), which is an autosomal recessive genetic diseases that leads to infant and child deaths. SAM has been included on the List of Rare Diseases (First Batch) jointly released by the National Health Commission of the PRC and other four authorities of the PRC. This product is a Class 1 innovative drug for the treatment of RDs in children. It can directly target the potential molecular defects of diseases and increase the production of functional SMN protein in central and peripheral tissues.

25. Dinutuximab Beta Injection is indicated for the treatment of pediatric patients aged 12 months and above with high-risk neuroblastoma and relapsed or refractory neuroblastoma with or without residual lesions. Neuroblastoma (NB) is one of the common malignant tumors in children, and no immunotherapy products for NB treatment have been approved for marketing in China. This product is included in the List of Overseas New Drugs Urgently Needed in Clinical Settings.

26. Cisplatin Injection was previously approved for the palliative treatment of small cell lung cancers (SCLC) and non-small cell lung cancers (NSCLC); non-seminomatous germ cell cancer (NSGCC); advanced refractory ovarian cancer; advanced refractory bladder cancer; refractory head and neck squamous cell carcinoma (HNSCC); gastric cancer and esophageal cancer. It was recently approved for administration and dosage in children, and its approval for marketing guarantees the rational clinical use in children.

27. Ambroxol Hydrochloride Spray is indicated for the treatment of viscous sputum and difficulty in expectoration in children aged 2-6 years. This variety is a modified new drug in a dosage form suitable for use in children. Compared with oral preparations, this variety is less likely to cause vomiting. It is for children who are young and do not cooperate while drugs are being administered.

28. Cefcapene Pivoxil Hydrochloride Granule, is indicated for the treatment of the following infections caused by bacteria sensitive to cefcarbamate in children: skin soft tissue infection, lymphangitis, chronic pyoderma, pharyngitis, laryngitis, tonsillitis (including peritonitis and peritonsillar abscess), acute bronchitis, pneumonia, cystitis, pyelonephritis, otitis media, sinusitis and scarlet fever. This variety is a third-generation oral cephalosporin antibacterial drug. Its dosage form has a higher medication compliance and is suitable for children, especially infants and young children.

Drugs for public health:

29. Quadrivalent Influenza Vaccine (Split Virion) is for the prevention of influenza caused by vaccine-associated types of influenza viruses in people aged 3 years and older. This variety is a split vaccine made from the influenza A (H1N1 and H3N2) and influenza B (B/Victoria and B/Yamagata) strains recommended by the World Health Organization (WHO). The influenza vaccines previously used in China are mainly trivalent influenza virus split vaccines. On this basis, an influenza B antigen is added in this variety to increase the antibody protection rates and seroconversion rates against influenza B. Its approval for marketing is conducive to further addressing the demand gap for quadrivalent influenza vaccines.

30. ACYW135 Meningococcal Polysaccharide Conjugate Vaccine (CRM197 vector) is indicated for the prevention of meningococcal meningitis caused by Neisseria meningitidis groups A, C, Y and W135. This variety is the first tetravalent meningococcal polysaccharide conjugate vaccine approved for marketing in China. Its approval for marketing fills addresses the widespread need for a Group Y and Group W135 meningococcal polysaccharide conjugate vaccine for children aged under 2 years in China.

31. Freeze-dried Rabies Vaccine (Vero Cells) for Human Use is indicated for the prevention of rabies. Currently, vaccines from only two drugmakers in China have been approved for use in the four-dose immunization procedure. The rest vaccines are used in the five-dose immunization procedure. The drugmaker applied simultaneously for approval for use in the five-dose immunization procedure and the 2-1-1 four-dose immunization procedure. Its approval for marketing will further alleviate the shortage of rabies vaccine in the market.

Antineoplastic drugs:

32. Furmonertinib mesylate tablets are indicated for adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) who developed disease progression on or after previous treatment with epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI) and were confirmed by testing to be positive for the EGFR T790M mutation. This is a Class 1 innovative drug independently developed by a Chinese manufacturer who holds independent intellectual property rights thereof. It is a third-generation epidermal growth factor receptor (EGFR) kinase inhibitor.

33. Pralsetinib Capsules are indicated for the treatment of adult patients with locally advanced or metastatic rearranged during transfection (RET) fusion-positive non-small cell lung cancer (NSCLC) after platinum-based chemotherapy. This product is a Class 1 innovative drug of receptor tyrosine kinase RET (Rearranged during Transfection) inhibitor, which can selectively inhibit the activity of RET kinase, inhibit the phosphorylation of RET and its downstream molecules in a dose-dependent manner and effectively inhibit cell proliferation of expression RET (wild type and multiple mutant types).

34. Savolitinib Tablets are indicated for the treatment of the adult patients who suffer from locally advanced or metastatic non-small cell lung cancer with mesenchymal-epithelial transition (MET) exon 14 mutation and are intolerant to standard platinum-containing chemotherapy or whose conditions are further developed after receiving platinum-based chemotherapy. This product is a Class 1 innovative drug whose intellectual property rights are held by a Chinese manufacturer. It is the first small molecular inhibitor specifically targeting MET kinase in China. It can selectively inhibit the phosphorylation of MET kinase and has a marked inhibitory effect on the proliferation of tumor cells with MET exon 14 skipping mutation.

35. Sugemalimab Injection, in combination with Pemetrexed and Carboplatin, is indicated for the first-line treatment of patients with metastatic non-squamous non-small cell lung cancer featuring EGFR mutation-negative and ALK-negative. It is also used in combination with Paclitaxel and Carboplatin for the first-line treatment of patients with metastatic squamous non-small cell lung cancer. This product is a recombinant humanized anti-PD-L1 monoclonal antibody, which can block the interaction between PD-L1 and PD-1 on T cells and CD80 on immune cells. It exerts anti-tumor effects by eliminating immunosuppressive effects of PD-1 on cytotoxic T cells.

36. Utidelone Injection, in combination with Capecitabine, is indicated for the treatment of patients with relapsed or metastatic breast cancer who have received at least one chemotherapy regimen. This product is a Class 1 innovative drug independently developed by a Chinese manufacturer who holds independent intellectual property rights thereof. As a derivative of epothilone, it can promote tubulin polymerization, stabilize microtubules, and induce apoptosis. Its approval for marketing provides a new treatment option for patients.

37. Dalpiciclib Isetionate Tablet, in combination with Fulvestrant, is indicated for the treatment of patients with relapsed or metastatic breast cancer who still have further developed conditions after receiving endocrine therapy and are positive for hormone receptor and negative for human epidermal growth factor receptor 2 (HER2). This product is a Class 1 innovative drug of cyclin-dependent kinase 4 and 6 (CDK4 and CDK6) inhibitor, which can reduce the phosphorylation level of retinoblastoma protein downstream of CDK4 and CDK6 signaling pathways, and induce G1 phase arrest of cells, thereby inhibiting proliferation of tumor cells.

38. Pamiparib Capsules are indicated for the treatment of relapsed advanced ovarian cancer, fallopian tube cancer or primary peritoneal cancer in patients with germline BRCA (gBRCA) mutation who have undergone second-line or above chemotherapy. This product is a Class 1 innovative drug and a potent and selective inhibitor of PARP-1 and PARP-2. It has a synthetic lethal effect on tumor cells by inhibiting the restoration of DNA single strand damage and HRD in tumor cells, especially sensitive to DNA repair-deficient tumor cells carrying BRCA gene mutation. Its approval for marketing provides a new treatment option for patients.

39. Donafenib Tosilate Tablet is indicated for patients who suffer from unresectable hepatocellular carcinoma and have not received systemic therapy in the past. This product is a Class 1 innovative drug independently developed by a Chinese manufacturer who holds independent intellectual property rights thereof. It is a small molecule antitumor drug falling in the category of multikinase inhibitor. Its approval for marketing provides a new treatment option for patients.

40. Disitamab Vedotin for Injection is indicated for the treatment of patients who suffer from HER2 overexpression locally advanced or metastatic gastric cancer (including adenocarcinoma of the esophagogastric junction) and have received at least two kinds of systemic chemotherapy. This product is an innovative antibody-drug conjugate (ADC) developed independently by China, which contains HER2 antibody part, connexon and cytotoxic drug MMAE.

41. Axicabtagene Ciloleucel Injection is indicated for the treatment of adult patients who suffer from relapsed or refractory large B cell lymphoma (including diffuse large B-cell lymphoma (unspecified), primary mediastinal large B cell lymphoma, high-grade B-cell lymphoma and diffuse large B-cell lymphoma transformed from follicular lymphoma) and have received second-line or above systemic therapy. This product is the first cell therapy product approved for marketing in China and an autologous immune cell injection, which is prepared by chimeric antigen receptor T cells (CAR-T cell) targeting human CD19 genetically modified by the retroviral vector carrying the CD19 CAR gene.

42. Relmacabtagene Autoleucel Injection is indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after second-line or above systemic therapy. This product is the first cell therapy product developed independently by a Chinese manufacturer and the second cell therapy product approved for marketing in China. It is an autologous CAR-T cell immunotherapy product targeting CD19.

43. Olverembatinib Tablet is indicated for treating the adult patients with chronic myeloid leukemia accompanied with T315I mutation in the chronic phase or accelerated phase by the fully proved testing method and are tyrosine kinase inhibitor resistant. This product, a small molecule inhibitor for PTK, is a Class 1 innovative drug developed independently by a Chinese manufacturer who holds independent IPRs. It can effectively inhibit the activity of Bcr-Abl tyrosine kinase (wild type and multiple mutant types) and inhibit the phosphorylation of Bcr-Abl tyrosine kinase and downstream proteins STAT5 and Crkl, block the activation of downstream pathways, induce cell cycle arrest and apoptosis of Bcr-Abl positive and Bcr-Abl T315I mutant cell lines. It is the first drug approved in China for chronic myeloid leukemia accompanied with T315I mutation. Its approval for marketing provides an effective treatment means for the patients with drug resistance due to T315I mutation.

