Current ATMP regulation in China

Center for Drug Evaluation,
National Medical Products Administration

December 2023

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1 Advanced therapy medicinal products (ATMPs) in China

◆ **Cell therapy products**

Immune cells, stem cells, mesenchymal stromal cells, myoblasts, pancreatic islets, hepatocytes

◆ **Gene therapy products**

Plasmids, viral vectors, bacterial vectors, DNA/RNA

◆ **Oncolytic virus**

◆ **Tissue-based products**

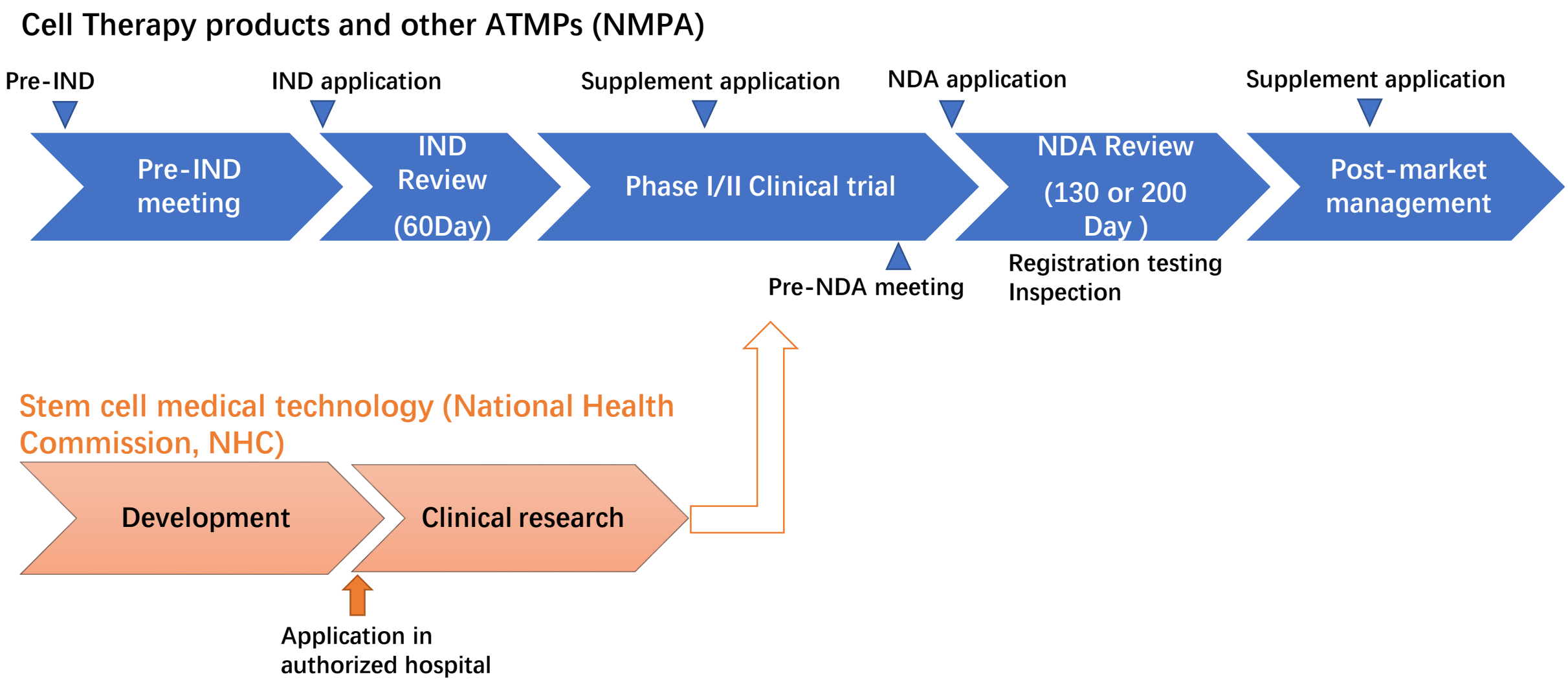
◆ **Others**

Immunotherapies (cells, tumor tissue-derived products, peptides, DNA/RNA)

Combination products (device-cell, drug-cell, etc.)

