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Active Temperature-Controlled Systems:
有源温度受控系统:

Qualification Guidance
确认指南

PDA Active Temperature-Controlled Systems: Qualification Guidance Technical Report Team

美国注射剂协会有源温度受控系统：确认指南技术报告团队

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Table of Contents

目录

1.0 Introduction
第一章：简介

1.1 Purpose and Scope
第 1.1 节：目的与范围

Fundamental to any temperature-controlled process is the expectation that materials that are stored and shipped within a controlled environment are maintained within a defined temperature range. Typically, this temperature range is within the recommended product storage requirements derived from stability data. The temperature within a temperature-controlled vehicle; temperature-controlled ocean container; active unit load device (ULD); or walk-in, temperature-controlled stores (e.g., a cold room, refrigerator, freezer, or standalone unit) is expected to be maintained:

对于任何一种温度控制过程来说最重要的是期望是在一个受控制的环境储藏与运输物料，将温度控制到一个规定的温度范围内。典型地，该温度范围处于来自稳定性数据所推荐的产品储存范围。诸如，在温度控制运输车、温度控制远洋运输集装箱、有源成组装运设备(ULD)、大型温度控制冷库(例如，冷藏间、冷库、冰箱或独立单元)都是需要维持以下要求：

- Reliably and consistently through the period in which the product is stored within the controlled environment (i.e., over time)

  在整个期间可靠、持续地将储存产品的温度控制在一定范围内(例如，全部时间)

- In compliance with the product requirements for temperature at all locations in which the product might be stored (i.e., temperature and location or storage boundary)

  所有产品可能储存的点都符合产品对温度要求(例如，温度与位置或者存储边界。)

The qualification process proves that the transportation system can consistently meet product temperature requirements. Strategies for conducting qualification studies should be based on the product's temperature and stability requirements as well as the transportation and storage process for that product.

确认过程证明运输系统可持续满足产品温度需求。进行确认研究策略应基于产品温度和稳定性要求以及运输和储存过程。

Qualification is part of a validation program with a validation master plan (VMP) for the transportation system in question that defines the design qualification (DQ), installation qualification (IQ), operational qualification (OQ) and performance qualification (PQ) requirements. The VMP is discussed in more detail in Section 4.0.

确认是所考虑运输系统验证总计划(VMP)的验证程序的一个部分，规定的设计确认(DQ)、安装确认(IQ)、运行确认(OQ)、以及性能确认(PQ)要求。验证总计划(VMP)在第4.0章进行详细讨论。

This guidance discusses the process of qualifying actively controlled spaces that are designed to maintain a stable and uniform temperature around the cargo for the duration of transportation or storage at any temperature range. Specifically, this guidance addresses best practices for qualifying temperature-controlled trucks or trailers (hereafter referred to simply as "trucks"), temperature-controlled ocean containers, active ULDs, and walk-in temperature-controlled stores that are used to quarantine, hold, or store raw materials, intermediates, or products. It provides details on selected temperature controlled units and their qualification testing, and it identifies best practices for performing and documenting the qualification activities, including temperature mapping studies, that are part of an overall validation program, whether that program is conducted by the pharmaceutical shipper or a service provider.

本指南讨论确认用来在运输或储存期间货物周围在任何温度下维持一个稳定、均匀温度的有源式控制温度空间的过程。特别的，本指南是为确认温度受控卡车或拖车(此后统称为运输车)、温度受控远洋运输集装箱、有源成组装运设备(ULD)、用来待检、保存，或储存原料、中间体，或产品的大型温度受控储存设施建立最佳规范。它提供了一个选择温度控制单元或确认测试详细方法，其辨识了实施与记录确认活动的最佳规范，包括作为整个验证规程的温度分布研究，而不论该程序是由药品承运人还是服务商来实施。

1.2 Aircraft Cargo Compartments
第 1.2 节：飞机货运仓

The environment of packages or freight in aircraft cargo compartments can be influenced by the transportation process. Transportation processes can be combined with other temperature-controlled packaging processes (active or passive) to help reduce the extremes of temperature for commodities during transit. In marketing their aircraft equipment and procedural controls, some air carriers are claiming that the aircraft cargo hold can serve as an active temperature-controlled system for cargo that is less sensitive to temperature variations (e.g., for products that are stable in a controlled room temperature range of 15°C to 25°C with allowable excursions). Although the temperature inside many current aircraft compartments can be regulated, aircraft themselves are not designed as temperature control systems. Thus, they are not discussed as such in this guidance.

在运输过程中飞机货运仓内的包裹或货物环境将受到影响。运输过程可与其它温度受控包装过程(有源或无源)合并，来帮助减少大宗商品在运输过程中的极端温度。在订购飞行设备或程序控制时，一些空运承运人会声称空运货物可用一个有源温度受控系统，温度变化不会产生较大影响(例如，对于产品在受控室温15℃到25℃范围并允许偏离)。虽然在许多目前使用的飞机货运仓内的温度都可调节，但航空器本身没有设计成温度受控系统。所以，本指南不对其进行讨论。

Pharmaceutical shippers with cargo that is sufficiently stable to withstand the rigors of air travel without additional protection by an active container or passive packaging system should perform shipping temperature studies to ensure that process controls are sufficient to protect the product within the air planes used. Such studies are outside the scope of this guidance.

在没有有源集装箱或无源包装系统附加保护下，经受严酷空运条件而足够稳定货物的药品承运人应实施运输温度研究来确保过程控制能够足够保护在所使用飞机内的产品。这样的研究也在本指南之外。

2.0 Glossary of Terms
第二章：术语

Definitions are provided to help clarify the concepts used in this report. Some of the definitions vary between companies; however, the definitions below are used consistently within this document.

提供定义来帮助澄清在本报告中所使用的概念。在公司之间，一些定义会有所不同，但，以下定义在本报告内是一致的。

Acceptance Criteria

可接受标准

Numerical limits, ranges, or other suitable measures for acceptance of test results (1).

检测结果可接受数字限度范围。

Active Temperature-Controlled System

有源温度受控系统

Actively powered system that uses electricity or other fuel source to maintain a temperature-controlled environment inside an insulated enclosure under thermostatic regulation (e.g., cold room, refrigerator, temperature-controlled truck, or refrigerated ocean or air container).