44. Envolizumab injection is for the treatment of adult patients with advanced solid tumors with unresectable or metastatic microsatellite instability (MSI-H) or mismatch repair gene deficiency (dMMR), including patients with advanced colorectal cancer whose disease has progressed after previous treatment with fluorouracil, oxaliplatin and irinotecan. It is also for patients with other advanced solid tumors whose disease has progressed after prior therapy and have no satisfactory alternative treatment options. This product is an innovative PD-L1 antibody drug developed independently by a Chinese manufacturer and is a recombinant single domain antibody Fc fusion protein injection targeting human PD-L1. It can bind to human PD-L1 protein and block its interaction with the receptor PD-1 to relieve the inhibitory effect of tumors on T cells through PD-1/PD-L1 pathways and motivate the antitumor activity of immune system to kill tumor.

Anti-infective drugs:

45. Azvudine Tablets, used together with nucleoside reverse transcriptase inhibitors and non-nucleoside reverse transcriptase inhibitors, are indicated for the treatment of HIV-1 positive adults with a high viral load. This product is a novel Class 1 innovative drug of nucleoside reverse transcriptase and accessory protein Vif inhibitor, and is also the first anti-HIV-1 drug with the above-mentioned dual targets. It can selectively enter the CD4 or CD14 cells in the peripheral blood mononuclear cells of HIV-1 target cells to inhibit virus replication.

46. Ainovirine Tablets are indicated for the treatment of untreated adult patients with HIV-1 infection together with nucleoside antiretroviral drugs. This product is a novel Class 1 innovative drug of non-nucleoside reverse transcriptase inhibitor for HIV-1 infection. It inhibits the replication of HIV-1 virus through non-competitive binding to HIV-1 reverse transcriptase.

47. Tenofovir Amibufenamide Tablets are indicated for the treatment of adult patients with chronic HBV infection. This product is a Class 1 innovative drug independently developed by a Chinese manufacturer who holds independent intellectual property rights thereof. It is a nucleoside reverse transcriptase inhibitor. Its approval for marketing provides a new treatment option for patients with chronic hepatitis B.

48-49. Omadacycline Tosylate Tablets and Omadacycline Tosylate for Injection are indicated for the treatment of community-acquired bacterial pneumonia (CABP) and acute bacterial skin and skin structure infection (ABSSSI). Omadacycline Tosylate is a novel tetracycline antibacterial drug with broad spectrum antibacterial activity. It has oral and intravenous dosage forms.

50. Contezolid Tablets are indicated for the treatment of complicated skin and soft tissue infections caused by Contezolid-sensitive staphylococcus aureus (methicillin-sensitive and -resistant strains), streptococcus pyogenes or streptococcus agalactiae. This product is a Class 1 innovative drug independently developed by a Chinese manufacturer who holds independent intellectual property rights thereof. It is a new totally synthetic oxazolidinone antibiotic.

51. Neinofloxacin Malate Sodium Chloride Injection is indicated for the treatment of adult community-acquired pneumonia (CAP) patients (≥ 18 years) caused by nemonoxacin-sensitive Streptococcus pneumoniae, Staphylococcus aureus, Haemophilus influenzae, Haemophilus parainfluenza, K. pneumoniae, Pseudomonas aeruginosa, Mycoplasma pneumoniae, Chlamydia pneumoniae and Legionella pneumophila. This product is a fluoroquinolone-free antibacterial drug, which has a different action site from fluoroquinolone-containing antibacterial drugs.

52. Levoornidazole Phosphate Disodium Phosphate for Injection is indicated for the treatment of severe intestinal and liver amebiasis, post-operation infection caused by ornidazole-sensitive anaerobic bacteria, and for the prevention of sensitive anaerobic infection caused by surgical operation. This product is the latest generation of nitroimidazole anti-infective drugs, and its approval for marketing provides a new treatment option for anaerobic infections.

Endocrine system drugs:

53. Chiglitazar Sodium Tablets are indicated in combination with diet control and exercise for improving blood glucose control in adults with type 2 diabetes. This product is a Class 1 innovative drug independently developed by a Chinese manufacturer who holds independent intellectual property rights thereof. It is a full agonist of peroxisome proliferator-activated receptor (PPAR). It can simultaneously activate three subtypes (α, γ and δ) receptors of PPAR, induce downstream target gene expression related to insulin sensitivity, fatty acid oxidation, energy conversion and lipid transport and inhibit PPARγ receptor phosphorylation associated with insulin resistance.

54. Henagliflozin Proline Tablets are indicated for improving blood glucose control in adults with type 2 diabetes. This product is a Class 1 innovative drug independently developed by a Chinese manufacturer who holds independent intellectual property rights thereof. It is an inhibitor of sodium glucose co-transporter 2 (SGLT2). By inhibiting SGLT2, it reduces the reabsorption of glucose filtered through renal tubules and the renal threshold of glucose, thus increasing urinary glucose excretion (UGE).

Circulatory system drugs:

55. Hybutimibe Tablets are indicated for adjuvant therapy other than dietary control. They can be used alone or in combination with HMG-CoA reductase inhibitors (statins) for the treatment of primary (heterozygous familial or non-familial) hypercholesterolemia and can lower the levels of total cholesterol, LDL cholesterol and apolipoprotein B. This product is a Class 1 innovative drug independently developed by a Chinese manufacturer who holds independent intellectual property rights thereof. It can inhibit the cholesterol absorption dependent on the sterol carrier Niemann-Pick C1 – like1 (NPC1L1), thus reducing cholesterol transport from small intestine to liver, reducing blood cholesterol levels and liver cholesterol storage. Its approval for marketing provides a new treatment option for patients with primary hypercholesterolemia.

Circulatory system drugs:

56. Herombopag Olamine Tablets are indicated for adult patients with chronic primary immune thrombocytopenia who failed to respond to the treatment by glucocorticoid, immunoglobulin, and other therapies due to thrombocytopenia and clinical conditions that increase the risk of bleeding. It is also indicated for treatment of adult patients with severe aplastic anemia (SAA) who failed to respond to immunosuppressive therapy. This product is a Class 1 innovative drug independently developed by a Chinese manufacturer who holds independent intellectual property rights thereof. It is a small molecule human thrombopoietin receptor agonist.

Drugs forrheumatic diseases and immunization:

57. Telitacicept for Injection, in combination with conventional therapy, is indicated for the treatment of adult with systemic lupus erythematosus (SLE) featuring high disease activity and positive autoantibodies after conventional therapy. An innovative therapeutic biological product independently developed by a Chinese manufacturer, it is a fusion protein formed by combining specific extracellular soluble part of transmembrane activator and CAML interactor (TACI) of B-lymphocyte stimulator (BLyS) with fragment crystallizable (Fc) region of human immunoglobulin G1 (IgG1). Since TACI receptors have a high affinity to BLyS and A proliferation inducing ligand (APRIL), this product can prevent the interaction between BLyS and APRIL and their cell membrane receptors, B cell maturation antigens, and B cell activation molecular receptors, thus inhibiting biological activity of BLyS and APRIL.

Drugs for Skin and ENT:

58. Apremilast Tablets are indicated for the treatment of adult patients with moderate to severe plaque psoriasis who meet the indications for phototherapy or systemic treatment. This is a product included on the List of Overseas New Drugs Urgently Needed in Clinical Settings. It is a small-molecule phosphodiesterase 4 (PDE4) inhibitor, which can promote the increase of intracellular cyclic adenosine monophosphate (cAMP) content by inhibiting PDE4, thereby increasing anti-inflammatory cytokine and down-regulating inflammatory response. Its approval for marketing provides patients with a new alternative treatment option that is convenient to administer.

Chapter 6: Efficient Emergency Review

In 2021, the global COVID-19 epidemic was still raging. The constant emergence of new variants cast a shadow of uncertainty the situation. Increased pressure to "prevent the coronavirus from re-entering China to cause a new epidemic" increase the need for epidemic prevention and control in China, and the bar was raised for vaccines. The international community increasingly recognized that COVID-19 vaccines produced in China were safe and effective. The Party and the Chinese government have continuously raised review and approval standards for COVID-19 vaccines and drugs. Chinese Vice Premier Sun Chunlan and State Councilor Xiao Jie went to the Center for Drug Evaluation of the NMPA ("CDE") to conduct an inspection and hold a symposium for epidemic prevention and control. The CDE held fast to the principle of "People First and Life First, respecting science, following laws, and efficient response to changes in epidemic situation". It provided support for epidemic prevention and control efforts, by completing the emergency review and approval of COVID-19 therapeutic drugs and COVID-19 vaccines.

(1) The CDE redoubled its efforts in driving R&D and marketing of COVID-19 therapeutic drugs

The CDE implemented the requirements deployed by Chinese Vice Premier Sun Chunlan and State Councilor Xiao Jie during their inspection and symposium. It strictly adhered to the safety and efficacy standards for the R&D of COVID-19 therapeutic drugs. It accelerated the emergency review and approval processes for key drugs, and provided scientific and technological guarantees for responses to public health emergencies and major COVID-19 epidemic.