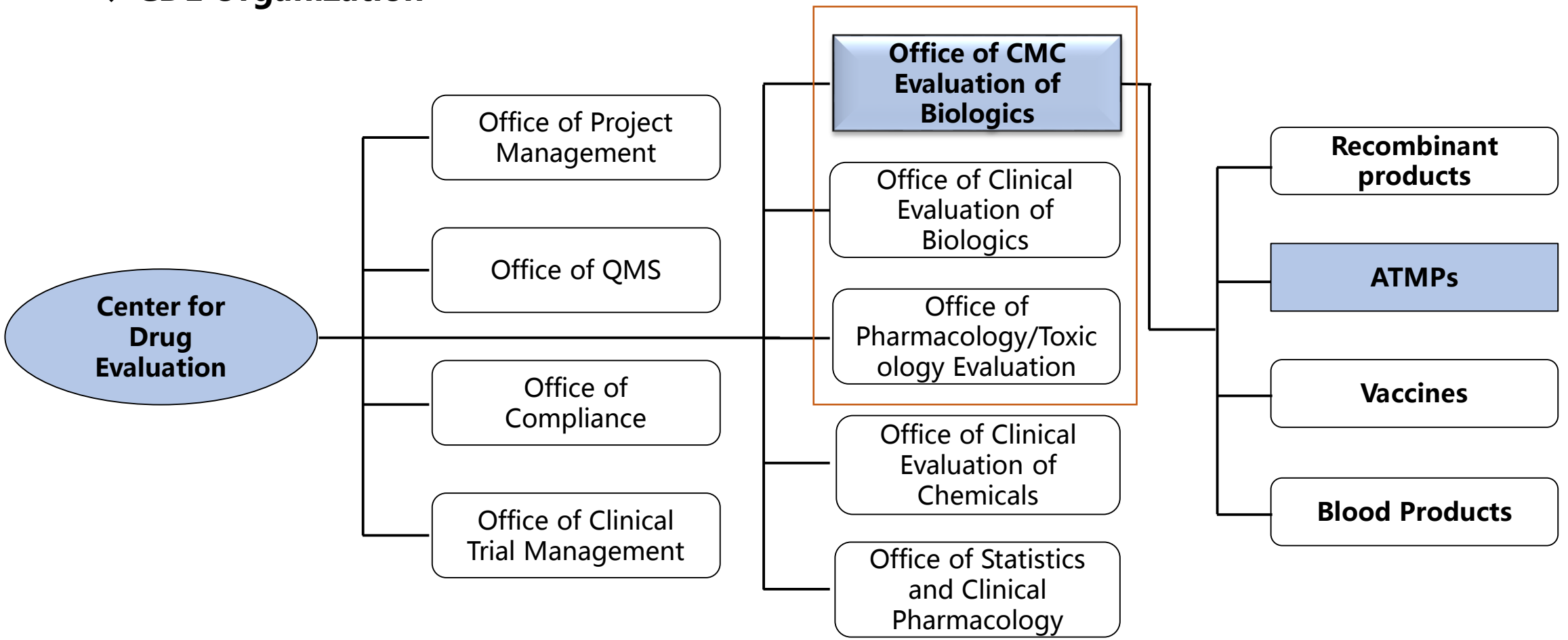
Organelles (exosome, etc.)

1 The regulatory framework of ATMPs in China



1 Center for Drug Evaluation (CDE), NMPA

◆ CDE Organization



1 The regulatory framework of ATMPs in China

Statues

Drug Administration Law (2019)

Regulations

Regulation for the Implementation of Drug Administration Law (Draft, 2021)

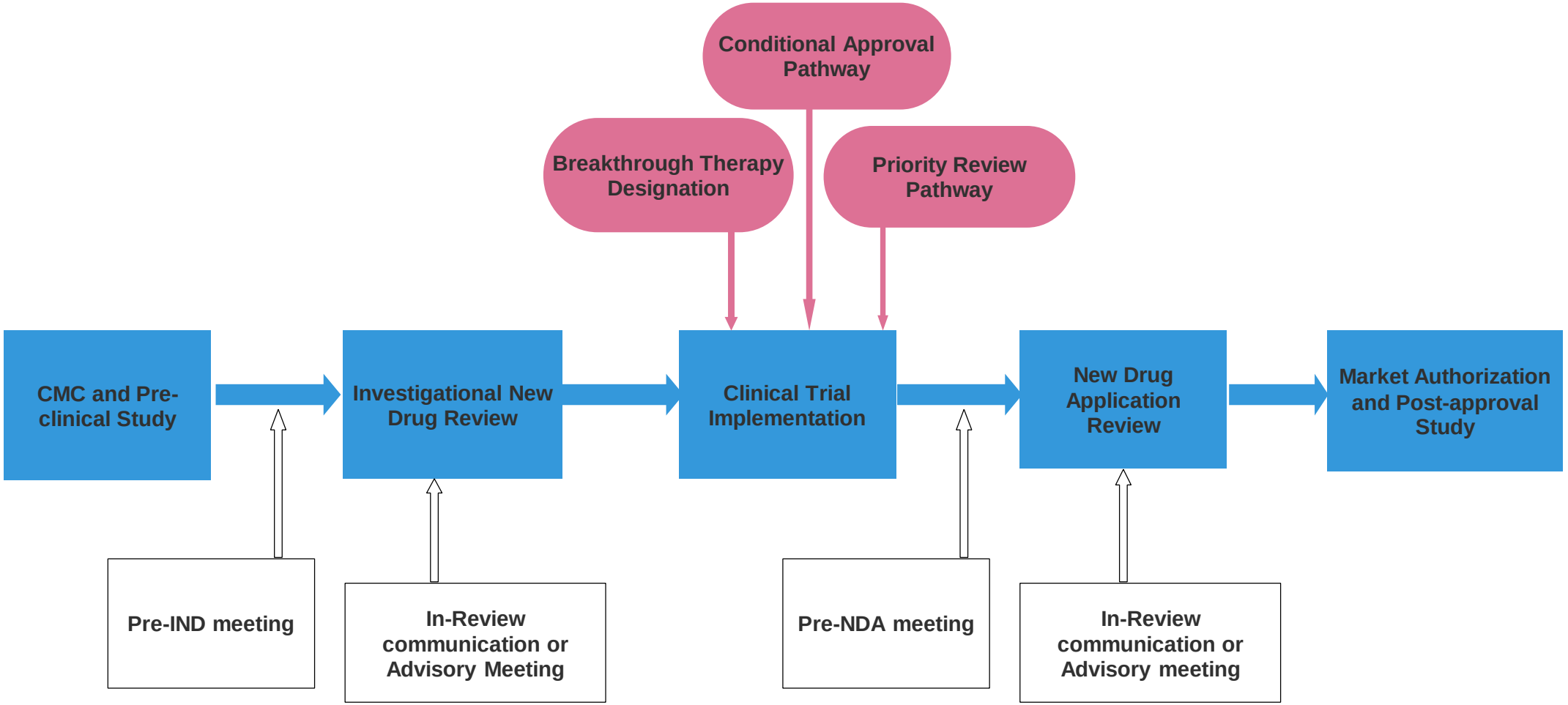
The Provisions for Drug Registration (NMPA Order No.27, 2020)