用电力或其它燃料来源来维持一个处于温度调节(例如，冷库，冰箱，温度控制运输车，制冷的远洋或空中仓储集装箱)保温密闭空间温度受控环境的有源动力系统。

Active Unit Load Device (Active ULD)

有源成组装运设备(有源ULD)

A unit load device with an active heating and/or cooling system that is typically used in air transportation, usually operated from externally supplied AC or DC power or from internal batteries.

一个拥有有源式制加热，和/或，制冷系统的成组装运设备，其典型用于空运，通常用外部供的直流或交流电源或内部电池来运行。

British thermal unit (BTU)

英制热量单位

The amount of heat (measured in Joules) required to raise the temperature of one pound of water by 1°F.

把一镑水提高一华氏度所需要的热量(焦耳)。

Change Control

变更控制

The process and procedures used to manage changes.

管理变更的过程与规程。

Compressor

压缩机

Components used to pump refrigerant through the active temperature-controlled system.

将冷剂用泵输送到有源式温度受控系的一个部件。

Condenser

冷凝器

Component that removes the heat absorbed by the refrigerant from the compressor and temperature-controlled area.

转移由制冷剂从压缩机与温度受控区域所吸收热量的部件。

Controlled Environmental Space (CES)

受控环境空间(CES)

An area that is controlled by regulating temperature.

一个通过调节温度受控区域。

Design Qualification (DQ)

设计确认(DQ)

Documented verification that the proposed design of the facilities, equipment, or systems is suitable for the intended purpose (1).

文件确证，所提议的设施、设备或系统设计适用于与其目的(1)。

Distribution Thermocouple

布置热电偶

Device placed in the interior of the controlled environment space (CES) to measure air temperature but is not placed in the product (see penetration thermocouple).

用来测量空气温度放置在受控环境空间(CES)内部的装置，但它不放在产品内部(见穿透型热电偶)。

Evaporator

蒸发器

Component that transfers heat out of or into the CES (to control the area temperature).

将热转移出或转移进入受控环境空间(CES) (以便控制区域内的温度)部件。

Full Loop Calibration

全闭环校准

A calibration process that includes all measurement system components, from sensor to measurement value (e.g., temperature calibration of a data logger and attached thermocouple wires).

包括所有测量系统部件的校准过程，从传感器到测量数值(例如，数据记录仪器与附带热电偶导线的温度校准)。

Generator Set (Genset)

发电机组(Genset)

A generator unit that is used to provide electrical power to maintain the temperature in a container/trailer in transit and is not attached to a stationary power source. Gensets consist of a diesel or electrically powered engine that produces the required voltage to operate the temperature control unit (TCU; reefer) on the container/trailer.

发电机组用于不依附固定电源来提供维持在运输中集装箱/拖车内温度电源。发电机组是由产生需要的电压来运转在集装箱/拖车的温度控制单元(TCU, 冷藏箱)。

Installation Qualification (IQ)

安装确认(IQ)

Documented verification that the equipment or systems, as installed or modified, comply with the approved design, manufacturer’s recommendations, and/or user requirements (1).

文件确证所安装或维修的设备或系统与已经批准的设计、生产企业推荐，和/或，用户需求修相符合。

Intermodal Container

多式联运集装箱

A shipping container used to ship cargo through more than one of the four traditional modes of transportation (road, air, ocean, and rail).

一个用于通过一个以上的四个传统运输模式方式中一个来运输货物运输集装箱(陆运、空运、海运、与铁路)。

Microprocessor

微处理器

One of the five major components of a TCU, the unit interfaces with temperature sensors in the discharge and return air and adjusts the output rate of active cooling or heating to achieve the setpoint temperature.

温度控制单元(TCU)的五个主要部件的之一，该单元与排放与回风温度传感器连接，并调整有源式制冷或制热输出的速率来达到设置温度。

Operational Qualification (OQ)

运行确认(OQ)

Documented verification that the equipment or systems, as installed or modified, perform as intended throughout the anticipated operating ranges (1).

文件确证所安装或修改的设备或系统按照在预期的操作范围内实施(1)。

Passive Holdover

被动维持

The length of time that the temperature remains within the acceptable range when power is lost.

在断电情况下，温度维持在可接受范围内的时间长度。

Passive Temperature-Controlled Transportation Systems

被动温度控制运输系统

Transportation systems without active temperature control (e.g., insulated containers with or without refrigerants).

无有源式温度控制的传输系统(例如，有或没有制冷剂保温集装箱)。

Penetration Thermocouple

穿透型热点偶

A thermocouple that is placed in or against the material/product to measure the material/product temperature.

进入或紧靠物料或产品来测量物料和产品的温度的热电偶。

Performance Qualification (PQ)

运行确认(PQ)

Documented verification that the equipment and ancillary systems, when connected, can perform effectively and reproducibly based on the approved process method and specifications (1).

文件确证设备与辅助系统连接后，可按照已经批准的工艺方法与规格标准有效并重现实施(1)。

Protocol

方案

A predefined, written procedural method for the design and implementation of experiments to define and document the methodology and criteria required to assess the capability of a temperature controlled system to achieve the desired result.

预定义的、 书面程序方法来设计与实施实验来定义并记录所需要的方法与标准来评估的温度控制系统的能力，以实现所需的结果。

Protocol Deviation

方案偏差

A deviation that occurs when a result is unexpected (i.e., fails to meet the predetermined acceptance criteria) or a procedure in the protocol cannot be executed as written (e.g., when a challenge is conducted using a methodology other than that described in the protocol or a process/ piece of test equipment fails).

当非预想的结果出现时产生的偏差(例如，不能满足预定的可接受标准)或方案中的规程不能按照书面要求实施(例如，当实施挑战使用的方法不是方案里所描述的方法，或者参与的检测设备/部件发生故障时)。

Protocol Summary Report

方案总结报告

A report generated at the completion of the activities identified in an individual validation protocol that summarizes deviations and conclusions.

在一个单独的验证方案内已经辨识的活动完成后，生成一个汇总偏差与结论的报告。

Qualification

确认

Documented testing that demonstrates, with a high degree of assurance, that a process or system function will meet its predetermined acceptance criteria.

