



Overview | Project research and project approval | POC | CMC | Registration | Application 1: Plasmid | Application 2: Lentiviral vector | Application 3: CAR-T cells

**01 Intellectual property and patents**  
Chinese patents, US patents, European patents and other relevant national patents  
Scope of the patent, the applicant for the patent, the status and duration of the patent, and circumvention of the patent

**02 Market**  
Product sales data, market share comparison of similar products/regional market share distributions in the world and in China  
Investigate dosage forms and specifications that are easy to sell or bid on. Conclusion should provide the product dosage forms and specifications with development priority

**03 Domestic and foreign laws and regulations**  
Approval time, original manufacturers, approved product dosage forms and specifications of similar products  
Whether the product has administrative protection, whether there are legal barriers to registration, and the proposed category of registration in China

**04 Pharmacology**  
Information on the pharmacokinetics, pharmacodynamics and safety tests on the product  
Information on the reference drug products for animal experiments

**05 Information on drug substance**  
Information on the drug substance process route, quality research content, availability of starting materials, need of specific equipment and facilities for commercial production

**06 Information on drug product**  
Study on physicochemical characterization, stability, etc. of the drug product  
Feasibility of the drug product process, availability of excipients, need of specific equipment and facilities for commercial production

**07 Clinical application**  
Investigate the clinical indications, application scope and side effects of the product  
Investigate the advantages and disadvantages of the product in the clinical application compared with similar products, and the requirements for clinical studies of the product

**In vivo evaluation**

**01 Safety**  
No observed adverse effect

**02 Efficacy**  
Present tumor growth inhibition effect  
Dose dependence

**03 PK**  
Significant cell expansion observed, preferably higher peak product cells and survival duration

**01 Production**  
Manufacturing protocol of pharmacology/toxicology, registration and clinical batches  
Batch production record  
Scale-up study report  
Process validation report

**02 Quality**  
Product testing of pharmacology/toxicology, registration and clinical batches  
Batch verification record  
Stability study protocol  
Validation protocol of analytical procedures  
Validation report of analytical procedures  
Impurity profile report

**01 Process**  
Seed solution  
Fermentation  
Pyrolysis  
Size-exclusion chromatography  
Use stability  
Affinity chromatography  
Ion exchange chromatography  
Ultrafiltration  
Drug substance  
Drug product (studies on filling process and formulation)

**02 Specification**  
Establishment of Ecoli cell bank  
Primary Cell Bank  
Master Cell Bank  
Working Cell Bank  
Verification of cell bank  
Stability of cell bank  
Passage stability  
Storage stability

**03 Stability**  
Long-term test  
Stress: Freeze-thaw  
Accelerated

**01 Process**  
Single blood collection  
Magnetic bead sorting (CD4/CD8)  
Activation  
Transfection/electrotransfer  
Culture (< 14 days)  
Drug substance  
Drug product (studies on packaging material screening, filling process, formulation and programmed freezing condition)

**02 Specification**  
Appearance  
pH  
Osmolality  
CAR%  
Phenotyping  
Cell density  
Process related impurities  
Activity  
Integration site  
Copy number  
Sterility  
Endotoxin  
RCL  
Mycoplasma

**03 Stability**  
CD4 / CD8  
CAR +  
Depletion  
Apoptosis  
Differentiation  
.....  
Dead cell density  
Viable cell density  
Cytokine residue  
Lentivirus virus (lentivirus transfection process)  
mRNA residue (transposition process)  
Magnetic bead residue  
.....  
Killing  
Proliferation  
Cytokine secretion  
Copy number of vectors  
Copy number of CARs  
Single blood collection  
Transport stability  
Stability at Room Temperature  
Resuscitation stability  
Long-term stability  
Transport stability  
Use stability

▶ **Illustrated Handbook: Cell Therapy R&D Illustrated Handbook** ◀

**Give thanks**  
Editor @ David (David has been engaged in pharmaceutical research and development for more than 10 years; David is now working in the head of gene therapy R&D enterprise, and good at peptide, CAR-T, virus, mRNA and other drug CMC works)  
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