The CDE took instruction from the symposium from the start, studying and carrying out implementation measures, sorting out the emergency review process for COVID-19 drugs, formulating emergency review work plans for key according to the principle of "one policy and one team for one drug". It established a working mechanism and clarified the technical standards, working nodes, countdown schedule and roadmap for marketing review. It also formulated the Work Plan for the Marketing Review of COVID-19 Drugs.

The CDE strengthened the link between research and review, guided drugmakers, and continuously tracked the progress of COVID-19 therapeutic drugs under R&D. It efficiently reviewed COVID-19 drugs according to the applicable laws and regulations, and accelerated their marketing. At the same time, the CDE paid close attention to the R&D, review and approval of COVID-19 therapeutic drugs internationally to better guide the R&D and marketing application of imported and generic drugs manufactured in China.

Third, CDE implemented the major responsibilities of applicants. For the varieties under application for conditional approval for marketing, CDE urged the applicants concerned to complete relevant studies and submit relevant materials/dossiers on time according to their commitments, and efficiently conducted scientific supervision over COVID-19 therapeutic drugs in their whole life cycle.

The CDE formed the Special Working Group for Emergency Review of TCMs to Fight the COVID-19 Epidemic. It clearly understood the pathological features, evolution patterns, syndrome differentiations and treatment principles of COVID-19. It also kept abreast of the use of TCMs at the front lines fighting against COVID-19 as well as the latest trends in TCM R&D. Moreover, it deepened the understanding of the unique role TCM can play in the fight against COVID-19 in combination with the Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia issued by the National Health Commission of the PRC.

The CDE improved technical guidance and registration services for applicants. In keeping with the principle of "submission immediately after R&D, and review immediately after submission", the CDE optimized review process and completed the review of 84 project establishment applications. Each project establishment application was completed within 24 hours of submission. As such, CDE accepted questions from applicants on a 24-7 basis, providing prompt answers. The CDE also gave full play to the guiding role of the Special Expert Group composed mainly of TCM academicians and front-line clinical experts fighting COVID-19, resulting in the "Three TCM Prescriptions".

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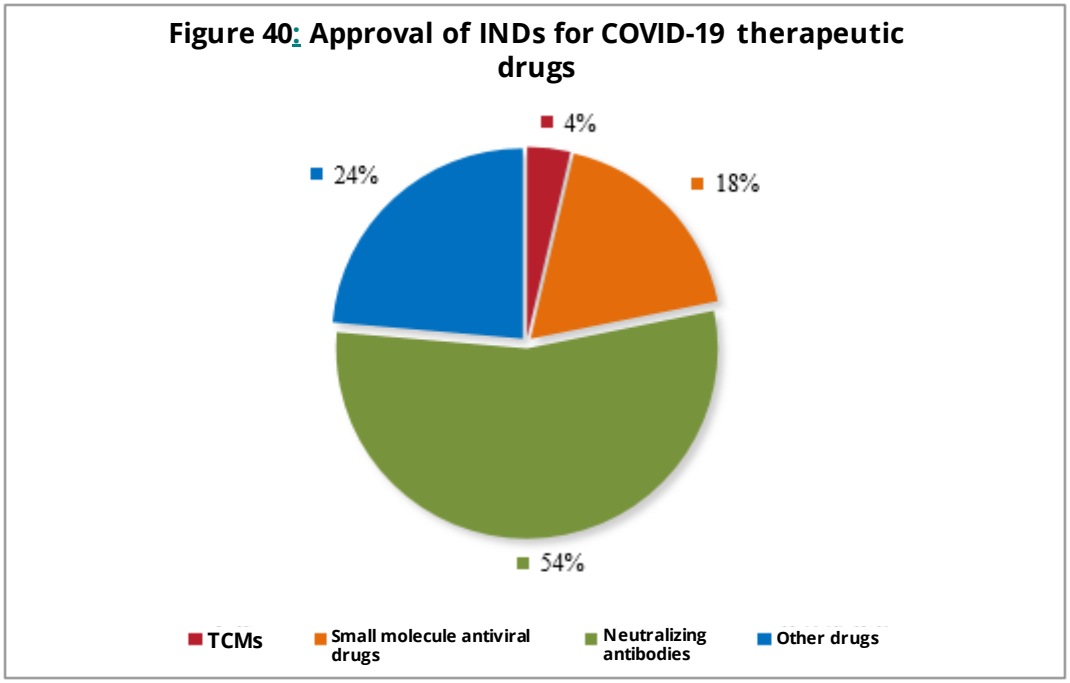
Figure 40: Approval of INDs for COVID-19 therapeutic drugs



(2) The CDE maintained the link between research and review, innovated its workflows and efficiently completed the emergency review of COVID-19 vaccines

The CDE also thoroughly implemented the deployment of the CPC Central Committee, the State Council and the NMPA, continuously optimized its 24x7 emergency review and approval system through early intervention, continuous tracking, linkage research and review, and scientific review.

The CDE redoubled its efforts in driving conditional approval for marketing four COVID-19 vaccines, approved clinical trials of 27 vaccine varieties in five technical routes (wherein, nine varieties entered Phase III clinical trials), and made major breakthroughs in the review of COVID-19 vaccines.

It served vaccine makers, provided them with full-process guidance, actively communicated with the WHO, fully supported the inclusion of two COVID-19 vaccines made in China into the WHO Emergency Use Listing (EUL), achieving historic breakthroughs. These efforts provided important guarantees for epidemic prevention and control, the resumption of labor and production and the promotion of economic and social development in China. These efforts provided solid support CPC General Secretary Xi Jinping's commitment to the "vaccine as a public good for all human beings", demonstrated the "quality of products made in China" and "accountabilities of a responsible major country" in emergency review and approval of vaccines while injecting strong confidence into the global joint endeavors in overcoming COVID-19.

The CDE promoted the expansion of production, guaranteeing the quality and supply of COVID-19 vaccines. It innovated workflows and assigned staff members to COVID-19 vaccine makers places like Jiangsu Province, Anhui Province and Beijing to study and solved technical problems. It conducted emergency reviews for expansion of production capacity, growing China's annual vaccine production capacity to several billion doses. It made vaccines more accessible and affordable, ensuring that supply would meet demand.

The CDE continued to strengthen service guidance and persistently tracked progress of COVID-19 vaccine R&D, especially focusing on clinical trials of recombinant protein and nucleic acid vaccines. It promoted the market approval of more COVID-19 vaccines, expanding the "arsenal" and supplementing the "ammunition" to fight COVID-19.

The CDE paid close attention to the emergence of new COVID-19 strains, provided technical guidance and urged makers to carry out studies and promptly adjusted R&D strategies.

The CDE urged marketing authorization holders (MAHs) of COVID-19 vaccines to fulfill their obligations upon conditional approval, keeping them informed about safety guidelines for conditionally approved products.

The CDE attended video teleconferences held by such organizations as the WHO and the International Coalition of Medicines Regulatory Authorities (ICMRA) to explore R&D and evaluation standards, to align China's standards for R&D and vaccine registration with the rest of the world. These efforts laid a solid foundation for COVID-19 vaccines made in China to enter the global market and contributed invaluable Chinese drug regulatory knowledge to help in the global fight against COVID-19. By the end of 2021, CDE personnel had attended 71 WHO-related meetings and 49 ICMRA-related meetings.

The CDE incorporated best practices into emergency review process, improving workflows that accelerated the review and approval of applications for the marketing of innovative drugs, new drugs and vaccines.

Chapter 7: Continued evaluation and approval system reforms

(1) The CDE took multiple measures simultaneously to meet urgent clinical needs for pediatric drugs and to promote the R&D and innovation of pediatric drugs

"Supporting the R&D of and practicing strict regulation of pediatric drugs" is one of Top Ten Projects of "Drug Regulation Benefiting Makers and People" in keeping with the principle "doing practical work for the masses". This is part of the NMPA's program for Learning and Education of the Party History. To solve the urgent medication problems the CDE carried out multiple measures simultaneously and made precise efforts to solve R&D problems in pediatric drugs, promote their innovation and meet clinical needs.

The CDE innovated its review system for pediatric drugs. It established a special working group that facilitated "unified deployment of tasks, overall deployment of forces and promotion of integrated work ". Moreover, it grew its capacity for identifying and solving problems.

The CDE conducted in-depth investigations and coordinated all stakeholders to tackle difficult problems in pediatric medication. Regulatory authorities, clinical institutions and drugmakers are required to work together. The CDE assigned staff members to the National Children's Medical Center of China to conduct inspection symposiums with scientific research companies with the aiming of improving China's R&D and regulation of pediatric drugs.

The CDE implemented a policy of priority review and approval of pediatric drugs applications, to make them safer and more accessible. It adhered to "high standards, strict requirements and enhanced services". It applied its learnings from the emergency review and approval of COVID-19 therapeutic drugs. It gave special designations to "pediatric drugs" in the review system. It optimized the allocation of review resources, assigning dedicated staff members for the review of their applications. It accelerated the marketing of pediatric drugs. 24 drug marketing authorization applications for drugs indicated for children were approved for marketing through the Priority Review and Approval Procedure (PRAP).

