IND*Ready*® produced plasmids exceed FDA and EMA regulatory guidelines for cGMP vector production

Background

Over the last decade, there has been confusion and differing opinions on the regulatory requirements for plasmids starting material in cGMP vector production. Some CGT vector manufacturers thought the regulatory agencies would enforce a cGMP plasmid regulation in later phase clinical studies, while others thought there was no requirement for cGMP starting material.

To clear the confusion, the FDA and EMA have both come out and definitively stated that there is no requirement for cGMP starting materials[1,2]. While both agencies have indicated that plasmid starting material does not need to be cGMP manufactured, they did state requirements for manufacturing and testing the plasmid starting materials[3-8]. Reviewing these agencies' requirements is vital to understand what these agencies require for plasmid starting material used in cGMP vector production.

In 2002, Puresyn started a service to provide high-quality, highly documented plasmids for cGMP vector manufacture. This service, IND*Ready*®, was designed to exceed FDA and EMA regulatory guidance and help keep collaborators' clinical studies on track. A review of the agencies' requirements and how Puresyn's IND*Ready*® produced plasmids meet each requirement was produced.

Table 1: IND*Ready*® adherence to regulatory requirements

	FDA Required	EMA Required	INDReady®
Cell Banking	Yes	Yes	Yes
Bank Characterization	Yes	**	Yes+
Identity	Yes	Yes	Yes
Sequencing	Yes	Yes	Yes+
Purity	Yes	Yes	Yes
Functionality	Yes	Yes	No
Safety	*	*	Yes+
Stability	Yes	Yes	Yes+
Audit of Vendor	Yes	**	Yes
Risk Assessment	Yes	Yes	Yes
Principles of cGMP	Yes	Yes	Yes

* Sterility, Endo, RNA, Host DNA, protein, Mycoplasma
** Not specifically stated but previously recommended to start by regulatory reviewers
+Samples collected per collaborator require and sent for third-party testing

References

1. Questions and answers on the principles of GMP for the manufacturing of starting materials of biological origin used to transfer genetic material for the manufacturing of ATMP, European Medical Agency (2021)
2. OTAT Town Hall on Cell Therapy Chemistry, Manufacturing, and Controls and Tissue-engineered Medical Products, 2022
3. Chemistry, Manufacturing, and Control (CMC) information for Human Gene Therapy Investigational New Drug Applications (INDs), US Department of Health and Human Services, FDA, Center for Biologics Evaluation and Research (2020)
4. Characterization and Qualification of Cell Substrates and Other Biological Materials Used in the Production of Viral Vaccines for infectious Disease Indications (2010)
5. ANCILLARY MATERIALS FOR CELL, GENE, AND TISSUE-ENGINEERED Product, Pharmacopeia, US, Vol USP <1043> (2012)
6. Guideline on quality, non-clinical and clinical requirements for investigational advanced therapy medical product in clinical trials, European Medical Agency (2019)
7. Raw Materials of Biological Origin for the Production of Cell-Based and Gene Therapy Products, EUROPEAN PHARMACOPOEIA9.0 (5.2.12)
8. Gene Transfer Medical Products for Human Use, EUROPEAN PHARMACOPOEIA9.0 (5.14)

About Puresyn

Puresyn incorporates a stringent Quality system in every aspect of our products and services and is committed to providing our collaborators with products and services of the highest quality. To meet that goal, all Puresyn functions are performed under the umbrella of our quality system. Puresyn maintains high standards to ensure that products meet or exceed our established specifications and those of our collaborators. We work with our collaborators to ensure the products and services we provide are of the highest quality possible to advance research. Puresyn can do this through adherence to all applicable Puresyn policies and procedures, utilizing good scientific practices, and adhering to all applicable government regulations.

Puresyn provides contract plasmid DNA manufacturing services including Transfection*Ready*, Research*Ready*, and IND*Ready*® DNA for applications from Transfections to GMP Vector production, and has over 30 years of DNA purification experience.

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