NMPA IND Submissions 2020

& JOINN's contribution

2020 Summary

Content

1. NMPA IND Submissions 2017-2020

1.1 JOINN's Share in Overall IND Submissions to NMPA CDE

In 2020, NMPA CDE accepted 629 IND submissions, of which 163 were evaluated by JOINN, accounting for 25.9% of total submissions. Between 2017 to 2020, the average share of NMPA INDs executed by JOINN was 28.4%.

Table 1 NMPA CDE Annual IND Acceptance 2017-2020.

Year	No.	Type	By JOINN	Rate
2017	619	352	101	28.7%
2018	679	419	146	34.8%
2019	715	380	95	25.0%
2020	1142	629	163	25.9%
Average				28.4%

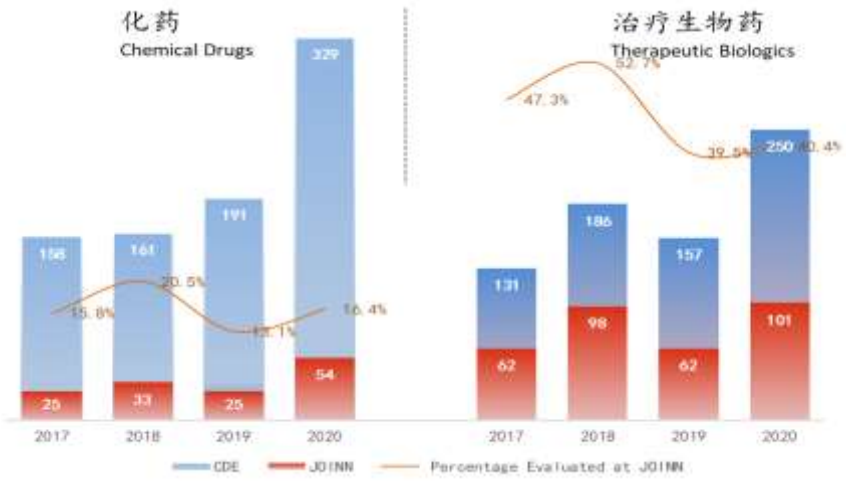
Table 2 NMPA CDE IND Acceptance by Month 2020

In 2020, NMPA CDE accepted 329 chemical drug INDs, of which 54 were evaluated by JOINN, accounting for 16.4%; accepted 23 INDs for preventive biologics, of which 7 were evaluated by JOINN, accounting for 30.4%; accepted 250 INDs for therapeutic biologics, of which 101 were evaluated by JOINN, accounting for 40.4%.

Table 3 NMPA CDE IND Acceptance by Therapeutic Class 2020

Therapeutic Class	Total INDs	By JOINN	Percentage	Average for 2017-2020
Chemical Drugs	329	54	16.4%	16.3%
Preventive Biologics	23	7	30.4%	43.3%
Therapeutic Biologics	250	101	40.4%	44.6%
TCM and Natural Compounds	27	1	3.7%	2.5%
Total	629	163	25.9%	28.4%

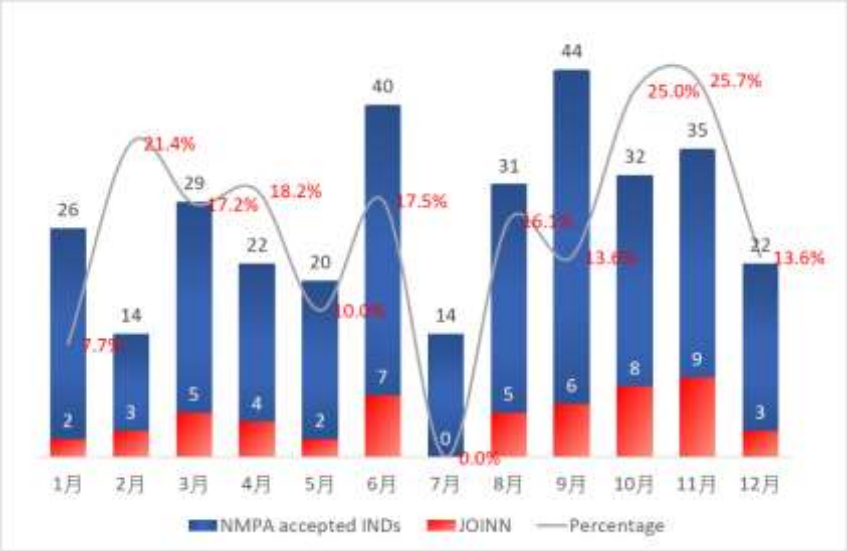
Table 4 NMPA CDE Chemical/Biological IND Acceptance 2017-2020



Chemical INDs

In 2020, the monthly share of accepted chemical drug INDs evaluated by JOINN varied between 0 and 25.7%, on average accounted for 16.4%.