Guidance

Cell Therapy products, gene therapy products, oncolytic virus, others

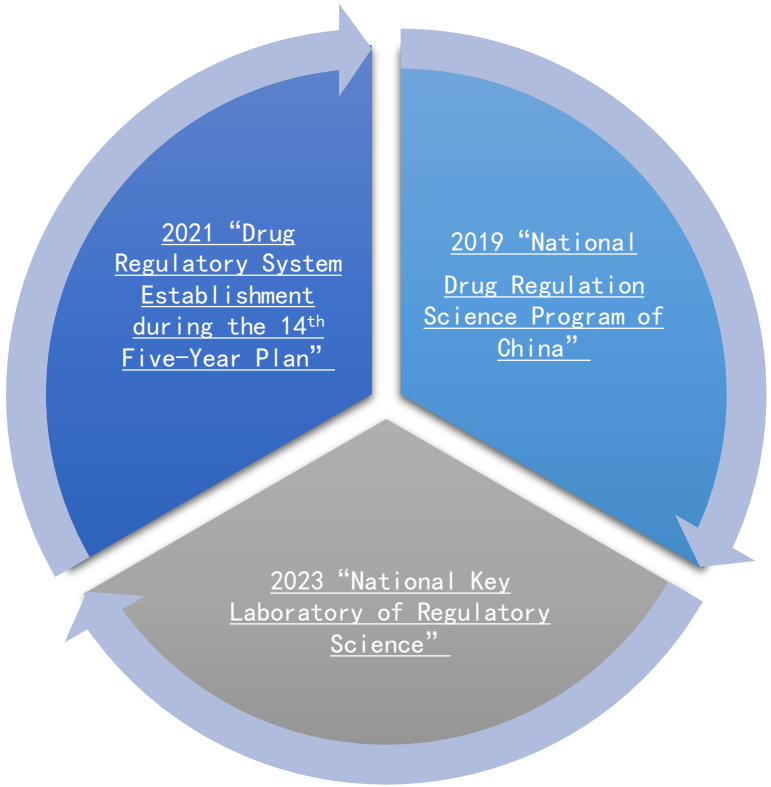
CMC　　Non-clinical　　Clinical

1 The expedited regulatory programs speed up the approval of ATMPs



1 The actions on ATMP regulation in China

- Focus on drafting CMC guidance on stem cell products, oncolytic virus and AAV products in IND and NDA stage
- Establish the clinical risk-benefit evaluation method of ATMP-targeting diseases (tumor, rare disease, regenerative medicine)



- To support the development and evaluation of new tools, new standards and new methods of ATMPs
- Including the study on risk control of Replication Competent Virus, risk control of stem cell products, etc.

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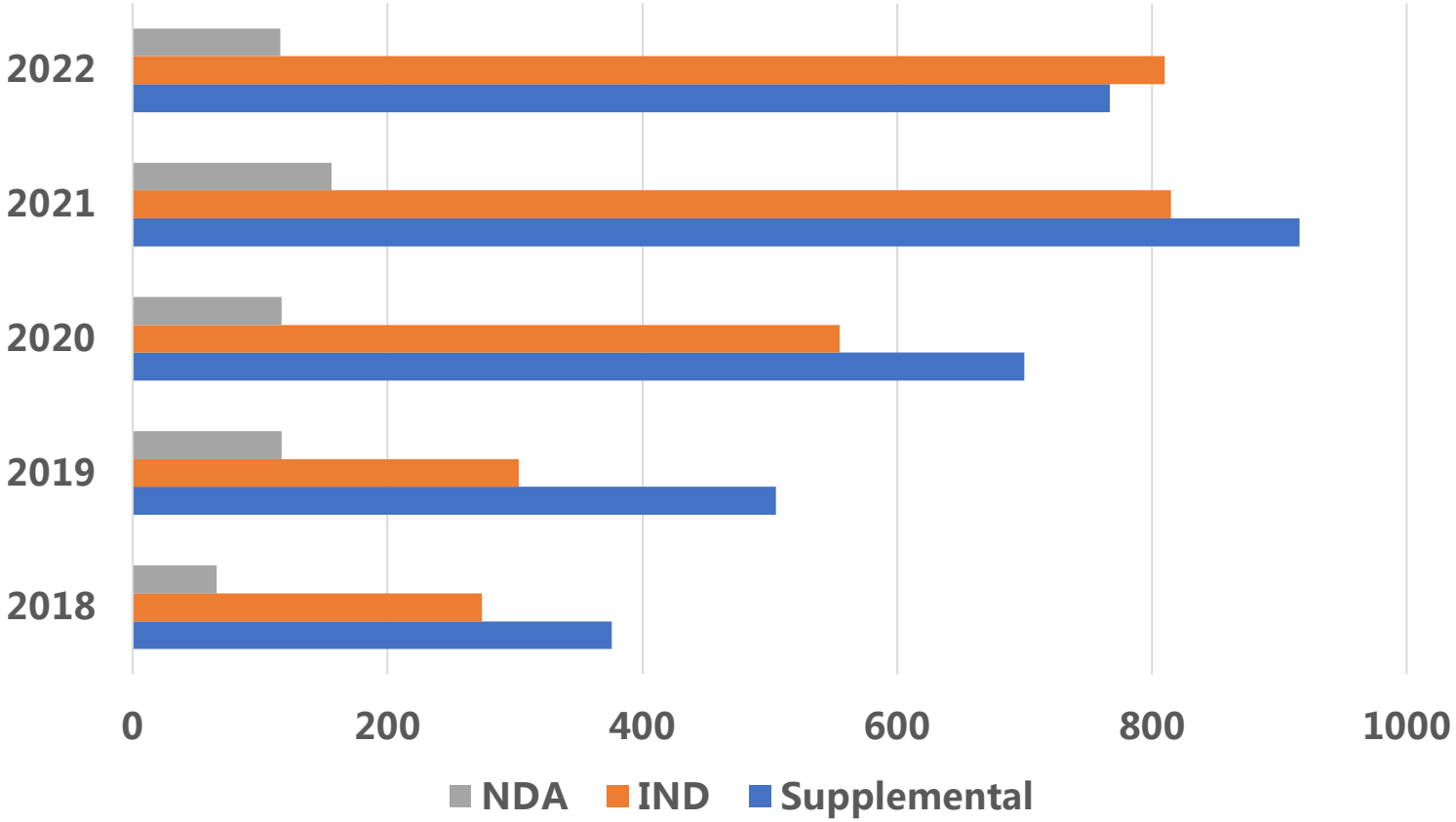
2 Recent trends of ATMPs application

