United Therapeutics
A PUBLIC BENEFIT CORPORATION

United Therapeutics Corporation's Quality Operations and Good Manufacturing Practices

We are committed to leading industry practice through our **GxP** Quality and Compliance program, supported by a digital Quality Management System (**QMS**). GxP refers to Good Manufacturing Practices (**GMP**[1]), as well as Good Clinical Practices (**GCP**), Good Distribution Practices (**GDP**), Good Laboratory Practices (**GLP**), Good Tissue Practices (**GTP**), and Good Vigilance Practices (**GVP**). Our Global Quality Policy and supporting policies and standard operating procedures (**SOPs**) together establish guidelines designed to assure quality, safety, and efficacy in the marketing and distribution of products.

Our **Quality Policy** covers all full- and part-time employees and extends to all contractors, sub-contractors, and temporary labor. Suppliers that could affect the quality and safety of our products are required to comply with GMP regulations, enforced by the U.S. Federal Drug Administration (**FDA**), and have their own Quality Policy, which is reviewed during qualification and subsequent monitoring.

Quality Policy Statement
Unitherians [United Therapeutics' employees] are committed to providing safe and effective therapeutic products to enrich the quality of life for our patients. We will continually achieve our mission through improving scientific innovation, enhancing the quality management system, complying with regulatory requirements, and meeting the expectations of our customers.

GP-001 Revision 02

Sam Mancuso
Quality Management System Representative
Senior Vice President, Global Quality

Dr. Martine Rothblatt
Chairperson and Chief Executive Officer

[1] We adhere to FDA GMP standards and are committed to improvement, striving to apply current Good Manufacturing Practices (**cGMP**) across our manufacturing operations.

Our Quality Organization

Our quality organization is composed of several different teams with different focus areas to help us maintain our high level of quality operations. Responsibilities include, but are not limited to, the following:

Quality Teams	Areas of Responsibility
Quality Assurance (**QA**) teams • Program Quality • Quality Engineering • Quality Operations	• Review product raw material and component specifications and controls in both manufacturing processes and final products to help assure the quality standards for safety and efficacy of each lot • Review production processes to comply with best manufacturing practices and drive ongoing improvements • Review master and executed records or Certificates of Compliance generated internally or externally to include ownership of documents for products manufactured on our behalf • Review supplier Certificates of Analysis to ensure that results meet label claims and specifications • Review test data reports to ensure accuracy of results • Design and review methods and protocols, including assurance procedures and reports • Approve product, raw material, or component specifications, test data, reports, and qualification/validation protocols, and signs and communicates release of the same for shipment
Quality Control (**QC**) team	• Inspect and test incoming materials, in-process materials, and finished product
GxP Compliance group	• Includes experts in GCP, GDP, GLP, GMP, GTP, and GVP • Responsible for establishing, implementing, and maintaining processes, infrastructure, tools, and resources for the QMS, and maintaining and leading the promotion, awareness, training, and remediation of regulatory quality throughout the organization • Conduct audits of external service provides and internal functions

Our QA methods encompass all corporate operations. All departments, such as but not limited to, Medical Device Design and Development, Fill/Finish, Production Materials, and Quality Control are responsible for adhering to GxP/Quality System Regulations (**QSRs**) and our internal procedures while performing GxP/QSR activities in a manner that enables us to incorporate and design quality into our products. Ongoing training and development is meant to provide employees with the tools to successfully fulfill their responsibilities while meeting our high quality and safety standards. We routinely evaluate our quality systems and processes at various levels of our organization to monitor key performance and quality indicators.

Our QMS provides guidance and best practices based on the current editions of applicable regulator standards, including the following:

- 21 FDA Code of Federal Regulations (**CFR**) Part 11 Electronic Records, Electronic Signatures
- 21 CFR Parts 210 and 211
- 21 CFR Part 314.81 Other postmarketing reports
- 21 CFR Parts 600 to 680 covering biological product cGMPs
- 21 CFR Part 803 Medical Device Reporting
- 21 CFR Part 4 Regulation of Combination Products
- 21 CFR Part 7 Subpart C Recalls (including Product Corrections)
- 21 CFR Parts 820.20 Management Responsibility, 820.30 Design Controls, 820.50 Purchasing Controls, and 820.100 Corrective and Preventive Action
- 21 CFR Part 830 Unique Device Identification
- International Conference on Harmonization (**ICH**) Guidelines Q7, Q9, Q10, and Q11
- USP General Chapter <7>
- USP or USP-NF Compendia associated with specific material and/or product testing requirements