证明高度确保一个过程或系统功能将符合预定的可接受标准的文件化测试。

Setpoint

设置点

The specific temperature programmed by the user into the TCU that establishes the target temperature in the CES (cold room, truck/trailer, intermodal container, or ULD).

由用户订立的输入温度控制单元(TCU)特定温度，以便建立(冷藏间、卡车/拖车、多式联运集装箱，或有源成组装运设备(ULD))目标温度。

Temperature-Controlled Truck or Trailer

温度控制卡车或拖车

A cargo box attached to a truck chassis or consisting of a trailer pulled by a truck that is equipped with a TCU to provide active cooling or heating control inside the box (refrigerated trucks or trailers are sometimes referred to as “reefers”).

一个装配有温度控制单元(TCU)来提供在货物箱内有源制冷或加热控制连接在卡车底盘货箱或由卡车牵引的拖车(制冷车或拖车有时被认为是一种“冷藏箱”)。

Temperature-Controlled Ocean Container (Reefer, Intermodal Container)

温度控制远洋运输集装箱(冷藏箱、多式联运集装箱)

An actively cooled metal box (commonly 20 or 40 ft long) that can be easily transferred between different modes of transportation, such as between ships, trains, and trucks.

一个有源式制冷金属箱(一般 20 英尺或 40 英尺长)，它可很容易的在几种不同运输模式之间转换，比如在船舶、火车、卡车。

Temperature Control Unit (TCU)

温度控制单元(TCU)

A unit that controls the refrigeration and heating systems contains a microprocessor and thermostat to maintain the set temperature.

一个内含微处理器和恒温器控制制冷和加热系统来维持设定温度单元。

Thermal Mass

热质量

The mass of material present multiplied by that material’s specific heat capacity

物体质量乘以物质单位热容量。

Validation

验证

A documented program that provides a high degree of assurance that a specific process, method, or system will consistently produce a result that meets predetermined acceptance criteria (1).

一个提供特定过程、方法或系统将持续产生符合预定验收标准结果高度保证的文件化程序(1)。

2.1 Acronyms

第 2.1 节：缩写

BTU	British Thermal Unit 英制热量单位
CES	Controlled Environment Space 受控环境空间
DQ	Design Qualification 设计确认
GDP	Good Distribution Practice 药品流通质量管理规范

GEP	Good Engineering Practice 药品工程质量管理规范
GMP	Good Manufacturing Practice 药品生产质量管理规范
IQ	Installation Qualification 安装确认
NIST	National Institute of Standards and Technology 美国国家标准与技术研究所
OQ	Operational Qualification 运行确认
PM	Preventive Maintenance 预防性维护
PQ	Performance Qualification 性能确认
RTD	Recording Temperature Device 温度记录装置
SLA	Service Level Agreements 服务水平协议
TCU	Temperature Control Unit 温度控制单元
ULD	Unit Load Device 成组装运设备
URS	User Requirements Specification 用户需求规格标准
VMP	Validation Master Plan 验证主计划

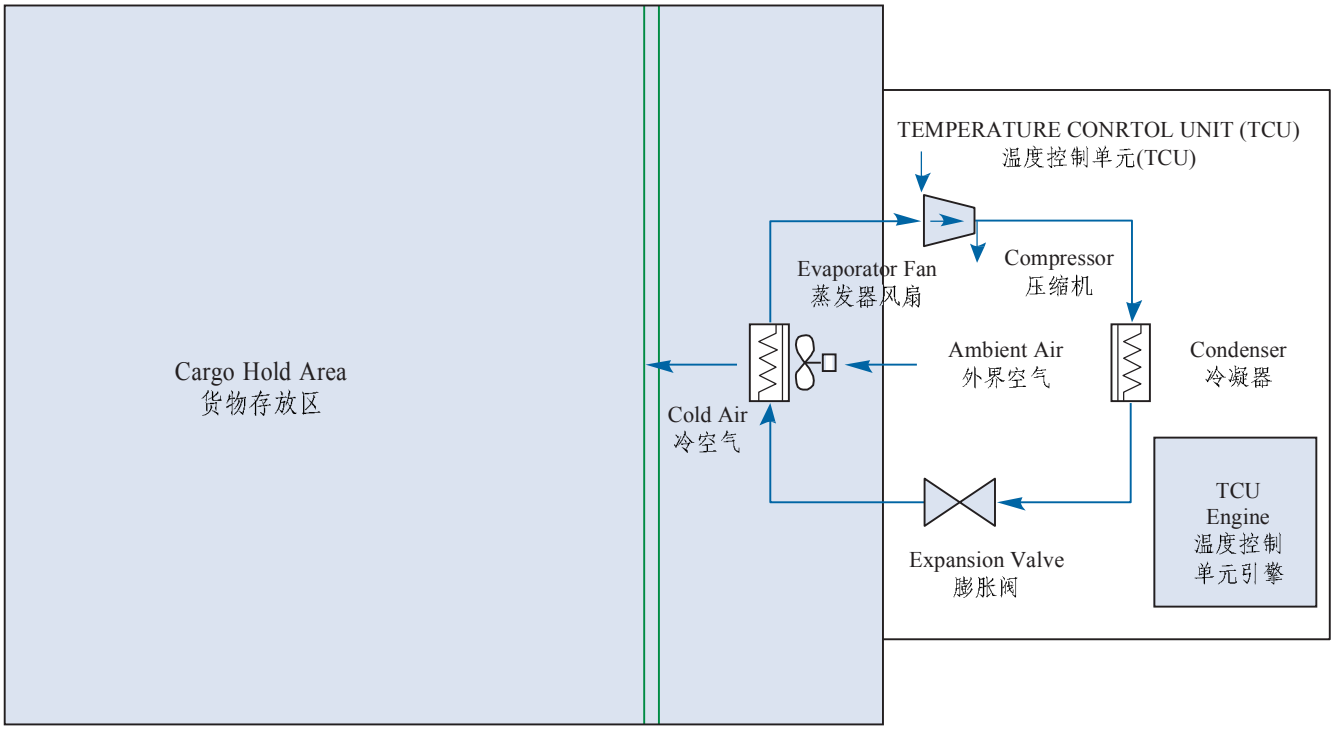
3.0 Overview of Active System Operating Characteristics
第三章：有源式系统运行特性概述