Number of therapeutic biological products reviewed from 2018-2022



2022

All biologicals

IND：859

NDA：131

Supplemental application：767

ATMPs

IND：112

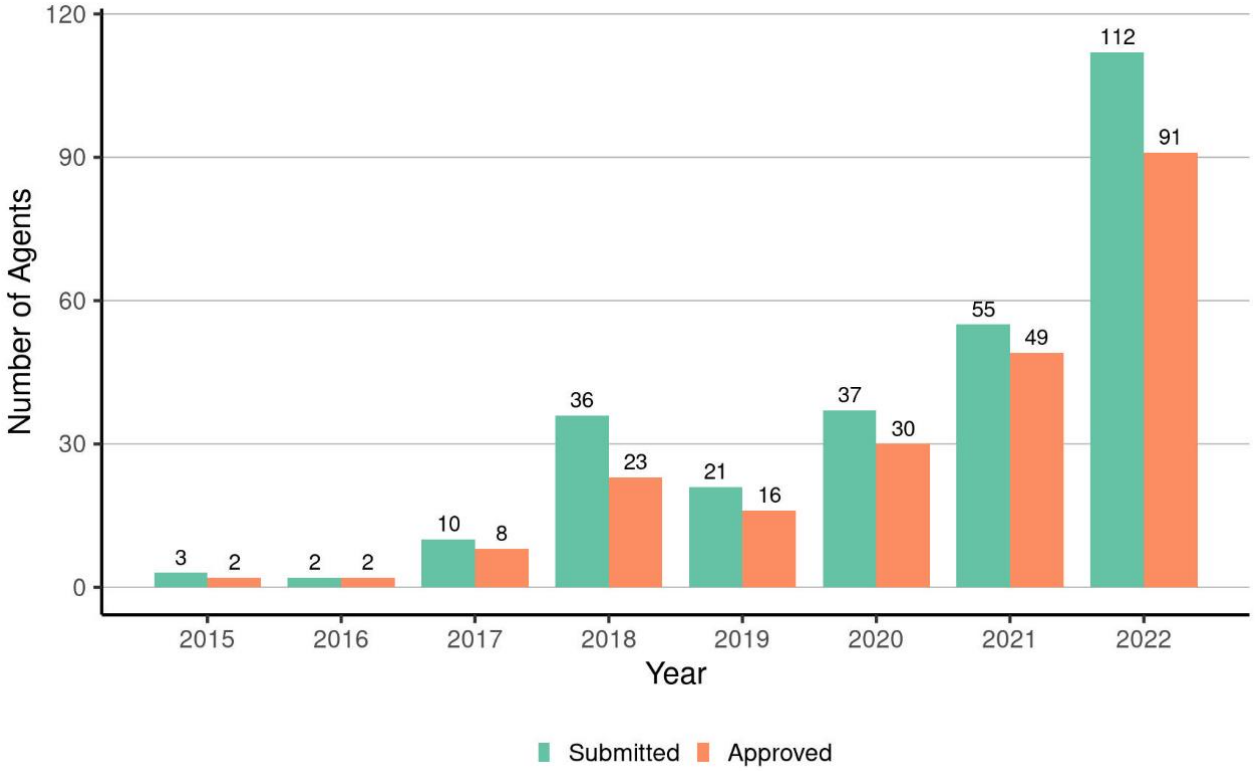
NDA：4

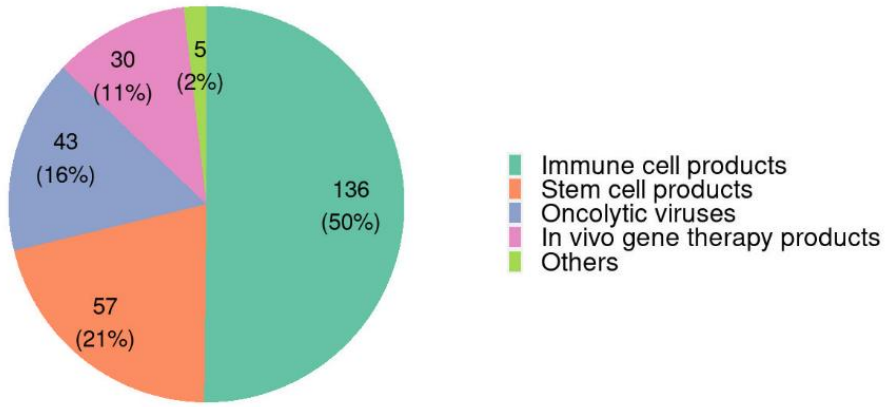
Supplemental application：8

Data source: The database of NMPA’s Registration and Information Disclosure Platform for Drug(https://www.nmpa.gov.cn/yaopin/index.html)