CDE further improved the system of review standards for pediatric drugs to guide scientific R&D. In line with the principle of "drugs for urgent use first" and in combination with clinical practice, reference to international experience, concentrated expert wisdom and bold exploration practice, CDE established an evidence system for review of R&D of pediatric drugs covering guidelines for support by real-world data, etc. As of the end of 2021, 12 special guidelines for pediatric drugs, such as Guidelines on Pharmaceutical Development of Medicines (Chemical Drugs) for Pediatric Use (Draft for Comments), Technical Guidelines for Using Real-World Evidence (RWE) to Support R&D and Regulatory Review of Pediatric Drugs (Draft for Comments) and Technical Guidelines for Clinical Trials of Drugs with Attention Deficit Hyperactivity Disorder (ADHD), have been issued, which improved the standards for evaluation of clinical trials and safety of pediatric drugs, provided important technical support and review basis for R&D and review of pediatric drugs, stimulated the R&D vitality of pediatric drugmakers, and better guided the scientific R&D of pediatric drugs.

The CDE information inserts for marketed drugs to ensure proper scientific use of pediatric drugs in clinical practice. It curbed off-label use and has worked to prevent inaccurate dosage from splitting pills. In conjunction with the National Children's Medical Center of China and its medical complex members, the CDE also established the Program for Standardization of Package Inserts for Children in China. So far, the CDE have compiled a list of two batches of pediatric drugs requiring package insert revisions.

The CDE intensified efforts in policy publicity and training on pediatric drugs. On June 1, 2021, it opened the "Pediatric Medication Column" on its official website. This was designed to release policies, regulations, guidelines, training materials, product approval information and other content related to pediatric drugs in a timely manner. It will make China's efforts in its review of applications for pediatric drugs more transparent. The *People's Daily* published an article titled "Multiple measures to encourage the R&D and production of pediatric drugs: meeting the demand for drugs and ensuring medication safety". Additionally, *China Medicine Daily* published an article titled "Fully tackling the difficult issue of shortages in pediatric drugs".

(2) Improving the clinical trial management system and the quality of clinical studies

1. Release of the Annual Report of the Status Quo of Registered Clinical Trials of New Drugs in China (2020)

To maintain the status quo for clinical trials for new drug registrations (NDA) in China, make the progress of clinical trials more transparent to the public, and provide a reference for R&D, resource allocation and new drug review and approval, the CDE conducted a comprehensive summary and analysis on the status quo of clinical trials for NDA in China for the first time. It was based on clinical trial information about NDAs on the Platform for Registration and Information Publicity of Drug Clinical Trials and was issued the Annual Report on the Status Quo of Clinical Trials for New Drug Registration in China (2020).

The CDE will focus efforts on regulatory innovation and improve regulatory efficacy based on clinical trial registration for NDAs in China. It will improve communication with the industry in promoting the modernization of drug regulation, increase transparency and promote the high-quality and healthy development of clinical trials for NDAs in China.

2. The CDE improved the progress clinical trials and safety regulation for COVID-19 vaccines and therapeutic drugs

The CDE adjusted and optimized safety regulation measures, implemented high-frequency pharmacovigilance and safety risk regulation. During clinical trials for COVID-19 vaccines and therapeutic drugs, it enhanced safety monitoring and risk mitigation for key drug products in strict accordance with regulations. By the end of 2021, 82 COVID-19 vaccines and therapeutic drugs approved for clinical trials were included in the special channel for clinical trial safety risk management.

3. Promoting Good Pharmacovigilance practice

Good Pharmacovigilance Practice of China ("CN GVP") was initiated on December 1, 2021. The CDE took part in the formulation of the CN GVP and its supporting documents as well as the publicity for its implementation, training, and technical interpretation. This was intended to improve applicants' awareness of major pharmacovigilance (PV) responsibilities and promote CN GVP's practical implementation.

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4. Improving Pharmacovigilance and Safety Risk Management during Clinical Trials

The CDE kept abreast of the latest dynamics of international PV practice. It improved new PV theories, methods and tools in line with the realities in China. It built the regulatory science system and working platform to develop PV discipline. First, it optimized the safety information review procedure; built a system for safety risk management during clinical trials (CTRiMS); electronically managed safety information detection and risk mitigation; and improved the coordination, orderliness, and standardization of safety risk management (SRM) during clinical trials. Second, it upgraded the PV receiving system to meet regional requirements for E2B (R3); improved safety database application functions; and promoted the transformation and implementation of ICH E2B (R3) and ICH E2A guidelines in China. Third, it optimized the SRM mechanism and set up the Safety Information Monitoring Team to monitor, identify, analyze, and preliminarily evaluate safety information to form opinions on risk mitigation. Fourth, it established the three-level risk mitigation approach for safety clinical trial safety information (i.e., letters of notification on clinical trial risk management, risk control and suspension or termination). Moreover, it strongly managed safety information reporting and evaluation during drug clinical trials.

5. The CDE steadily improved its capacity in risk identification for safety information

In 2021, the CDE received 7,197 initial reports of suspected unexpected serious adverse reactions (SUSAR) during clinical trials in China (up 54.51% YoY) and 2,568 annual development safety update reports (DSUR) (up 42.82% YoY). 15,075 entries were registered on the clinical trial registration platform (including initial registration and registration updates), up 22.95% YoY. The CDE issued 86 letters of notification on clinical trial risk management, 21 letters of notification on clinical trial risk control and one letter of notification on suspension of clinical trial). In addition, the CDE recommended five voluntary trial suspensions.

A rapidly advancing mode of R&D was adopted for both COVID-19 vaccines and COVID-19 therapeutic drugs, presenting some potential risks. Many subjects were included clinical trials over a short period of time. The CDE always prioritized the safety of COVID-19 vaccines and therapeutic drugs, strengthened safety regulation of clinical trials, increased the frequency of safety regulations, strengthened early risk warnings, improved the flexibility of safety regulations, and processed the warning information as quickly as possible. The CDE ensured that risks in clinical trials were controllable, and subjects were safe. It met public safety needs for COVID-19 vaccines therapeutic drugs as early as possible.

(3) Establishing China Patent Information Registration Platform for Marketed Drugs

To implement the Opinions of the General Office of the CPC Central Committee and the General Office of the State Council of the PRC on Deepening the Reform of the Review and Approval System and Encouraging the Innovation in Drugs and Medical Devices (No. T [2017]42) and the Announcement of the State Administration and the State Intellectual Property Office of the PRC on Issuing the Implementation Measures for the Early Resolution Mechanism for Drug Patent Disputes (Interim) (No.[2021]89), the CDE explored the establishment of an early resolution mechanism (ERM) for drug patent disputes. In accordance with the law, it set a waiting period, a patent protection period, or a market-exclusive period for drug products applicable to the ERM for patent disputes. The CDE also established the China Patent Information Registration Platform for Marketed Drugs.

1. The CDE solicited opinions and suggestions from all sectors of the community with a problem-solving mindset

The CDE strengthened communication and coordination by inviting relevant departments, authorities and industry experts for seminars on platform building. This was an effort to solicit professional opinions from the industry and identify and solve problems. During the commissioning of the Patent Information Registration Platform for Drugs Marketed in China, the CDE answered and addressed the problems raised from all sectors of society, simultaneously optimizing the functions of the platform.

2. The CDE released operation guidelines and other relevant documents, to improve the platform user experience

The CDE released guidance documents like Guidelines for User Operation of the Patent Information Registration Platform for Drugs Marketed in China and the Instructions on Filling out the Registration Form for Patent Information of Drugs Marketed in China to provide clear guidance for applicants. For the sake of full disclosure, 1,476 patent information entries were registered by 325 marketing authorization holders (MAHs), involving 1,090 drugs. 959 patent statements were disclosed, including 783 Class I statements, 65 Class II statements, 175 Class III statements and 97 Class IV statements.

(4) Solidly promoting the consistency evaluation of generic drugs

1. The CDE continuously selected reference preparations

The CDE continued to standardize the selection process. It improved work efficiency and selected reference preparations according to the requirements of the Work Process of the Center for Drug Evaluation of the NMPA for Selection of Reference Preparations of Chemical Generic Drugs. Since consistency evaluation was carried out in August 2017, a total of 49 batches of reference preparation lists have been released, involving 4,677 product specifications (involving 1,967 varieties), including 1,253 product specifications (involving 477 varieties) of reference preparations for injections. In 2021, the CDE released 850 product specifications (involving 527 varieties) of reference preparations.

2. The CDE continued optimize consistency evaluation

In 2021, 331 products passed consistency evaluations. To better carry out consistency evaluations, the CDE sorted relevant data of chemical drug marketed in China and analyzed drug varieties with clear clinical value but no original drug control, innovative drugs manufactured in China, and drugs unique in China. This provided reference for subsequent consistency evaluations. The CDE formulated technical requirements for pharmaceutical studies for 75 drug products, drafted 27 guidelines for bioequivalence of individual drugs, and gradually improved the system of review standards. Meanwhile, the CDE held a consistency evaluation symposium with drugmakers. It fully listened to opinions and suggestions they put forward and took in their pain points in their subsequent work.

3. Optimizing consistency evaluation column

CDE optimized the special column of “Consistency Evaluation of Quality and Efficacy of Generic Drugs” on CDE’s official website and assigned dedicated staff members to update and maintain this special column, and timely update the package inserts of oral solid preparations passing consistency evaluation, manufacturer’s study reports and bioequivalence trial data, lists of reference preparations, policies and regulations, technical guidelines, and other relevant information.