Table 5 NMPA CDE Chemical IND Acceptance by Month 2020



Between 2017 to 2020, an annual share of between 13.1% ~ 20.5% of chemical INDs were evaluated by JOINN.

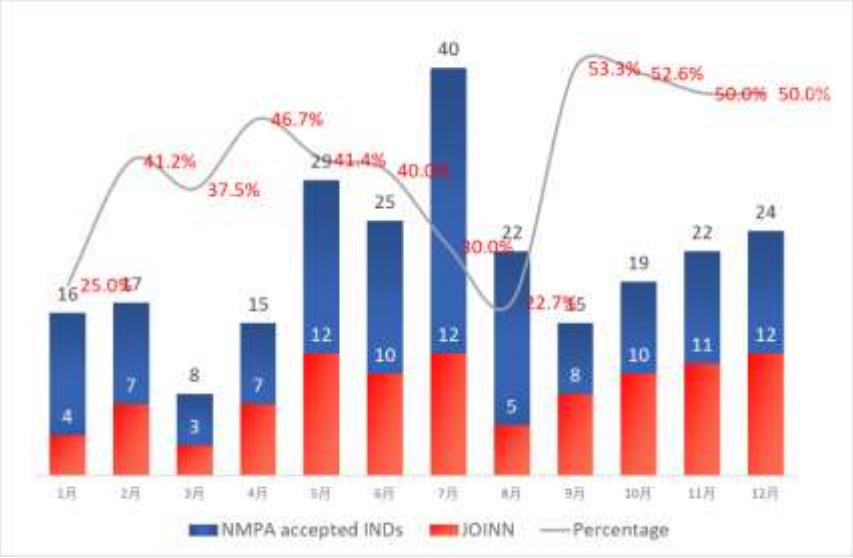
Table 6 Annual Chemical Drug IND Acceptance at NMPA CDE 2017-2020

Year	Chemical Drug	By JOINN	Rate
2017	158	25	15.8%
2018	161	33	20.5%
2019	191	25	13.1%
2020	329	54	16.4%
Average			16.3%

2 Therapeutic Biologic INDs

In 2020, JOINN accounted for between 22.7% ~ 53.3%, of monthly therapeutic biologic INDs accepted at the NMPA CDE.

Table 7 NMPA CDE Therapeutic Biologic IND Acceptance by Month 2020



Between 2017 ~ 2020, JOINN accounted for between 39.5% to 52.7% of the annual therapeutic biologic INDs accepted at the NMPA CDE.

Table 8 2017-2020 Therapeutic Biologic IND Acceptance at the NMPA CDE

Year	No.	By JOINN	Rate
2017	131	62	47.3%
2018	186	98	52.7%
2019	157	62	39.5%
2020	252	101	40.1%
Average			44.5%

2.1 Therapeutic Biologic INDs by Category

Among the major categories of therapeutic biologics accepted by the NMPA CDE (2000-present), JOINN evaluated significant shares in every category. See table below for details, in most cases accounting for greater than 50% of all INDs.

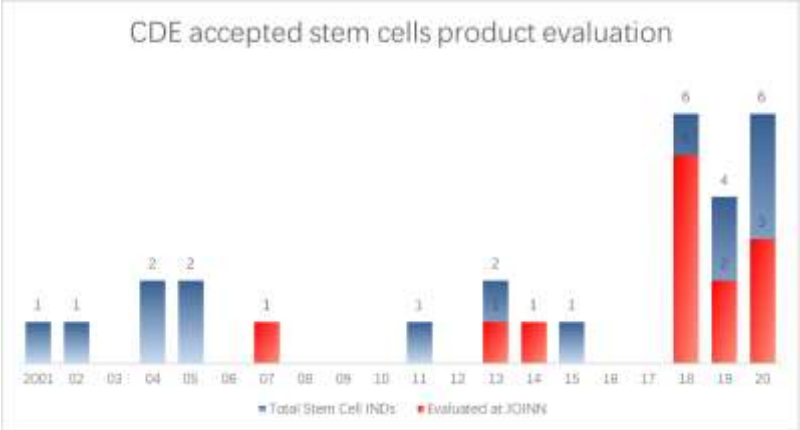
Table 9 Sub-Classes of Therapeutic Biologic INDs

Sub-Classes	CDE	By JOINN	Rate
Stem cells	28	13	46%
CAR-T	45	29	64%
Oncolytic Virus	32	17	53%
Monoclonal Antibody	392	143	36%
Bispecific Antibody	32	17	53%
ADC	30	16	53%

2.2 Stem Cells

Since 2001, the NMPA CDE has granted 28 stem cell INDs, of which 13 were evaluated by JOINN, accounting for 46.4% of the total. Amcellgene products were approved for clinical use in April 2020.