2 Recent trends of ATMPs application

Investigational New Drug Application





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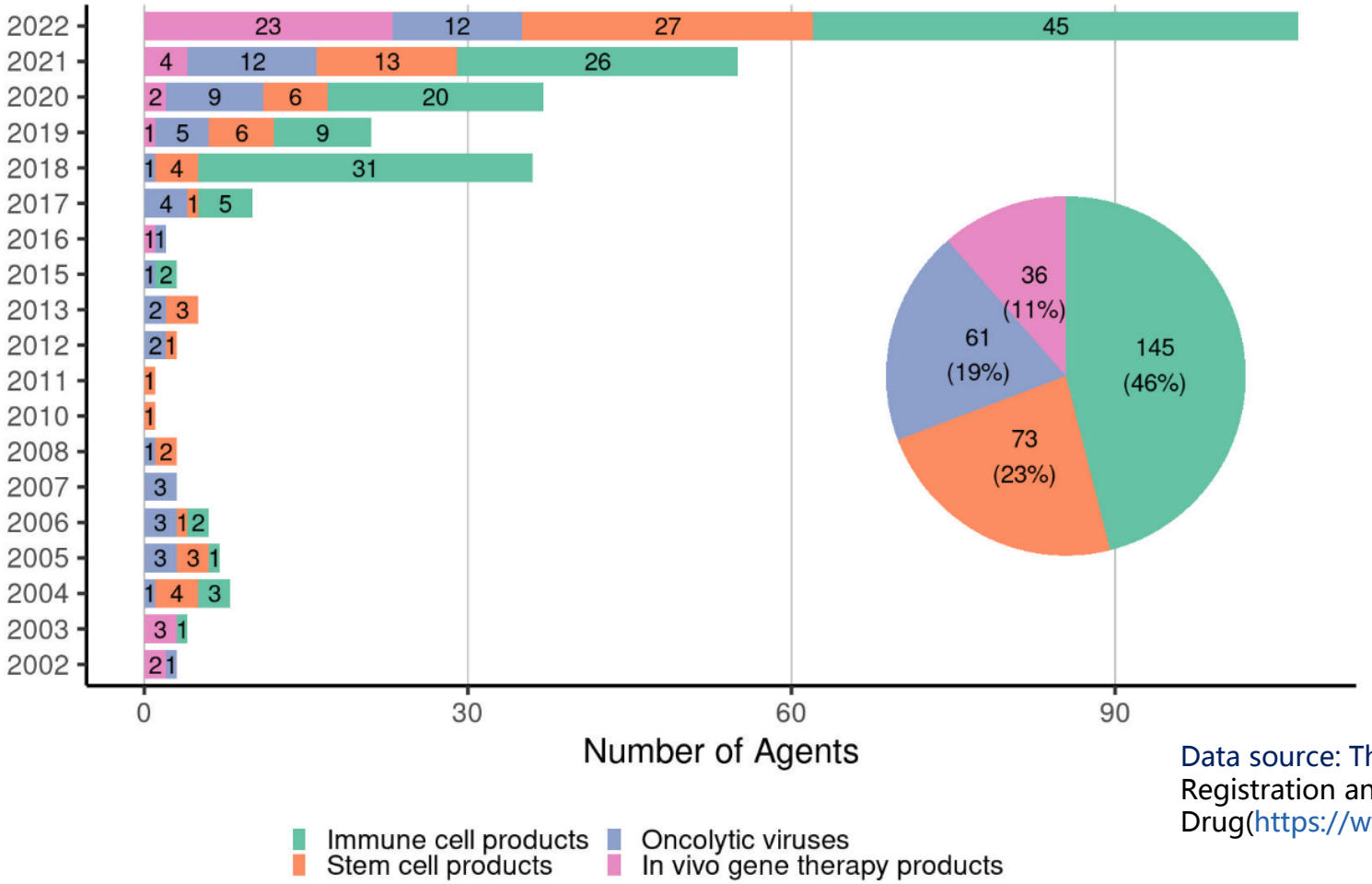
2 Recent trends of ATMPs application