(5) Increasing the transparency of review and approval[25]

First, CDE intensified efforts in disclosure of review information and established a long-acting mechanism for disclosure of review information. CDE formulated the Standards of the Center for Drug Evaluation of the NMPA for Disclosure of Technical Review Reports (Interim) and released the 2020 Annual Report for Drug Review, to improve review transparency. As of the end of 2021, CDE cumulatively disclosed 500 reports for technical review of new drugs. Second, CDE continuously promoted disclosure of review information. CDE added such columns as "Publicity of Breakthrough Therapy" on its official website to disclose the information of expedited drugs highly concerned by applicants; meanwhile, CDE launched the Objection Resolution System, functioning to open a channel for raising objections to review conclusions and timely respond to social concerns. Third, CDE constantly strengthened informatization. CDE upgraded and transformed its official website. CDE added such special columns as "Pediatric Drugs", "Administrative Acceptance Services", "Guidelines" and "Electronic Common Technical Document (eCTD) for Drugs", to enhance the proactivity of review information disclosure, convenience of information retrieval and timeliness of information update, and continuously meet the demands from the public and applicants. Fourth, CDE further deepened the reform of "delegating power, improving regulation and upgrading services", accelerated the realization of "access more government services via a single website" and promoted the overall linkage of drug regulatory services. With the goal of building an online service platform featuring overall linkage, high efficiency, and convenience for the people, CDE integrated the internal account system, connected it with the Online Service Hall of the NMPA, and achieved unified account, portal, and login.

In 2021, CDE disclosed 11,546 entries of registration application information already undertaken, publicized 112 entries of information on drugs included in priority review, 51 entries of information on drugs included in breakthrough therapy designation (BTD), publicized 3,757 entries of information on applications for communication, disclosed 2,873 entries of information on applications for approval of implied license for clinical trials, and disclosed 184 entries of information on review reports for marketed drugs. CDE disclosed 2,524 tasks of APIs, pharmaceutical excipients and pharmaceutical packaging materials that passed registration review or passed review after application acceptance. In 2021, CDE realized inquiries about the progress of review of APIs for the first time, realized related inquiries with related preparations, disclosed 927 tasks of inquiries on progress of separate review of APIs and 443 tasks of related inquiries on related preparations, and continuously promoted disclosure of review progress.

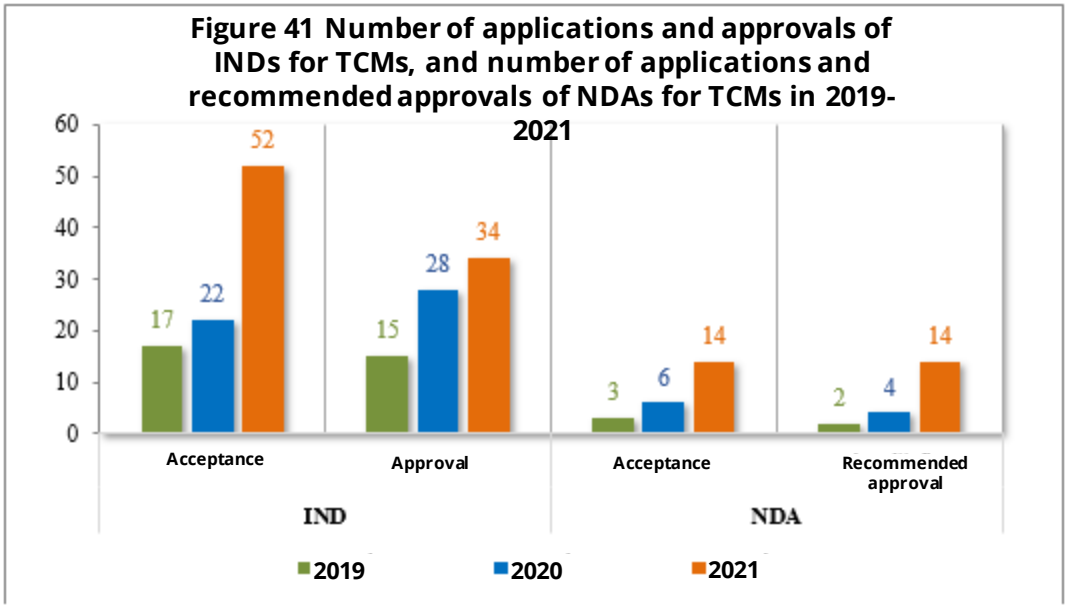
(6) CDE promoted electrification for submission drug registration applications

To promote the electronic submission of applications for drug registration and improve the service efficiency of "Internet plus Drug Regulation", CDE formally implemented the eCTD program. First, CDE released technical specifications to guide applicants in preparing eCTD dossiers. CDE formulated eCTD such technical documents as technical specifications and implementation guidelines, to provide technical guidance and compliance standards for applicants to prepare electronic submission dossiers. Second, CDE carried out publicity for implementation, to improve the enthusiasm of applicants for eCTD submission. CDE formulated a publicity and interpretation plan and carried out publicity to external stakeholders, to help applicants to understand the technical requirements and submission process of eCTD. Third, CDE made efficient efforts in relevant informatization, to facilitate eCTD submission by applicants. CDE built the special column of eCTD for centralized disclosure of domestic and overseas/international guidelines and work dynamics, etc., and built the eCTD submission system to dock with the drug business application system of the NMPA, to open the electronic channel for the whole process of drug registration application. Fourth, CDE carried out information security evaluation, to improve information security. CDE carried out multiple measures such as eCTD level protection assessment, password application security assessment and cybersecurity risk assessment, to effectively control and reduce information security risks.

Chapter 8: Promoting the heritage, innovation and development of TCMs

From 2019 to 2021, the number of INDs for TCMs (17, 24, 52), number of approved INDs for TCMs (15, 28, 34), number of NDAs for TCMs (3, 6, 14), and number of NDAs for TCMs recommended for approvals (2, 4, 14) saw a trend of year-over-year growth. See Figure 41 for the number of applications and approvals of INDs for TCMs, and the number of applications and recommended approvals of NDAs for TCMs in 2019-2021.

Figure 41 Number of applications and approvals of INDs for TCMs, and number of applications and recommended approvals of NDAs for TCMs in 2019-2021



(V) CDE implemented the requirements for reform and improvement of the mechanism for review and approval of TCMs, and promoted the establishment of the "Three-in-One"[26] Registration-Review-Evidence (RRE) System

CDE conscientiously implemented the Opinions of the CPC Central Committee and the State Council of the PRC on Facilitating the Inheritance, Innovation and Development of Traditional Chinese Medicine and the spirit of the instruction from CPC General Secretary Xi Jinping on reforming and improving the mechanism for review and approval of traditional Chinese medicine (TCM), deeply studied and summarized the practical experience in review and approval of TCM and the results of the reform of the drug review and approval system in line with the principles of "inheriting the essence, adhering to the right way while making innovations, and achieving high-quality development", proactively and actively studied the opinions on adjustment of registration classification for TCMs, accelerated the establishment of the "Three-in-One" RRE System, paving a smooth way for registration of new TCMs.

CDE formulated the review standards and guidelines for TCMs based on the "Three-in-One" RRE System. In view of the adjustment and communication focus of study strategies and methods under the "Three-in-One" RRE System, CDE translated the consensus on experience in human use already formed so far into the guidelines, and released two guidelines, i.e., Guidelines for the Preparation of Submission Dossiers of Traditional Chinese Medicine Theories for New TCMs and TCM Compound Preparations (Interim) and Guidelines for the Preparation of Package Inserts for TCM Compound Preparations in Ancient Classic Famous Recipes (Interim). CDE selected three specific indications (i.e., malignant tumor, chronic gastritis, and gastroesophageal reflux disease) as breakthrough points, introduced new tools and new methods (e.g., real-world study), worked together with authoritative experts in the fields of clinically relevant indications of TCM to conduct studies regarding the technical requirements for clinical efficacy evaluation in line with the characteristics of TCM, and formed the guidelines step by step.

(II) CDE studied to optimize the registration classification and opened a new path for the R&D and review of TCM compound preparations in ancient classic famous recipes

CDE conducted a systematic study on Class 3 "TCM compound preparations in ancient classic famous recipes" in the TCM classification in the current Provisions for Drug Registration, added the classification item "Class 3.2 Other TCM compound preparations derived from ancient classic famous recipes" based on the thought of the "Three-in-One" RRE System, and put forward a series of corresponding registration management requirements. This new classification item embodies the principle of "inheriting the essence and adhering to the right way while making innovations", and it is different from the R&D mode of innovative TCMs. This classification item is of a very positive significance for accelerating the transformation of the achievements in the fields of classic famous recipes (prescriptions) inherited in long-term TCM clinical practice, experience prescriptions from famous old TCM experts and hospital preparations as well as fully meeting the needs for TCM clinical treatment. Through the review of TCM varieties related to "Three TCM Prescriptions", CDE practiced the review procedure, key points for clinical and pharmaceutical review and technical requirements adapted to the classification item and won high appraisal from authoritative experts such as TCM academicians and national-level TCM masters.

In accordance with the work deployment of the NMPA and the State Administration of Traditional Chinese Medicine of the PRC ("NATCM"), CDE continued to promote the establishment of the Expert Review Committees for TCM Compound Preparations in Ancient Classic Famous Recipes.

(III) The CDE continuously enhanced studies on standards to build a whole-process quality control (QC) system in line with the characteristics of TCMs

The CDE followed TCM theories, traditional experience in TCM, and R&D. It conducted in-depth studies on TCM characteristics and TCM review standards. It established and improved the whole-process QC system for new TCMs, formulated the technical guidelines for research and evaluation in line with the characteristics of TCM, changed the TCM QC concept of "focusing on ingredients only", and basically built up the whole-process QC system for new TCMs covering TCM medicinal materials, prepared TCM in pieces and TCM preparations, etc. It also established requirements for the whole life cycle management of TCM. The CDE released the Technical Guidelines for Studies on Quality of New TCMs (Interim). The guidelines prioritized safety and effectiveness of long-term clinical use of TCMs, value-oriented clinical applications, and the unique characteristics of TCM in guiding drugmakers to formulate QC methods and strategies. The guidelines emphasize concepts like "quality originates from design" and "whole-process QC", to guide drugmakers to better control quality.