3.1 Temperature Control Unit System Components
第 3.1 节：温度控制单元系统组成

Every active temperature-controlled system has five major components:
每个有源式温度受控系统有五个主要部件部分:

- Microprocessor
  微处理器
- TCU engine
  温度受控系统(TCU)引擎
- Compressor
  压缩机
- Condenser
  冷凝器
- Evaporator
  蒸发器

Each component has a unique function (See Figure 3.1.1-1) that is discussed in the next subsection.
每个部件都有个独特功能(参见图3.1.1-1)，它们将会在下节介绍。



3.1.1 Cooling and Heating Cycle: How it all works
第 3.1.1 节：制冷与加热周期：其是如何工作的

A box containing the compressor, condenser, TCU engine, and microprocessor is located outside the controlled environment space (CES) (e.g., outside the trailer, temperature-controlled ocean container, active ULD, or cold room). The compressor works with the engine to change the phase of the refrigerant from gas to liquid by increasing its pressure. During compression, the refrigerant heats up due to the phase change. The resulting liquid refrigerant is pumped into the condenser, where the heat is removed from the refrigerant as it approaches thermal equilibration with the ambient air outside the CES. After the refrigerant has been cooled to a liquid, it passes through an expansion valve into the evaporator, where it changes phase back to a gas as it absorbs heat. The

warmed refrigerant then flows back through the compressor, where the cycle starts again. The heating process of a refrigeration unit is typically the reverse of the cooling process. The evaporator becomes the condenser and the condenser becomes the evaporator. Some systems, such as active ULDs, might be equipped with a separate heat source, such as an electric heater.

一个包括压缩机、冷凝器、温度控制单元引擎和微处理器的箱体位于受控环境区域(CES)以外(例如，在拖车外、温度控制远洋集装箱外、在有源成组装运设备(ULD)外、在冷库外)。 压缩机和发动机一起工作来使制冷剂变相，增压使其从气态到液态。在压缩过程中，制冷剂由于相变升温。然后液态的制冷剂被用泵打入冷凝器，由于和受控环境区域(CES)环境空气接触后达到热平衡，导致制冷剂的热量被带出。制冷剂被冷却成液体后，其通过膨胀阀时，然后进入蒸发器，当其相变回气态吸收热量。被加热的制冷剂重新流回压缩机，这样循环又再一次开始。制冷单元的加热过程，就是制冷过程的逆过程。蒸发器变成冷凝器，冷凝器变成蒸发器。一些系统，诸如有源成组装运设备(ULD)，可能安装了其它分离式加热源，诸如电加热器。

A defrost cycle, necessary to prevent the system from forming ice, is executed periodically based on measurements of the coil's temperature at given time intervals. A timer closes a circuit, which allows air to flow to a temperature sensing device. If the temperature falls within the temperature range that would allow ice to build up, the system starts a defrost cycle, in most cases using an electrical heater. The defrost cycle also begins if evaporator icing results in airflow obstruction.

防止系统结冰所必须的除霜循过程，基于对盘管在给定间隔的温度的测量，定期实施。一个计时器闭回路，使得空气留到温度传感器装置。如果温度不在可能结冰的范围，系统开启除霜模式。在大多数情况下使用电加热器进行除霜。如果蒸发器结冰而导致空气流通遏阻，那么也会开启除霜模式。

3.2 Operating Characteristics Affecting Qualification

第 3.2 节：影响确认的运行特性

Temperature-controlled spaces for storage and/or transportation are utilized to provide a stable temperature in the environment surrounding a temperature-sensitive material. As in passive systems, the temperature within a CES is affected by the thermal energy of the material placed inside it. Unlike passive systems, active systems do not use up their potential to maintain a stable temperature over time. Thus, active systems can be qualified using techniques that are different from those used to qualify passive temperature-controlled transportation systems and that are more suitable and effective for active temperature-controlled transportation systems. Design specifications and process characteristics affect active systems operations, and both of these parameters should be taken into consideration when designing this type of system. The critical design parameters of active systems are:

利用储藏，和/或，运输的温度受控空间来为温度敏感物料提供一个稳定温度环绕环境。在无源的系统，受控环境空间内的温度受放置在其中物料的自身热能影响。与无源系统不一样，有源式系统不会用光其在整个时间的潜能来维持稳定温度。因此，可用与确认无源式温度控制运输系统的不同技术对有源式系统进行确认，并且对于有源式温度受控系统更加适合并有效。设计规范与过程特性影响有源式系统运行，当设计这种系统时，应考虑这些参数。无源系统的关键设计参数为:

- Insulation
  保温
- Airflow
  气流
- Heat exchange capacity
  热交换容量
- Thermal integrity
  热完整性
- Monitoring systems
  监测系统
- Alarms
  报警

A system's performance in practice is also affected by the process used for loading and unloading its contents, the temperature immediately outside an open door, and the temperature and amount of material placed inside the CES.

系统实际性能同样受到装货和卸货过程、开门的外界温度、放置在受控环境空间内的物料温度和数量等因素影响。

3.2.1 Insulation

第 3.2.1 节：保温

Insulation can be categorized by its composition (material), form (structural or nonstructural), or functional mode (conductive, radiative, or convective). Nonstructural forms of insulation include blankets, loose fill spray foam, and panels. Structural forms of insulation include insulating concrete forms, structured panels and straw bales. Sometimes a thermally reflective surface, called a radiant barrier, is added to a material to reduce the transfer of heat through radiation as well as conduction. Reflective insulation and radiant barriers reduce the radiation of heat to or from a material's surface.