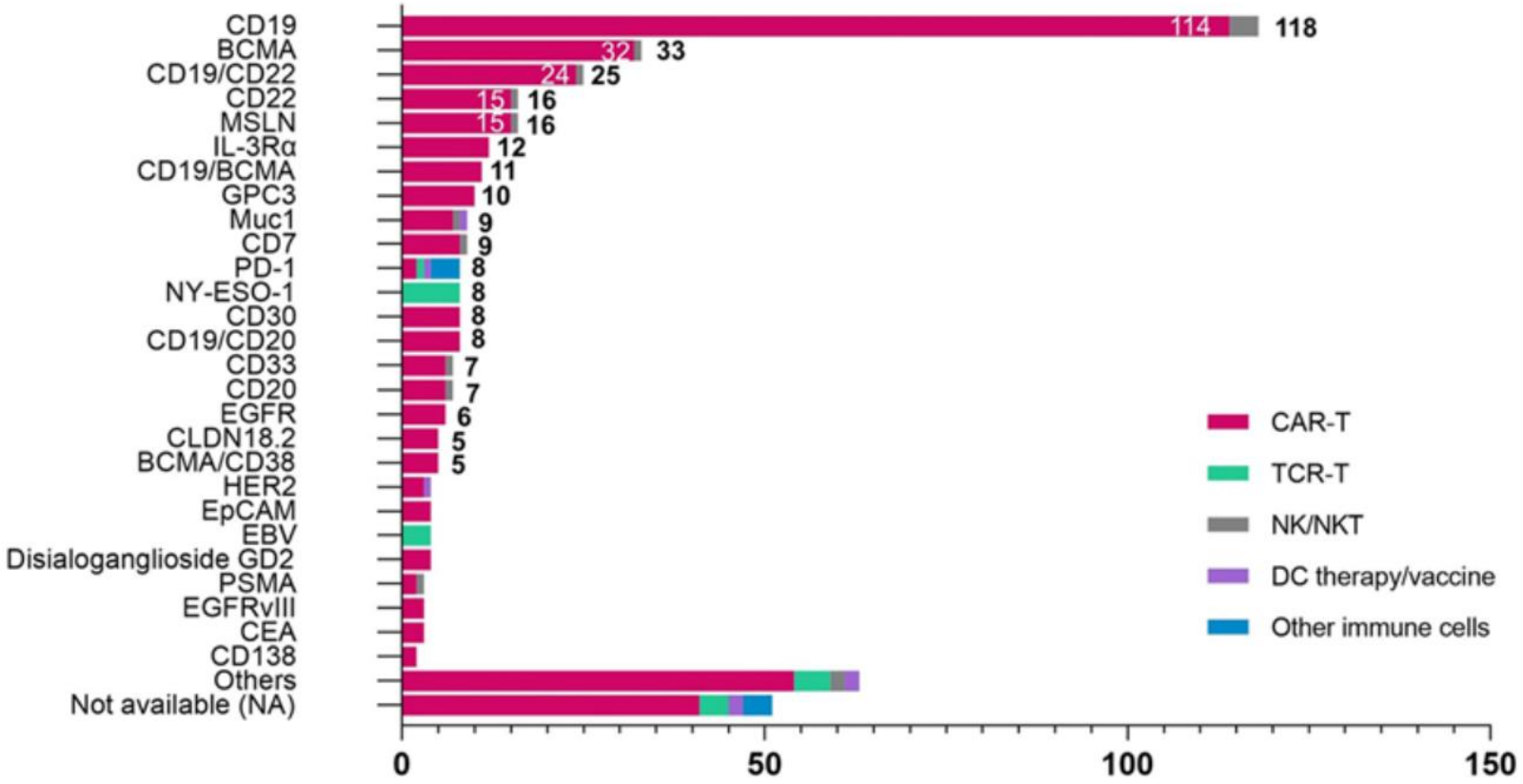
Investigational New Drug Application



Data source: The database of NMPA's Registration and Information Disclosure Platform for Drug(https://www.nmpa.gov.cn/yaopin/index.html)