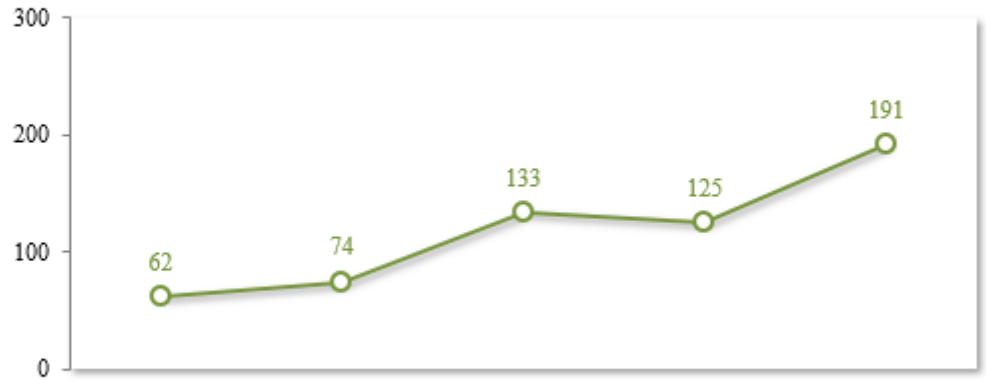
The CDE conducted an in-depth study and summary of the experience and achievements in research on TCM changes and regulations in recent decades. It abolished the TCM evaluation pattern of "focusing on ingredients only" and established new standards for evaluation of change studies based on production process, experience in human use and quality evaluation, and released the Technical Guidelines for Studies on CMC Changes of Marketed TCMs (Interim). This was done to promote the development of the TCM industry, optimize the technical requirements for CMC changes of marketed TCMs and address the challenges that have long plagued drugmakers..

(IV) The CDE strengthened guidance for applicants and accelerated the review of new TCMs with clinical value

The CDE included new TCMs with significant clinical value into the Priority Review and Approval Procedure. Through multiple manners such as inquiry-type communication, professional inquiry, and online video conference, the CDE proactively communicated with applicants on key technical issues/problems/concerns, to make applicants more focused in their reply at Expert Consultation Meetings (ECMs) and improved the quality and efficiency of preparation of review-required documents, such as supplementary materials, package inserts and quality standards. The CDE made every effort to accelerate the review of applications for marketing authorization of TCMs and give full play to the unique advantages of TCM in disease prevention and treatment.

Since the release of the Administrative Measures for Communication of Drug R&D and Technical Review, the number of CDE-processed applications for CMs for new TCMs has been increasing year after year, from 62 (cases) in 2017 to 74 in 2018, 133 in 2019, 125 in 2020 and 191 in 2021. Through communication with applicants, the CDE preprocessed concerns in submission dossiers, improving the quality of submission dossiers and the efficiency of review. See Figure 42 for the applications for CMs for new TCMs in 2017-2021.

Figure 42 Applications for CMs for new TCMs in 2017-2021



(V) The CDE actively assisted Xinjiang and Tibet to promote the development of ethnic drugs

According to the NMPA's deployment and work requirements, the CDE assigned staff members to Xinjiang, Tibet, and other ethnic regions to carry out investigations, trainings, and symposiums. This increased their understanding of existing problems in the R&D of ethnic drugs and spurred exploration of ways to adapt ethnic drug registration, and promote their R&D and uses in clinical treatments. The CDE answered hundreds of questions from ethnic drugmakers based in Xinjiang and Tibet online, to help address issues in R&D and the registration process. The CDE promoted the R&D of ethnic drugs, prioritized the allocation of review resources for them, strengthened service and guidance for their registration, and communicated efficiently throughout the review process.

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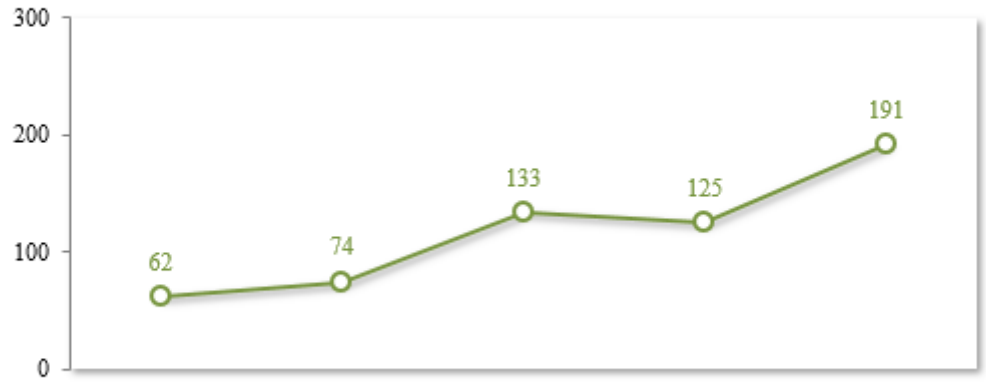

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Chapter 9: Modernizing Review System and Review Capacity

(I) Working to guarantee the NMPA's re-election to the ICH Management Committee

The CDE ICH Work Office has made the following efforts to ensure that the NMPA was successfully re-elected to the ICH Management Committee. First, it secured the understanding and support of all ICH members. It organized the "ICH China Progress and Outlook Conference" and showcased China's achievements in ICH work to international trade associations. It organized and participated in the ICH Theme Day event during the Chinese Annual Meeting of the Drug Information Association (DIA). It engaged in-depth exchanges with representatives from European, American, and Japanese institutions on promoting international coordination of ICH and other issues; and jointly held seminars with Japanese regulators to comprehensively deepen exchanges and cooperation with international regulators and industrial community. Second, it familiarized the public with the representative fields of the industry. Second, on April 28, 2021, it held the "Implementation Presentation of ICH's Guidelines". 14,000 people viewed it online and 11,000 viewed recording of the presentation. Third, it paid close attention to the ICH Management Committee election process. It conducted in-depth research, and prepared the application materials for the election. These actions have laid solid foundations for the NMPA's successful re-election to the ICH Management Committee on June 3, 2021.

(II) Promoting the transformation and implementation of ICH guidelines and coordination of issues

The CDE's ICH Work Office has further promoted the implementation of the ICH guidelines in China. In 2021, the NMPA approved and issued six ICH guidelines. These identified the timeline for implementing nine of ICH's guidelines. As of the end of 2021, the NMPA has fully implemented 53 ICH guidelines, 84.13% of the total. The CDE ICH Work Office was also deeply involved in the coordination of ICH issues. At present, ICH has a total of 28 active issues. 53 experts have been assigned to the Expert Working Group for Coordination of ICH Issues. The Office has participated in 379 telephone conferences held by the Working Group.

(III) Building a more reasonable and process-oriented scientific management system

With the support and guidance of the Discipline Inspection and Supervision Team under the National Supervisory Commission of CPC Central Commission for Discipline Inspection to the State Administration for Market Regulation and the Party Group of the NMPA, the CDE's pilot scientific management system has been running smoothly. The CDE has established and revised 28 scientific management system plans, release 17 systems, and advanced 58 reform measures. The CDE built up a process-oriented scientific management system for internal review. It further improved the institutional standard systems and risk prevention and control mechanisms. The review process has become clearer and reviews and approvals have become more efficient. Service awareness and applicant satisfaction increased, and the CDE's reputation significantly improved. A process-oriented, solution-driven drug review and approval system has taken shape. Moreover, the CDE revised its Good Review Practices (GRP). Taking this as a new starting point the CDE will continue to leverage the working mechanism for building a process-oriented scientific system, to constantly solve new problems, study new measures, and continuously modernize the CDE's review system and review capacity.

(IV) Building a talented team

The CDE has made great efforts to build a talented team. It has established a clear employment orientation, adhering to strict management and great kindness, placing equal emphasis on incentives and constraints, and encouraging staff to take initiative. As such, the CDE build up its review team and its capacity. It effectively recruited talent and ensured that staff received thorough training. It made development channels available for staff members. The CDE put in place a more efficiently review and application system for senior professional titles. It reviewed and appointed staff for technical positions and chief reviewers. It identified intermediate professional titles and management levels removing the bottleneck for career development. The CDE continued to build the institution with 11 systems, such as Provisions for Staff Resignation, Provisions for Staff Members Engaged in Part-time (Full-time) Jobs, Provisions for Attendance and Leave, and Provisions for Going Abroad for Private Purposes. Additionally, the CDE improved performance evaluations and further standardized incentive and restraint mechanisms for all staff members.