可按照保温的构成(物料)、形式(有结构或无结构)或功能模式(热传导、辐射、对流)进行分类。无结构的形式包括毯子、松散填充的泡沫塑料、嵌板。有结构的保温形式包括保温混凝土形式、结构嵌板和草包。有时候，一种被称作辐射屏障的热反射表面被加入到物料中去来减少通过热辐射与对流传递。反射保温和辐射屏障可减少热辐射或来自物料表面的热辐射。

Radiant barriers reflect radiant energy but do not affect heat conducted through a material by direct contact or heat transferred by moist air rising or convection. For this reason, trying to associate R values with radiant barriers is difficult and inappropriate. The R-value test measures heat transfer through the material and not to or from its surface. The resistance of each material to heat transfer depends on the specific thermal resistance [R value]/[unit thickness], which is a property of the material and the thickness of that layer.

辐射屏障反射辐射能量，但不影响直接接触物料传导，也不影响因为潮湿空气导致热转移或对流。由于这个原因，对辐射屏障尝试用R值是很困难的也不合适。R值测量通过物料热传递，而不是从其表面的热传递。每个物料对热传递的阻力取决于特定的热阻[R值]/[单位厚度]，其与物料性质以及厚度有关。

The polyurethane insulation commonly used in trucks/trailers and temperature-controlled ocean containers degrades by a small percentage each year. The urethane in the wall tends to break and become powdery over time (usually several years), which can leave large areas of the container without insulation. Over time, this loss of insulation can reduce the system's ability to hold a stable, uniform temperature inside the CES and result in the need for corrective repair or requalification (see Section 4.6.1.5).

聚氨酯保温材料曾经通常用于卡车/拖车及温度控制远洋集装箱，但现每年小比例的下降。在墙内的氨基甲酸乙酯在一定时间(一般是几年)的使用后，会开始崩解变成粉末，这样会导致集装箱的一大块区域没有保温材料。经过一段时间后，保温能力减弱会降低系统保持稳定能力，使受控环境空间内的温度不均匀，并导致需要维修和再确认(见第4.6.1.5节)。

3.2.2 Airflow

第 3.2.2 节：气流

Because thermal energy moves from warm to cold areas, heat energy ceases to flow between two objects once their temperatures are equal (phase changes excluded). When a CES is maintained at a temperature that is different from the outside ambient temperature (or if there is positive or negative latent heat energy within the cargo), the TCU produces an inflow of air that must be slightly above or below the setpoint to compensate for thermal gains or losses. To create a uniform temperature in the entire area, the air should be completely replaced often enough to remove the influence of heat from the material inside the area and to reduce heat transmitted from outside through the walls, floor, and ceiling. As a result, the entire volume of product within the CES is exposed to the newly conditioned air. Care must be taken not to load products too high or in positions that block the flow of air to prevent the formation of stagnant air pockets and the consequent hot or cold spots.

由于热能从高温区流向低温区，两个物体一旦其温度相等，热能就停止流动(不包括相变)。当受控环境空间维持的温度与环境温度不同时(或者如果在货物中有正或负潜热)，那么温度控制单元会产生气流，这个气流必须略高于或低于设定值，来补偿这种热增加或热损失。为了在整个区域形成均匀的温度，空气应经常足够完全替换来消除来自在这个区域内物料影响，并减少来自外部通过墙、地面与天棚进行的热传递。所以，在受控环境空间内的产品必须完全与新鲜空调风接触。必须小心不要让产品放置的过高或阻碍气流的位置，防止形成滞留空气口袋，形成热或冷点。

Sufficient air velocity is also important to ensure uniform airflow throughout the CES. In smaller spaces, an unassisted temperature control unit (TCU) can push air with sufficient speed and direction to reach from front to rear and from top to bottom of the space's interior. For larger spaces, additional air distribution systems such as fans, chutes, or both are recommended to maintain enough air velocity to reach all interior areas. The air is then recycled back to the return air vents. The temperature of this return air is measured by the TCU to calculate the necessary input air temperature.

足够的风速度对于确保在受控环境空间内形成均匀气流是非常重要的。在较小的空间内，一个独立的温度控制单元(TCU)可提供足够速度和方向的气流，从而在整个空间内部从前至后、从上到下能能够达到。对于较大的空间，推荐使用额外气流分配系统诸如风扇，沟槽或两者同时存在，从而保证足够的风速达到内部空间的所有角落。然后，空气循环到回风口。温度控制单元测定这个回风温度来计算所需的进风温度。

3.2.3 Thermal Integrity

第 3.2.3 节：热完整性

Thermal integrity refers to a completely closed space. Gaps around doors, cracks in door seals, and gaps or cracks in walls or ceilings allow unconditioned air to enter the CES, making it more difficult for the active system to maintain a stable temperature.

热完整性是对于全封闭空间而言的。门四周的缝隙、门密封破损、墙缝隙或破损，及天花板的类似情况，都会使得未经过空调处理的空气进入受控环境空间，这样就使有源式系统维持稳定温度变得很困难。

3.2.4 Capacity for Heat Exchange

第 3.2.4 节：热交换容量

The capacity for temperature control measured in British thermal units (BTUs) determines how much heat energy can be delivered or removed by the TCU. The ability to produce the correct amount of BTUs is essential for any TCU. The capacity required in a given situation depends primarily on the temperature difference between the air inside and outside the CES. The thermal mass of the stored/ transported products and their temperature also has an impact. The required temperature control capacity within a temperature stable ambient condition, such as a walk-in cooler inside a warehouse, is very different from required capacity for the wide range of conditions that a moving temperature controlled trailer might experience. The wider the range of ambient temperatures around a unit, the harder the temperature-control unit must work to produce the correct air temperature for the material or product being stored.