2 Recent trends of ATMPs application

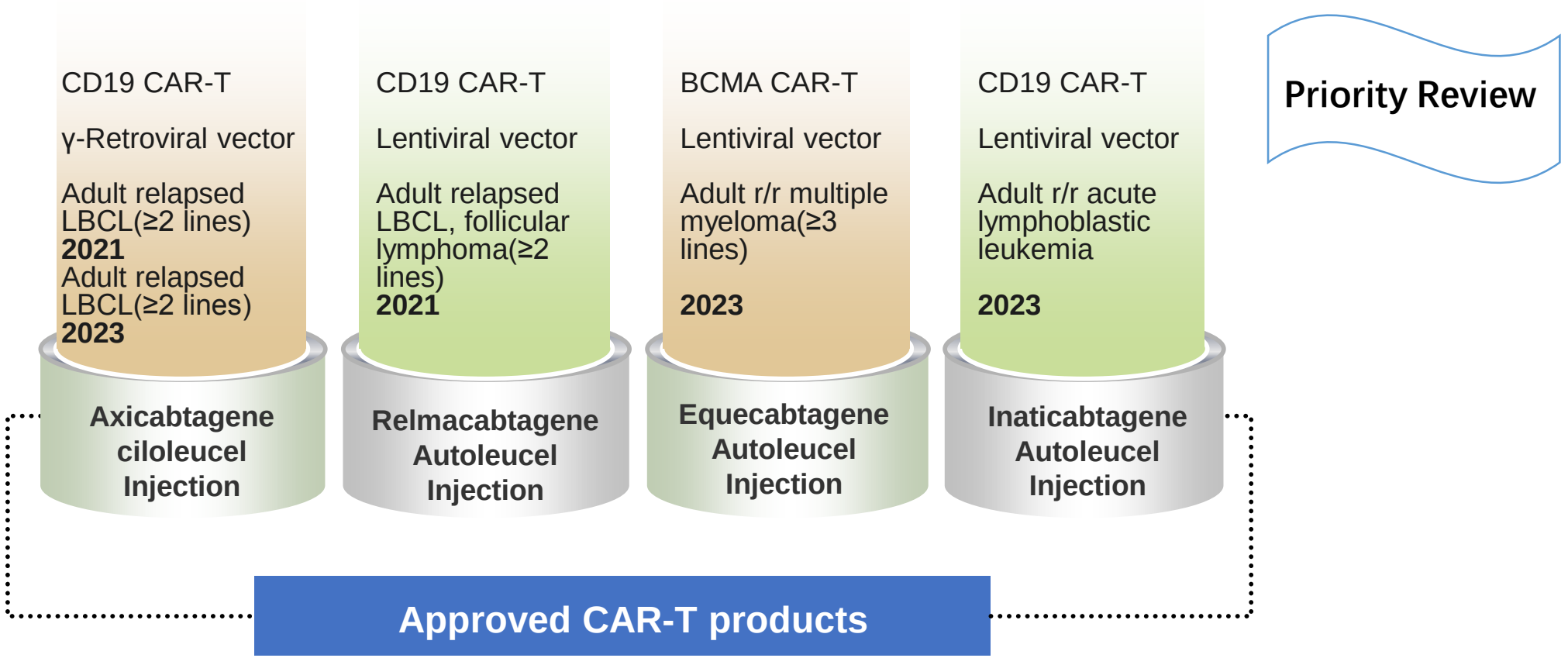
Targets of ATMPs



Yin et al. Journal of Hematology & Oncology (2022) 15:139

2 Recent trends of ATMPs application

Market authorization



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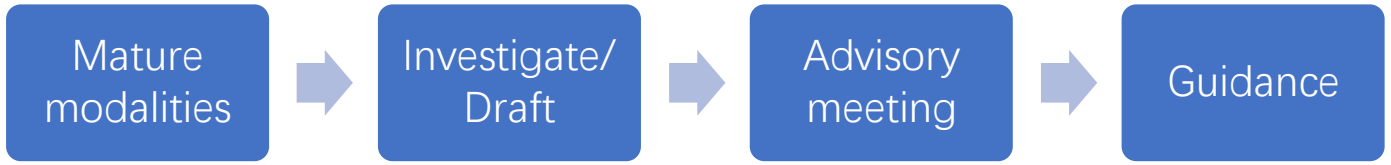
3 The regulatory guidance for ATMPs in China

Some key points of ATMP development

CMC	Nonclinical	Clinical
Raw materials	Species selection	Innovative design of clinical trails
Innovative manufacture process and control	Bio-distribution/Persistence	Long term Follow-up
Impurities	Shedding studies	Shedding studies
Critical quality attributes	Off-target toxicity	Virtual clinical trials
Replication Competent Virus	Tumorigenicity	
Comparability		

3 The regulatory guidance for ATMPs in China

Traditional biologics



ATMPs

3 The regulatory guidance for ATMPs in China

The structure and points to address in CMC guidance

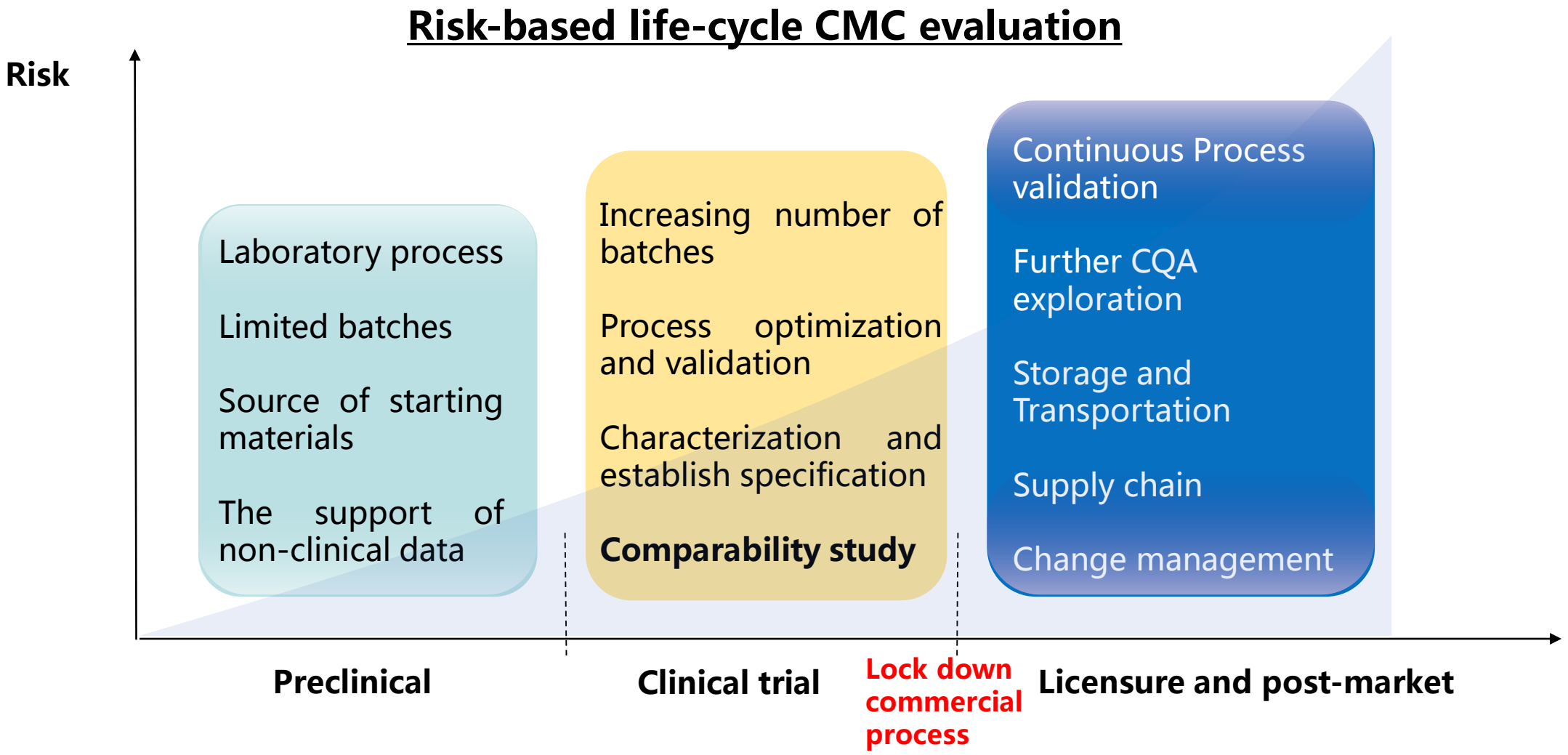
Materials
Molecular Design(Vectors, Plasmids…)
Adventitious agents
Human-derived
Donor-to-donor variations