(V) Guiding and standardizing the work of Sub-Centers for Drug Evaluation (sCDEs)

Establishing sCDEs in the Yangtze River Delta and the Greater Bay Area was an important measure proposed by the CPC Central Committee and the State Council. The measure was intended deepen reform and deploy strategic development plans. This provides comprehensive support for the reform, innovation, and capacity building of drug reviews. Under the unified leadership of the NMPA, the CDE implemented national and regional strategies, fulfilled the requirements of “unified review team, unified business management, unified review system, and unified review standards”, and improved planning design and support for the construction of these sCDEs. The CDE also intensified operational support and guidance, enhanced professional training, encouraged sCDEs to play their roles as soon as possible, and facilitated the regional development of the pharmaceutical industry. The CDE has accomplished the following:

First, the CDE established a work coordination framework for sCDEs. It established a special work group to study and promote their operational development and talent recruitment. The CDE enabled sCDEs to conduct review work. Second, the CDE organized a variety of one-on-one training sessions both on- and offline. It has trained sCDE staff in review task management, expert meetings, communication, technical review and more. Third, the CDE supported and guided sCDEs in communication-related work. For key varieties with clinical value, the CDE provided sCDEs with technical support to guide applicants in their respective regions. The CDE organized 17 CMs, released its “Notice Regarding Starting the Work of Answering General Technical Questions at the Sub-Center for Drug Evaluation in the Yangtze River Delta and the Greater Bay Area Under the NMPA”. It opened ports for applicants to submit general technical questions to sCDEs, and guided sCDEs in answering 1,415 of these questions. Fourth, it held seminars and trainings on post-marketing changes in Shanghai and Shenzhen. It established a communication and coordination system between the CDE, sCDEs, and provincial NMPA offices for determining post-marketing changes for drugs. The CDE dispatched staff to two sCDEs to train teams in guidelines for post-marketing changes of drugs. Approximately 2,000 people in the Yangtze River Delta region participated. 500 took part in the Greater Bay Area.

Since their inception, these two sCDEs have provided services, conducted in-depth research to understand drugmakers’ needs, and addressed prominent problems that drugmakers encountered in drug R&D and registration. Looking ahead, the CDE will work with these two sCDEs to continue reforming the review and approval system, improve their quality of service, and encourage innovation in the pharmaceutical industry. It will also guide and support the sCDEs in ensuring that teams work efficiently and maintain political and personal integrity.

Chapter 10: Improving the technical guideline system for drugs at an accelerated pace

In recent years, with the rapid development of the pharmaceutical industry, new technologies, new targets, new mechanisms, and new achievements continue to emerge. There are more drug RAs, and several innovative high-tech drugs have entered the registration review and approval process. To keep up with this unprecedented change of pace and meet the pharmaceutical industry's development needs, technical guidelines for drugs must also be forward-looking yet standardized, instructive and effective in application. With the aim of meeting drug R&D needs and fostering innovation, the CDE continuously promoted system and review capacity modernization. It was committed to building a scientific, authoritative and transparent review standard system. This would address issues that affect and restrict drug R&D innovation, quality, and efficiency.

In accordance with the Notice of the Department of Comprehensive Affairs of the NMPA on Printing and Issuing the Release Procedure of Technical Guidelines for Drugs (DCA (2020) No. 9), the CDE enhanced efforts to draft and formulate guiding principles. The NMPA reviewed and approved 87 guiding principles in 2021. Since the establishment of the drug review standard system, the CDE has released 361 guidelines, covering the fields of TCM, chemical drugs and biological products, etc. These address challenging issues in R&D, such as COVID-19 therapeutic drugs, ancient formulations (prescriptions), cell and gene therapies, etc. At present, a technical standard system of guidelines have been formed. It provides powerful and scientific technical support for the innovation and development of the pharmaceutical industry and drug review. See Annex 7 for the technical guidelines the CDE completed in 2021.

In terms of accelerating the R&D and marketing of COVID-19 therapeutic drugs, the CDE has issued the Technical Guidelines for Non-clinical Studies on COVID-19 Neutralizing Antibody Drugs (Interim), the Technical Guidelines for Non-clinical Pharmacodynamic Studies and Evaluation on Drugs Against COVID-19 Inflammation (Interim) and the Technical Guidelines for Non-clinical Pharmacodynamic Studies and Evaluation on Chemical Drugs Against COVID-19 (Interim). It stayed current on domestic and international developments in COVID-19 and the clinical needs for its treatment. It prioritized COVID-19 neutralizing antibody drugs, anti-inflammatories, and chemical drugs for R&D, review and approval and improved its guidance on the R&D of related drugs.

In an effort to support and promote the heritage, innovation and development of TCM, the CDE released the Guidelines for the Preparation of Submission Dossiers of Traditional Chinese Medicine Theories for New TCMs and TCM Compound Preparations (Interim), the Guidelines for the Preparation of Submission Dossiers of Traditional Chinese Medicine Theories for New TCMs and TCM Compound Preparations (Interim) and the Technical Guidelines for Pharmaceutical Studies on TCM Compound Preparations Managed as per the List of Ancient Classic Famous Recipes (Interim). It developed a registration-review-evidence system featuring TCM theories, experiences in human use and clinical trials. It also standardized the preparation of TCM theory submission dossiers and the contents of package inserts for compound preparations of ancient formulas.

In the interest of meeting urgent clinical needs for pediatric drugs and promoting their innovation and, the CDE released the Technical Guidelines for Clinical Trials for Modified New Chemical Drugs for Children (Interim) and the Technical Guidelines for the Preparation of Information Related to Pediatric Medication in the Package Inserts of Chemical Drugs and Therapeutic Biological Products (Interim). It encouraged drug developers to develop dosage forms and strengths suitable for pediatric use. The CDE created package inserts to provide clinical information about pediatric drugs. It has also continued to address the issue of pediatric drug shortages in clinical practice.

For cell and gene therapies, the CDE released the Technical Guidelines for Non-clinical Studies on Genetically Modified Cell Therapy Products (Interim), the Technical Guidelines for Non-clinical Studies and Evaluation on Gene Therapy Products (Interim) and the Technical Guidelines for Clinical Studies on Long-term Follow-up for Gene Therapy Products (Interim). These standardized studies and evaluations of cell and gene therapy drugs in China. They also further improved drugmakers' R&D efficiency and guided the healthy development of the industry.

For the anti-tumor drug R&D, the CDE released its Guidelines for Clinical Value-oriented Clinical Research and Development of Antitumor Drugs, the Technical Guidelines for the Application of Biomarkers in Clinical Research and Development of Antitumor Drugs and the Technical Guidelines for Expanded Cohort Studies on First-in-Human Trials for Anti-Tumor Drugs (Interim). These put forward suggestions on the clinical R&D of anti-tumor drugs from the perspective of patient, guiding drugmakers to implement the clinical value-oriented and patient-centered R&D processes and promoting the scientific and orderly development of anti-tumor drugs.

For the treatment of RDs, the CDE released the Technical Guidance for Clinical Research and Development of Drugs for Rare Diseases. This was intended to promote the R&D of drugs targeting more low-incidence diseases and demonstrated the CDE's confidence and determination in promoting the R&D of drugs for rare diseases (DRDs) in China. The CDE strives to bring more DRDs previously neglected by the market into the R&D fast lane to bring more hope to marginalized RD patients. Also, to counter the generally low enthusiasm for R&D of DRDs, the CDE encouraged drug makers to focus more R&D on RDs. The ultimate objective of these measures was to prevent and treat RDs and meet the needs of patients suffering from them.

The CDE released its Guidelines for Real-World Data Used to Generate Real-World Evidence (Interim). This clarified requirements for data used in answering clinical scientific questions during review. It emphasized that real-world data is not equivalent to real-world evidence, and offered recommendations to the industry for using real-world data to support R&D. The guidelines will elevate China's real-world data to the global forefront of policy regulation.

To address post-marketing changes of drugs, the CDE released the Technical Guidelines for Studies on CMC Changes of Marketed Traditional Chinese Medicines (Interim), the Technical Guidelines for Studies on CMC Changes of Marketed Chemical Drugs (Interim), and Technical Guidelines for Studies on CMC Changes of Marketed Biological Products (Interim). The aim was to implement the whole lifecycle management (WLCM) of drugs, and guide studies on CMC changes of marketed TCMs, chemical drugs and biological products in China as well as provide applicants with referenceable technical standards.

The formulation and release of the guidelines further improved the drug review system of China and provided strong technical support for scientific and fair review decision-making. Meanwhile, the CDE encouraged scientific research institutions, applicants, and industry associations to participate more in the preparation of drug guidelines, to form a virtuous cycle for the building of the drug guidelines system, to better promote further consummation of China's drug guidelines system.

Chapter 11: Building of Party Administrationand Incorruptible Government is Effective and Efficient

Under the guidance of Xi Jinping Thought on Socialism with Chinese Characteristics for a New Era, the CDE strengthened its political consciousness of loyally supporting the "Two Establishments" and steadfastly practicing the "Two Safeguards", implementing the powerful results of political responsibilities for managing and governing the Party and provide a solid political guarantee for promoting the reform and innovation of drug review.

First, it formulated the Implementation Scheme for CDE Party Committee to Carry out Learning and Education of the Party History. It convened a mobilization and deployment conference and set up a supervision team to guide all Party branches to promote learning the Party history. This manifested in several forms, such as the "Three Meetings and One Lesson" (i.e., regularly holding Party branch member conferences, Party branch committee member meetings and Party group meetings as well as attending Party classes) and Party group life meetings.

Second, the CDE carried out activities in the spirit of "I am willing to do practical work for the masses." To solve problems of an "urgent, difficult, worried and desired" nature, the CDE implemented the NMPA's Top Ten "Drug Regulation Benefiting Manufacturers and People" Projects. It engaged in 25 practical work projects (e.g., accelerating and promoting the review of applications for COVID-19 vaccines; encouraging the R&D and innovation of pediatric drugs; promoting the disclosure of review information; continuously optimizing communication channels; continuously improving the quality of services for applicants, etc.). These efforts ensure that the CDE continuously met the demands of industry and the public.