温度控制容量用英制热量单位来测量(BTU)，通过它确定多少热能可从温度受控系统传入或传出。产生正确英制热量单位量的能力对于任何温度受控系统尤为重要。在给定的状况下，所需容量主要依赖于在温度受控系统内外空气的温差。储存或运输的产品的热质量及其温度也会产生影响。在一个温度稳定环境条件下，所需的温度控制容量，例如在仓库内的大制冷机与一个移动的温度控制拖车所需的热量是完全不同的。在单元外环境温度范围越宽，温度控制单元就越难产生正确对于所储存的物料或产品空气温度。

Relevant processes should also be controlled sufficiently so as not to exceed the system’s capability to maintain constant, uniform temperatures. In an ideal transportation process, heating or cooling capacity is affected only by ambient temperature conditions (heat loss or gain caused by conditions external to the temperature-controlled cargo area), which requires the goods and the cargo area to be at the desired storage/transportation temperature before they are loaded. Hence, an active temperature control system used in a transport container does not need the capacity to cool the contents. For example, in this ideal transportation process, materials might be moved from a temperature controlled warehouse (maintained entirely at the required product temperature) directly into a temperature- controlled, preconditioned, active temperature-controlled transport container. Similarly, a walk-in cooler might have procedural limits developed to limit “open door” situations, and a warehouse might have added measures, such as air curtains, to reduce the impact of loading and unloading materials on its temperature. However, the effects of each process on the air surrounding the materials should be examined individually to assess the system’s capacity to control the temperature of that air. Evaluations of each process should identify some capacity to cool or heat the system’s contents to compensate for loading/unloading in conditions that are less than ideal.

应对相关过程进行足够的控制，来保证不超过系统维持恒定、均匀温度的容量。在一个理想的运输过程中，加热与制冷能力只受环境温度条件的影响(温度受控货物区域从外部环境条件损失或获得热量)，其需要货物与装货区域在装载前处于所要求的储存/运输温度。因此一个在运输集装箱内的有源式温度受控系统不需要冷却货物的能力。例如，在一个理想的运输过程中，物料可能从温度受控仓库(完全保持在产品要求的温度)直接进入一个温度受控的、已经温度调节好了的、有源式运输集装箱。类似的，大型冷库也许有程序的限制，来限制“开门”状况，并且仓库可能有附加措施，诸如风幕，来减少装货和卸货对物料温度的影响。然后每个对于物料环境的过程影响，都应进行单独测定来评估系统空气温度控制能力。对每个过程的评估应辨识某些对系统内的物料制冷或加热能力，以便对在低于理想条件下货物装载/卸载进行补偿。

3.2.5 Temperature Monitoring Systems

第 3.2.5 节：温度监测系统

Considerations for temperature monitoring systems are:

对温度监测系统的考量是为:

- Location of temperature sensors
  温度传感器位置
- Ease and method of sensor calibration and/or verification of calibration
  减缓传感器校准，和/或，校准确证与方法
- Ability to store and retain temperature data and method for doing so
  存储于保存温度数据能力与相关方法

- Intervals used between temperature measurements
  温度测量的时间间隔

Most modern monitoring systems are digital and therefore are not “continuous.” It is useful to measure the temperature in a transportation system frequently enough to identify trends that lead up to any alarm events to support investigations of these events. Commonly, a 15- or 30-minute interval is therefore selected for the qualification test and/or transport data log.

大多数现代监测系统来说，他们都是数字化的，也就是不“连续”的。在运输系统内有足够频率的温度测量对该系统报进行辨识导致任何报警事件趋势来支持相关调查是非常有帮助的。一般的，因此对于确认测试，和/或，运输数据记录仪选择15或30分钟的时间间隔。

3.2.6 Alarms

第 3.2.6 节：报警

For each CES, upper and lower temperature alert and/or action limits need to be defined for temperature sensors. If a temperature exceeds one of the limits, an alarm is generated, and this alarm can be visual (light), audible (sound), and/or a text message/email.

对于每一个受控环境空间，都要为温度传感器设置上下报警线与行动线。当温度超出限度时，产生报警，这种报警可是视觉(灯)、听觉(声音)，和/或，文字信息/电子邮件。

3.3 Temperature Control Accuracy

第 3.3 节：温度控制准确度

Temperature control accuracy is assessed during the temperature mapping study. Ideally, temperatures are maintained with very little variance; however, the costs of purchasing and/or operating such systems is generally higher.

在温度分布研究中评估温度控制准确度。理想的，温度控制在一个非常小变动范围内，然而这种系统的采购成本，和/或，运行成本通常会比较高。

The more advanced temperature control systems employ active analog control, which actively regulates air temperature continuously. Simpler control systems employ an “on/off ” temperature control system in which the TCU is only activated and deactivated at predetermined high and/or low temperatures (similar to the thermostats in most homes). The “on/off ” control strategy tends to be more fuel efficient because the TCU is not in constant operation. Note that the bandwidth of TCU activation and deactivation can greatly affect the accuracy and efficiency of the system’s ability to control temperature. For example, a very tight bandwidth, in which the TCU is activated at one degree higher than a setpoint and deactivated at one degree below a setpoint, could result in very tight control, but it could also result in constant cycling of the unit.

更高级的温度受控系统运用有源式模拟控制，它主动连续调节空气温度。温度受控系统内使用更简单的控制系统使用“开/关”温度控制系统只是在超过，和/或，低于预设的温度时开启或关闭(类似族用的恒温器)。“开/关”控制策略趋向于更节省燃料，这是因为温度受控系不是持续工作。注意到温度受控系的动作范围可很大的影响到系统控制温度能力的准确度精度与效率。例如，一个非常窄的控制温度范围，温度受控系统在高于设定值1度时开始动作，在低于设定值1度时停止动作，这就造成一个非常窄的控制，但它也造成一个常态的单元循环。

Temperature control accuracy tends to be more challenging for systems in dynamic conditions and/ or that contain relatively small volumes of materials. In large warehouses, for example, the mass and volume of airspace might be sufficient to dampen the impact of heat gain or loss, and, thus, simpler control systems can be employed. Control temperature probe location should be based on the controlled space’s volume.

对于动态系统，和/或，相对包含少量物料系统，控制温度准确度趋于更挑战。对于大型仓库，例如，航空运输中的大质量与大体积货物足够可抑制热量获得/损失的影响，因此，可使用较为简单的控制系统。控制温度传感器的位置是基于受控空间的体积大小。

In summary, an actively temperature-controlled system is designed to maintain the air temperature within a defined space, thereby insulating the stored or transported goods from the effects of outside conditions. To accomplish this, the air inside the system must be able to move throughout the area being controlled. Thermal integrity, sufficient capacity for heat exchange, proper airflow, and air velocity are as essential to a temperature control system, including monitors and alarms, as they are to the refrigeration process.