Table 10 2001-2020 CDE accepted stem cells product evaluation

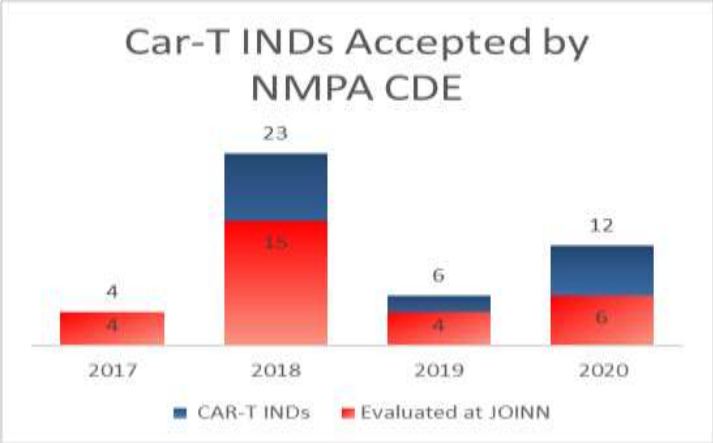


2.3 CAR-T

Since 2017, CDE has accepted 45 CAR-T products, 29 of which were evaluated at JOINN, accounting for 64% INDs overall.

In 2017, FDA approved two marketing authorizations for CAR-T products. The four CAR-T INDs accepted by CDE in that year were all evaluate by JOINN; In 2018, the number of INDs granted for CAR-T is up to 23, and 15 are evaluated by JOINN; In 2019, there were only 6 Car-T INDs granted, and 4 were evaluated by JOINN.

Table 11 CAR-T Evaluation



In 2020, the NMPA CDE accepted 12 Car-T INDs, 6 of which were evaluated by JOINN.

Of all CAR-T INDs, more than 53 percent targets CD19, 13 percent targets BCMA. All the two dual-target CAR-T products were evaluated at JOINN.

Table 12 CAR-T Targets and JOINN Evaluation Experience

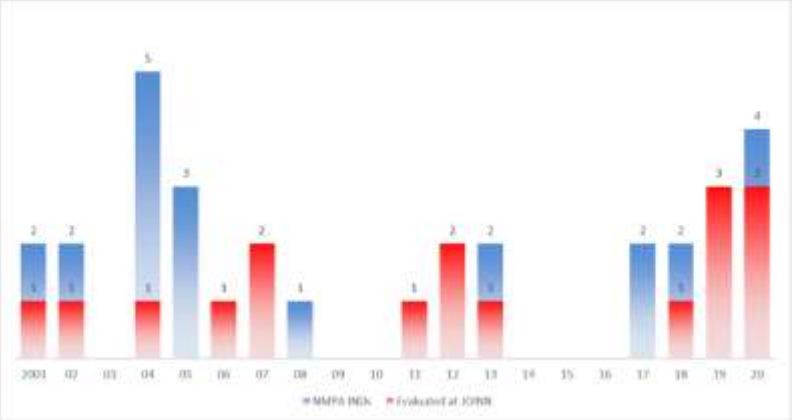
Target	CAR-T INDs	JOINN
CD19	24	16
BCMA	6	6
CTLA4	2	1
CD19&PD1	1	1
CD19&CD22	1	1
CD30	1	1
GPC3	1	1
NY-ESO-1	1	1
CD20	1	1
CLDN18	1	
CD269	1	
HLA	1	
Unknow	4	
Total	**45**	**29**

2.4 Oncolytic Virus

Between 2017-2020, NMPA CDE has accepted 11 Oncolytic Virus INDs, 7 of which were evaluated by JOINN, accounting for 64% of the total INDs accepted at the NPMA CDE.

The vectors evaluated are mostly adenovirus (70%) and herpesvirus. Other vectors evaluated include alphavirus, poxvirus, and naked plasmid.

Table 13 Oncolytic Virus INDs



2.5 Therapeutic Monoclonal Antibodies

Table 14 NMPA CDE Acceptance of Therapeutic Antibody INDs since 2000.