We also take into consideration the following international regulations as they apply to our facilities, processes, and products, and we align as appropriate and necessary to contractual agreements with non-U.S. partners:

- EudraLex – Volume 4 – EU Guidelines for Good Manufacturing Practices for Medicinal Products for Human and Veterinary Use, Part 1 and Part 2, and applicable Annexes
- Guidelines on Good Distribution Practice for Medicinal Products for Human Use (2013/C 343/01)
- Health Canada Therapeutics Products Programme Guidelines – Good Manufacturing Practices
- EP Compendial Requirements
- JP Compendial Requirements

Additional regulation requirements are incorporated into our QMS as deemed applicable and necessary to support our work.

Onsite Inspections, Audits, and Testing

We conduct audits in accordance with the GxPs relevant to the work. Our GxP Compliance team is responsible for auditing our suppliers, service providers, distributors, and internal functions to verify that they are qualified to meet global regulations and our own standards. Our GxP team also works closely with our Environmental Health, Safety, and Sustainability (**EHSS**) team in completing product stewardship and industrial hygiene audits and testing across our facilities.

Corrective and Preventative Action Program

Our Corrective and Preventive Action (**CAPA**) program has established methods to complete the following:

1. Analyze processes, work instructions, quality and audit reports, quality records, service records, patient complaints, returned product, and other sources of quality data to identify existing and potential causes of nonconforming product or other quality issues
2. Investigate the causes of nonconformities or other quality issues
3. Identify actions needed to correct and prevent the recurrence of nonconformities or other quality issues
4. Verify or validate that CAPAs have the intended effect and no unintended adverse effects
5. Notify QA and QC leaders about nonconformances or quality issues to enable regular improvement

All full- and part-time employees, contractors, subcontractors, and temporary labor are required to initiate CAPA requests upon confirmation of quality issues. Designated individuals are assigned responsibility for coordinating, documenting, and monitoring the CAPA process.

Employee Training

We maintain a comprehensive set of SOPs and training programs to guide and serve as best practices for our employees with respect to GxP requirements. All *Unitherians* receive annual GMP refresher training and new hires receive introductory GMP training as part of the onboarding process. *Unitherians* with GxP-related roles and responsibilities conduct additional training exercises.

Our Supply Chain

We maintain a robust GxP Quality and Compliance program covering those aspects of our supply chain that could impact the quality and safety of our products. Raw material vendors and service providers are pre-qualified to support our clinical and commercial business operations. Supplier audits focus on quality and safety aspects of the products and services supplied. After initial assessment and qualification, we periodically re-evaluate supplier compliance with GMP norms and quality standards at a frequency defined in internal procedures. For example, we conduct remote or onsite audits of certain qualified suppliers if there is high impact level of product or service provided, if there have been issues with product or service quality, and/or if there have been changes that may result in increased potential risk (e.g., change in manufacturing location).

References

- United Therapeutics Code of Conduct: https://ir.unither.com/~/media/Files/U/United-Therapeutics-IR/documents/corporate-governance/Code-of-Conduct-and-Business-Ethics.pdf
- See our Global Product Safety and Pharmacovigilance Overview: https://corporateresponsibility.unither.com/~/media/Files/U/Unither-Corp/reports-and-resources/ut-patient-safety-vigilance-program-overview.pdf
- See the latest Corporate Responsibility and Public Benefit Report for additional details about our public benefit goals, objectives, and targets, and our sustainability and ESG progress: https://corporateresponsibility.unither.com/

United Therapeutics Corporation rechartered as a public benefit corporation (**PBC**) in 2021—the first publicly-traded biopharmaceutical company to do so. Our **PBC purpose** has two parts: ***to create a brighter future for patients through the development of novel pharmaceutical therapies and technologies that expand the availability of transplantable organs.*** Our first purpose helps delay or avoid the need for a transplant, while the second purpose enables a patient to have a transplant when they need one.

Corporate website: https://www.unither.com/home
Corporate Responsibility website: https://corporateresponsibility.unither.com/
Investor Relations website: https://ir.unither.com/