总的来说，一个有源控制温度系统的设计是用来维持特定空间的空气温度，因此货物的储藏和运输的保温性就受到外界环境的影响。为了达到此目标，系统内的空气必须能够穿越整个受控区域。热完整性、足够热交换能力、适当的气流和空气流速是对一个温度控制系统是必须的，对于冷冻过程，要包括监测与警报系统。

3.4 Risk and Criticality Assessment of Systems

第 3.4 节：系统的风险与关键性评估

During equipment and utility (e.g., water, electric) qualification, quality risk management tools should be used to determine the relative criticality of systems and their components and to achieve efficiencies (2). Process equipment and utility systems should

be assessed to determine their potential to affect product quality. Systems that are deemed to have that potential should undergo qualification. Evaluation of criticality for individual components of a direct impact system supports the development of the qualification approach for that system. A risk assessment should be considered for use with this type of evaluation because it can provide a significant benefit in the form of a more in-depth evaluation of the system (3).

在设备与公用设施(例如，水、电)确认中，应用质量风险管理工具来确定系统及其组成部分的相对关键性并达到效果(2)。应对工艺设备与公用系统进行评估来确定其对产品质量潜在影响。对于那些已经认为有生潜在风险的系统，应对其进行确认。用直接影响系统单一部件关键性评价来支撑该系统确认方法的开发。因为可对系统的深度评价提供一个非常显著益处，应考虑风险评估使用这类工具(3)。

3.4.1 Risk Assessment

第 3.4.1 节：风险评估

In the past, the risk assessment was primarily executed using only a system and/or component impact assessment. The GMP impact assessment can be considered a triage risk tool that provides a method to identify elements that are and are not GMP. An additional step is needed to provide the general level of the equipment or utility system's risk to product quality. This level of risk helps further determine the level of testing required and when in the project testing will be executed (i.e., during commissioning or qualification) (4). It is also acceptable to forgo the impact assessment portion and assess the risk of the equipment or plan for qualification because most indirect systems can be qualified utilizing commissioning activities.

在过去，风险评估主要用于对一个系统或一个部件的影响评估。药品生产质量管理规范影响评估可认为是一个会审风险工具，其提供了一个方法来辨识每个是与不是药品生产质量管理规范的因素。必须采取一个额外步骤来提供设备或公用设施系统对产品质量总体风险水平。这个风险水平将帮助进一步确定需要的测试水平，及什么时候进行项目测试(例如，在调试或确认)(4)。放弃影响评估这一部分而去评估设备或确认计划的风险是可被接受的，因为大多数非直接系统可利用调试来被确认。

Table 3.4.1-1 Risk-Based Qualification Planning with Typical Assessment Categories (Adapted from TR60) (4)

图3.4.1-1：带有典型评估分类的基于风险的确认策划(根据第60号技术报告改编)(4)

Risk Assessment Output Rankings 风险评估输出评级	Qualification Planning Typical 确认策划	Typical Impact Assessment Categories 典型影响评估分类
High 高	Testing to satisfy validation requirements occurs during qualification. Documentation and sampling requirements are high. 在确认期间，测试满足验证要求。文件和取样要求为高。	Direct 直接
Medium 中	A blend of qualification and commissioning activities can be used to satisfy validation requirements. Sampling requirements are moderate, given appropriate controls and risk reviews. 确认与调试活动协调可满足验证要求。采样要求为中，给出适当的控制和风险审核。	Direct or indirect 直接或间接
Low 低	Testing to satisfy validation requirements can occur during commissioning phases. Appropriate controls and risk reviews should be in place. 在调试阶段通过测试来满足验证要求。应有适当控制与风险审核。	Indirect 间接

The triage begins with an initial GMP impact assessment (Figure 3.4.1). Systems found not to have a GMP impact can be tested using Good Engineering Practice (GEP) and commissioning tests alone. Systems and components found to have a GMP impact (either direct or indirect) should be evaluated for the level of risk they impose. Table 3.4.1-1 provides the typical risk levels of direct and indirect systems.

该会审始于最初的药品生产质量管理规范影响评估(图3.4.1)。发现对药品生产质量管理规范没有影响的系统可使用工程质量管理规范(GEP)来测试，并单独进行调试测试。发现对药品生产质量管理规范有影响的系统部件(即包括直接也包括间接)应对其呈现的风险水平进行评价。表3.4.1-1提供了直接与间接系统典型风险水平。

The amount of testing and when it should take place (i.e., during the commissioning or qualification project stages) is determined by the relative risk associated with the GMP system or component. Low risk items can be qualified through testing during the commissioning phases, whereas high-risk items need to be qualified. Medium- or moderate-risk systems can be tested during both commissioning and qualification stages (Figure 3.4.1) (2,4).

测试数量与应当测试时间(例如，在调试与确认期间)由与药品生产质量管理规范所关联的系统及部件的相对风险决定。低风险的项目可在调试期间通过测试进行确认，而高风险的项目必须经过确认，中度风险的系统可既在调试阶段又可在确认阶段进行测试(表3.4.1)(2,4)。

Figure 3.4.1-1 Risk-Based Qualification Approach to Determine Testing Requirements with Impact Assessment Triage.

图3.4.1-1：带有影响评估会审的基于风险确认方式来判断测试需求

Adapted From PDA Technical Report 54 (2).