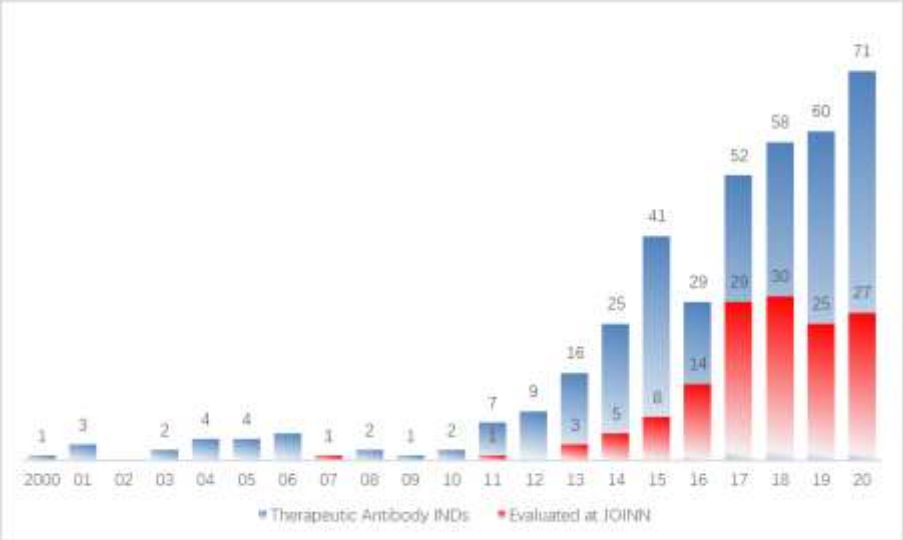
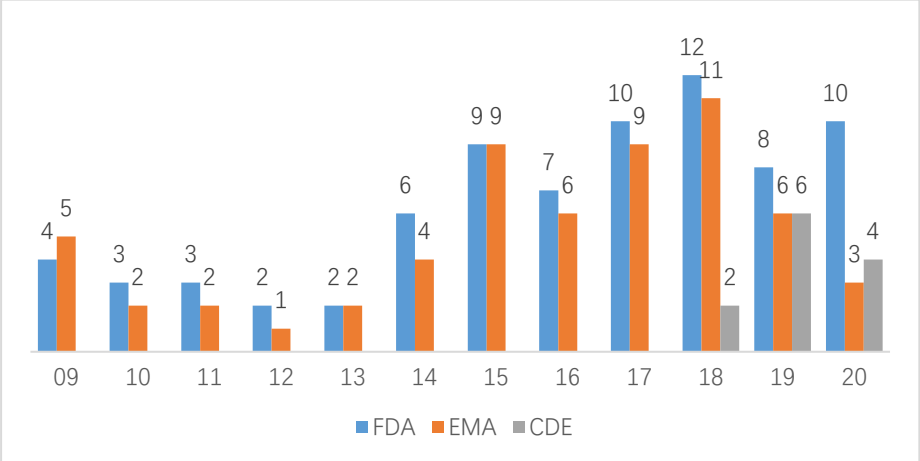
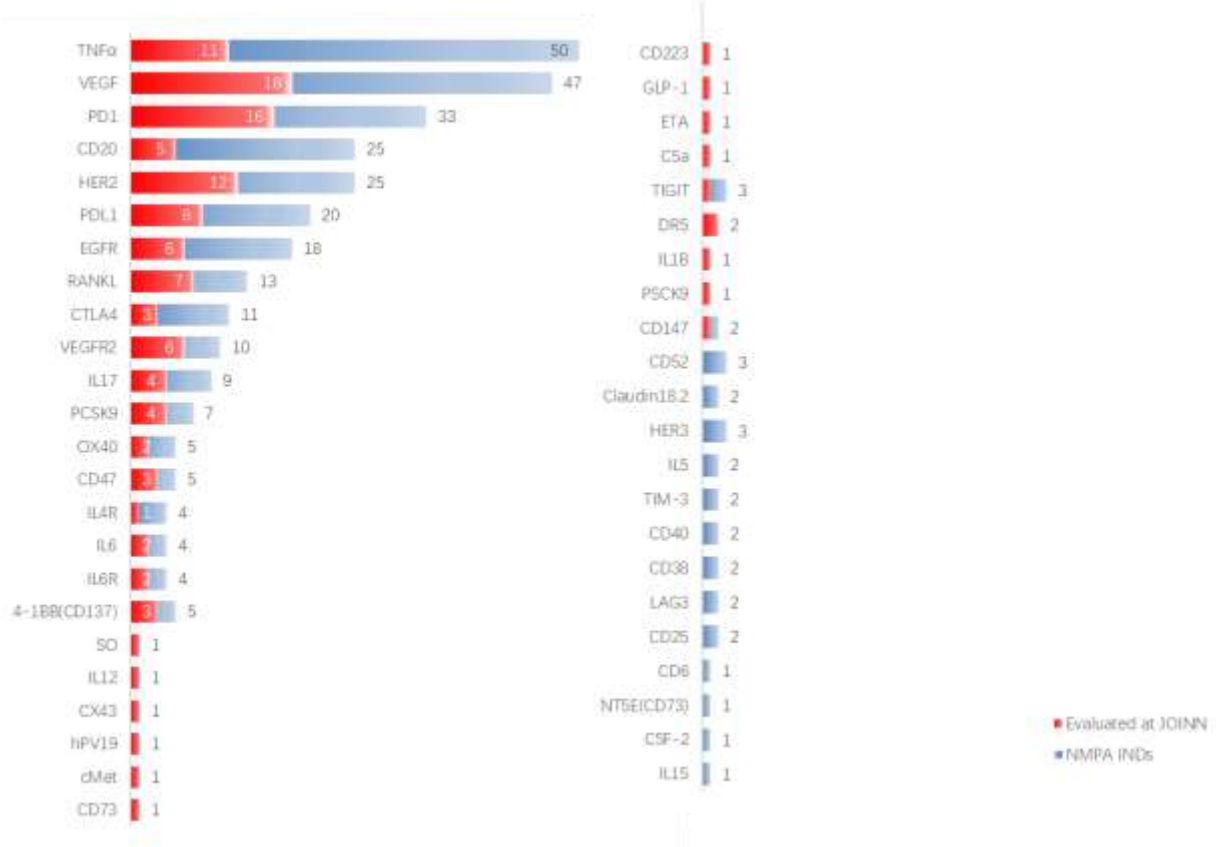