Manufacture
Innovative modes
Specialized techniques
Small scale
COI/COC for autologous products

Quality
Analytical methods of variations
Potency assay(Matrix)
Comparability study

Stability and closure system
Representative samples
Storage in freezer
In-use stability

3 The regulatory guidance for ATMPs in China



3 The CMC regulatory guidance for ATMPs in China

Guidance for Pharmaceutical Research and Evaluation of Oncolytic Virus Products (Trial), 2023
Guidance for Research and Evaluation on Chemistry, Manufacture and Control of Human Stem Cell Products (Trial), 2023
Questions and answers-Manufacturing Change and Comparability Study for autologous CAR-T Cell Therapy Products, 2023
Guidance for Research and Evaluation on Chemistry, Manufacturing, and Control (CMC) changes for biological products (Draft), 2023

Guidance for Chemistry, Manufacturing, and Control (CMC) Development and Evaluation of in vivo Human Gene Therapy Products (Trial), 2022
Guidance for Chemistry, Manufacturing, and Control (CMC) Development and Evaluation of ex vivo Gene Modification System (Trial), 2022
Guideline for Chemistry, Manufacturing, and Control (CMC) Development and Evaluation of Immune Cell Therapy Products (Trial), 2022

Guideline for Chemistry, Manufacturing, and Control (CMC) Development and Evaluation of Cell Therapy Products (Trial), 2017

https://www.cde.org
https://www.ccfdie.org

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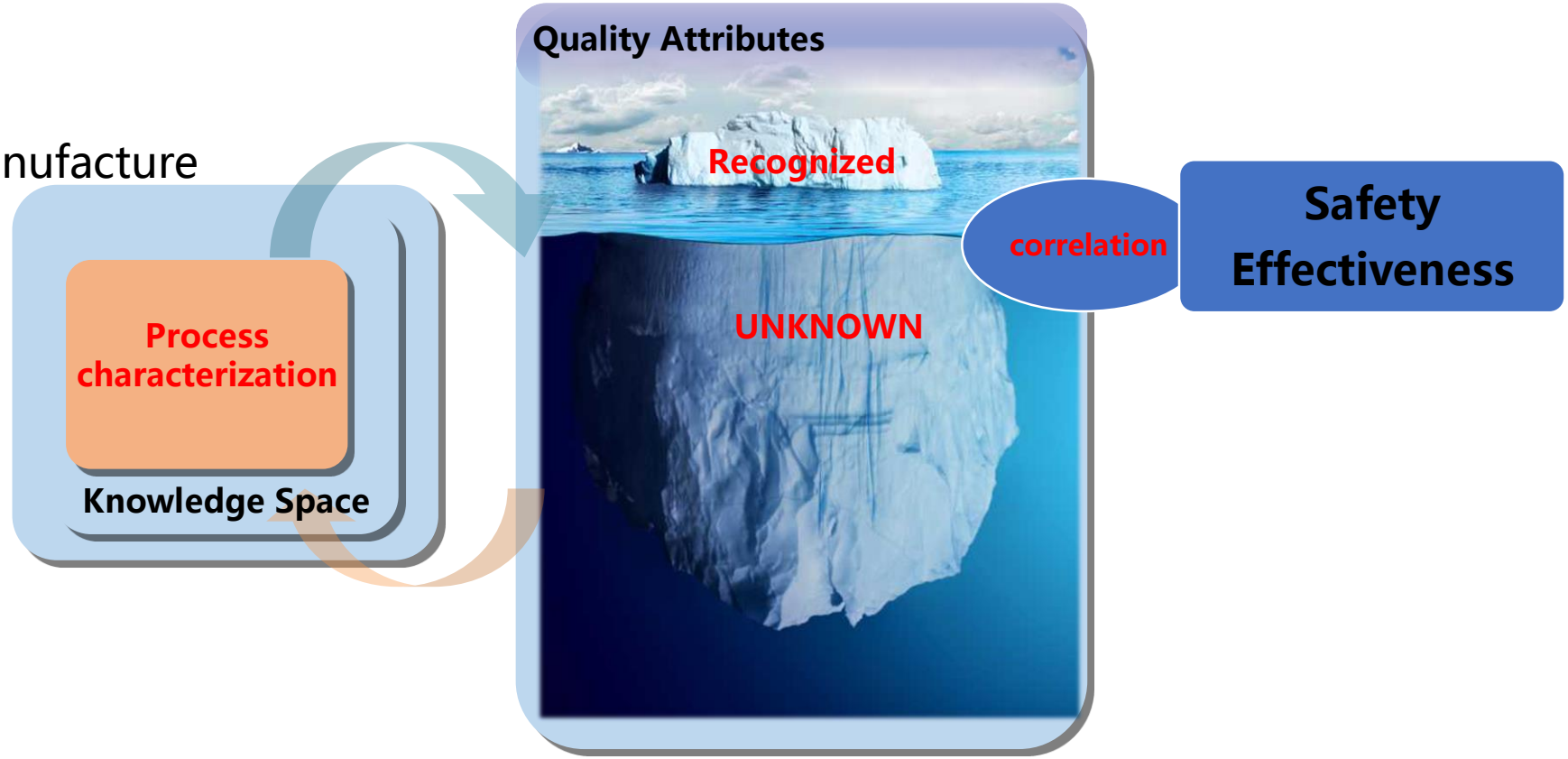
4 Challenges and perspectives

- ◆Individualized treatment
- ◆Highly varied materials
- ◆Complex design and manufacture
- ◆Understanding of CQA
- ◆Comparability Study
- ◆Small-scale lot
- ◆Statistics
- ◆Communications
- ◆…



Acknowledgements

Thanks for your attention!