Third, the CDE effectively coordinated tasks related to inspection-based rectification required by CPC Central Committee and the Party Group of the NMPA as well as special governance against violations of the spirit of the CPC Central Committee's "Eight-Point Regulation". It resolved challenging problems in the rectification process by establishing rules and regulations, optimizing processes, and strengthening supervision and processing. The CDE also continuously improved the overall quality of work through inspection-based rectification.

Fourth, the CDE carried out special supervision on key tasks. It implemented priority supervision over epidemic prevention and control, associated review, and approval of APIs, excipients, and packaging materials as well as review and approval of COVID-19 vaccines. It also promoted important work in drug review system reform. It regularly supervision communications regarding suspension of drug products such as breakthrough therapies under review. This helped to identify hidden risks and clearly assigned owners of responsibilities.

Fifth, the CDE continuously guarded against the risk of corruption. It conducted "inspections of those who offer and take bribes" and drafted the Letter of Commitment for Legitimacy and Compliance in Behaviors of Drug Registration Applicants. It also organized staff members to report any conflicts of interest, surveyed staff members who run business or hold equity therein, and promoted an honest and upright environment for review and approval.

Sixth, the CDE insisted on normalizing warning education . It drafted an annual plan for creating clean government culture, compiled and printed the Special Issue of Education on Incorruptible Review every two months, and disseminated anti-corruption slogans to all staff members every month. All these actions helped to create a vigorously honest organization that resists corruption.

Chapter 12: Key work arrangements in 2022

In the past year, technical drug review has made active contributions to encouraging pharmaceutical innovation, maintaining health of the people, and promoting public health security. It's role in ensuring the prevention and control of COVID-19 and accelerating the development of the pharmaceutical industry has grown dramatically. As system reforms continue, the people are demanding higher standards for drug quality and safety. Likewise, the pharmaceutical industry's demand for a fair, orderly and predictable review system is growing. These complex social dynamics are the backdrop for frequent public health crises around the globe and necessitate continuous innovation in drugs. China still faces many challenges concerning drug review institutions, drug review capacity and modernization of its drug review system.

Firstly, review teams are overloaded with excessive review tasks. At present, the disparity between capacity and workload is crippling. 10,000 RAs per year means lots of working overtime to reach deadlines. Secondly, drug review capacity still needs to be further modernization. With the ever-growing globalization of new drug R&D and innovation, and the number of "global new" drugs on the rise, innovative products put continue to put undue pressure on review capacity. Finally, the drug review process must still be made more efficient. Service quality must continue to be improved and modernized. This will continue to be salient concerns look ahead.

In 2022, under the strong leadership of the Party group of the NMPA and with a focus on the deployment of key work priorities, the CDE will carry out the following key tasks:

(I) Spare no effort in reviewing oCOVID-19 vaccines and drugs

The CDE will continue work toward the overall prevention and control of the epidemic, expanding the production capacity and ensuring the quality and supply of COVID-19 vaccines. It will strictly follow the safety and effectiveness standards for drug R&D, adhere to principles of early intervention, maintain the link between research and review, scientificity, rigorousness and compliance with laws and regulations. It will spare no effort to push marketing of COVID-19 vaccines and therapeutic drugs, and continue to track progress vaccine and drug R&D. It will accelerate and facilitate the R&D and innovation of key drugs and urge makers of conditionally marketed vaccines and drugs to conduct post-marketing studies. It will summarize and consolidate good experience and practices, optimize the emergency review mechanisms and put emergency review experience into practice. Moreover, it will closely supervise the development of safety information on COVID-19 drug trials subject to emergency review and approval.

(II) Continued deep reform of the evaluation and approval system

The CDE will promote basic studies in the pharmaceutical industry and encourage drugmakers to innovate. This will addressing developmental bottlenecks within the industry. It will continue to to encourage R&D and innovation in new and effective drugs that are clinical-value oriented, drugs for RDs and major infectious diseases as well as drugs urgently needed for public health. It will optimize procedures for drugs with breakthrough therapy designation, conditional approval, and priority review and approval. It will support R&D and innovation for pediatric drugs and improve their safety and availability. It will optimize and streamline the review process. It will increase awareness of "delegating power, improving regulations and upgrading services". It will the quality of service and communication. The CDE will optimize the implied licensing system for clinical trials. It will improve the CDE Expert Consultation Committee system. It will better coordinate verification and inspection for drug registration, and implement the supporting system for the Working Procedures for Starting Verification and Inspection for Drug Registration. It will bolster the pharmacovigilance system during clinical trials and improve the capacity for managing clinical trial information. Finally, the CDE will and make headway in raising the bar on its eCTD-related work.

(III) Accelerate and facilitate the reform of TCM review and approval mechanisms

The CDE will improve the review and approval mechanism for TCMs. It a review system that incorporates TCM theories, experience in human use and clinical trials. It will promote the development and revision of technical guidelines for TCMs and a establish a review system that meets the unique needs of TCM. This will serve to promote the heritage, innovation, and development of TCM. The CDE will also establishment an Expert Review Committee for TCM Compound Preparations in Ancient Formulas.

(IV) Promote consistency evaluation for the quality and efficacy of generic drugs

The CDE will promote the consistency evaluation for oral solid preparations and injections. It will strictly follow the evaluation criteria and improve technical guideline. It will accelerate the selection of reference preparations while promoting the sorting of drug varieties without reference preparations as well as self-verification of domestically manufactured innovative drugs.

(V) Modernize the review system and review capacity

The CDE will work with relevant authorities in special campaigns to enhance drug safety. It will accelerate service capacity, establishing sCDEs in the Yangtze River Delta and the Greater Bay Area under the unified leadership of the NMPA. It will build a process-oriented scientific management system to improve the scientific review system and will prevent various risks by standardizing the exercise of authority. The CDE will also build scientific management system with clear rules and regulations for implementation. It will improve the quality and efficiency of the review process. It will prepare for inspections by the National Regulatory Authorities (NRA) for vaccine assessment. It will develop clinical value-oriented guidelines and translate and implement ICH guidelines to align domestic industrial regulation with international standards. It will promote research on regulation-related topics, improve its legal operations, and raise awareness of the law among staff and decision makers. It will ensure a sufficient review capacity, optimize the structure of professional disciplines build up review teams. Finally, it will explore new solutions to improve the quality of staff training.

(VI) Steadfastly adhere to the Party model of clean government

The CDE will deepen its understanding of Xi Jinping Thought on Socialism with Chinese Characteristics for a New Era as it earnestly studies the spirit of the Party's 20th National Congress and apprehends the decisive significance of "Two Establishments". The CDE will conscientiously put into practice the essence of the important speeches and instructions by General Secretary Xi Jinping. It will constantly enhance "Four Awarenesses" and "Four Matters of Confidence" and practice the "Two Safeguards". The CDE will conscientiously follow the major decision-making and deployment of the CPC Central Committee and the State Council, consolidate and implement the spirit of the Central Committee's Eight-Point Decision, and continue to promote building of a system that is impervious to corruption. The CDE will work hard to prevent conflicts of interests. It will diversify it publicity tools to ensure the promotion of its achievements in drug review and approval reform.

Conclusion

Practice enriches knowledge and more knowledge leads to better practice. In 2022, the CDE will continue to look to Xi Jinping Thought on Socialism with Chinese Characteristics for a New Era for guidance, earnestly implement the important instructions issued by General Secretary Xi Jinping, and fully comprehend the full spirit of the 19th National Congress of the Communist Party of China and the plenary sessions of the 19th CPC Central Committee. The CDE will deepen its understanding of the decisive significance of "Two Establishments", the "Four Awarenesses" and the "Four Matters of Confidence" as it practices the "Two Safeguards". The CDE is determined to ensure that the plan for drug safety and development during the 14th Five-Year Plan is followed. It will comprehensively strengthen the Party and continuously further comprehensive and strict Party governance. The CDE will continue deepening drug review and approval system reforms, carry out in-depth special activities to enhance drug safety, and intensely manage review teams. The CDE will work hard to conduct emergency reviews for COVID-19 vaccines and drugs, strongly support the preservation and innovation of TCM and promote the consistency evaluation of quality and efficacy for generic drugs in an orderly manner. It won't stop modernizing its drug review system and review capacity. It will remain devoted to serving the overall epidemic prevention and control effort and will ensure drugs are safe and available for the people.

Innovation comes from staying true to the mission. The mission of drug review is glorious, and with this glory comes heavy responsibilities. More closely united around the CPC Central Committee with Comrade Xi Jinping at the core, seizing momentum and first opportunities, with heavy responsibilities, given by the new era, on its shoulders, and the whole nation its mind, the CDE will strive to create a new era of drug review, living up to the expectations of the people. It will quicken the pace of building a scientific, efficient and authoritative review institution that the people trust. The CDE will present its outstanding performance as a gift for the victorious opening of the 20th National Congress of the Communist Party of China and will continue on its path of making new contributions to safeguarding the health of the people, to building a modernized socialist country and to realizing the Chinese Dream of the Great Rejuvenation of the Chinese nation!

Conclusion

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About Tigermed

Tigermed (Stock code: 300347.SZ/3347.HK) is a leading provider of innovative clinical research solutions across full lifecycle of biopharmaceutical and medical device products globally. With a broad portfolio of services and a promise of quality, from clinical development to commercialization, we are committed to moving our customers and patients through their development journey efficiently and cost-effectively, embracing challenges to fulfill our commitment to serve unmet patients'needs, and eventually saving lives.

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About Yaxincheng

Beijing YaxinchengMedical 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. Yaxinchengnow has a strong network of linguists, project managers, DTP professionals and engineers with over 400 full-time employees and over 650 freelancers, and is providing services to over 600 global clients.

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