Table 15 The number of monoclonal antibodies approved for marketing by the FDA, EMA and the NMPA CDE between 2009 to 2020.



Among INDs accepted by the NMPA CDE, the most common target is TNF α, accounting for 22% of total INDs. Other high frequency targets are VEGF, PD1/PDL1, HER2. EGFR, IL17, PCSK9, and CD20.

Table 16 Monoclonal antibody target evaluation

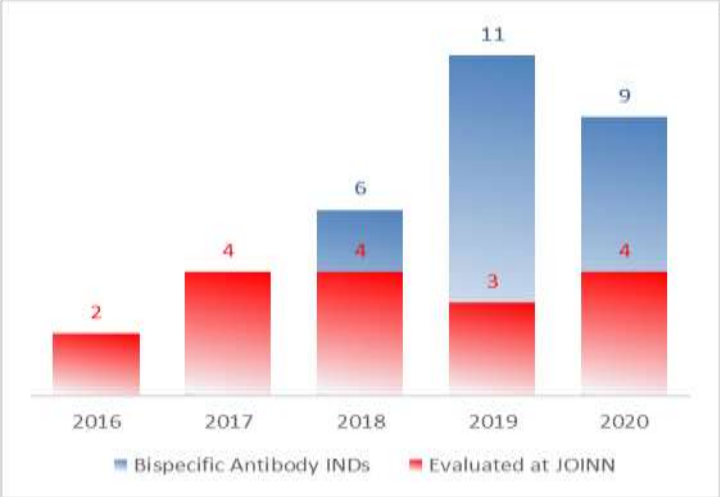


2.6 Therapeutic Bispecific Antibodies

Bispecific antibodies (including bifunctional monoclonal antibodies/ polyclonal antibodies) have been accepted since 2016. For the first two years, all INDs in this class were evaluated by JOINN.

The fastest progressing bispecific antibody developed in China has entered clinical Phase III: ALPHAMAB ONCOLOGY KN046. In clinical Phase II: EPIMAB BIOTHERAPEUTICS EMB-01, Akeso Inc. AK-104, Hengrui Medicine SHR1701, and Alphamab Oncology KN026.

Table 17 Annual bispecific antibody INDs.



2.7 Antibody-Drug Conjugates (ADC)

Acceptance of ADC INDs has surged since 2017, with half of the INDs targeting HER2. There are three clinical Phase III ADCs developed in China, all of which were evaluate by JOINN.

Table 18 ADC INDs at the NMPA CDE