根据美国注射剂协会第54号技术报告改编(2)。

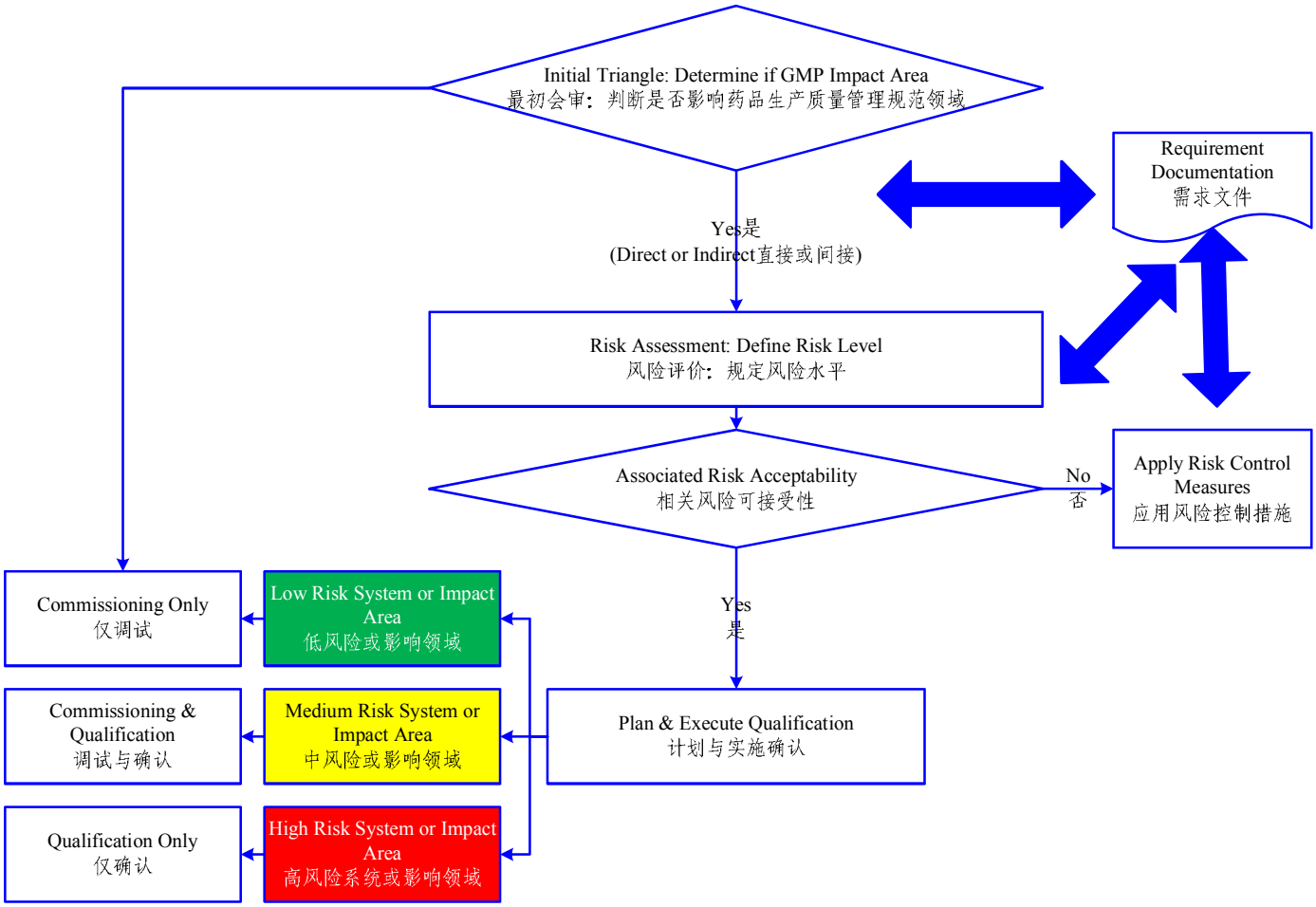


Table 3.4.1-2 illustrates how impact and component risk assessments can be used to focus the efforts of qualification for temperature-controlled systems. This table is not meant to be all inclusive.

表3.4.3.1-2说明了如何影响及部件风险评估用于关注温度受控系统确认工作付出。这个表格并不包含所有情况。

Table 3.4.1-2 Sample Assessment of Temperature Control System Impact and Component Criticality

表3.4.1-2：温度受控系统影响与部件关键性评估样本

System 系统	GMP Impact Areas 药品生产质量管理规范影响领域	Component(s)/Subsystems 部件/子系统	Component Risk to Product Quality 部件对产品质量风险	Rationale 基本原则	Scope of Testing 测试范围
Incoming walk-in-cooler (2 to 8°C, incorporates a single sensor to monitor internal temperature and a conventional compressor for cooling) 到货的大型制冷机(2-8°C，有一个传感器来监测内部温度，并有查压缩机来制冷)	Yes: the system preserves product's status. 是的，系统保持产品状态	Cooling system 制冷系统	Low 低	Gathers information on temperature uniformity to support independent monitoring locations 采集温度均匀性信息来支持独立监测位置	Temperature mapping during qualification to demonstrate temperature uniformity and to confirm the system's ability to produce consistent results in ongoing operations 在确认期间进行温度分布测试来确认温度均匀性来确认该系统在持续运行中产生一致性结果的能力
		Mechanical convection system 机械传热系统	Low 低		
		Insulation 保温	Low 低		
		Independent temperature monitoring instrument 独立温度监测仪器	High/medium 高/中 (direct) (直接)	Provides temperature record for the product 提供产品温度记录	Calibrate and test relevant alarms in OQ 在运行确认校准并测试相关报警
		Temperature control sensor 温度受控传感器	Low 低	Controls only (and not to provide a record of data) 仅控制(不提供数据记录)	Commission 调试 Thermal map to confirm system operation 热分布图来确认系统运行
		Automatic door lock 自动门禁	None 没有	Not part of temperature control system 不是温度控制系统的一部分	Commission for business need 按商业要求进行调试
ULD and independent monitoring system (used to transport highly critical products; each unit individually probed and	Yes: the system preserves product's status. 是的，系统保持产品	ULD and related mechanical systems 成组装运设备及相关的机械系统	Low 低	Records temperature data for each product unit 对每个产品单元记录温度数据	Qualify individual ULDs or groups of ULDs (family approach) 确认独立的成组装运设备或一组成组装运设备(族方法)

monitored) 成组装运设备与独立监测系统(用于运输高关键性产品；每个单元都有温度探头并进行监测)	状态				Temperature mapping during qualification to demonstrate temperature uniformity and to confirm the system's ability to produce consistent results in ongoing operations 在确认期间进行温度分布测试来确认温度均匀性来确认该系统在持续运行中产生一致性结果的能力
		Independent monitoring system 独立的监测系统	High/medium 高/中 (direct) (直接)	Provides data of record on each unit of the product 对每个产品的单元提供数据记录	Calibrate and test relevant alarms in OQ 在运行确认校准并测试相关报警
Temperature-controlled truck set to maintain 15 to 25ºC (when used to transport a ULD validated to comply with internal product requirements in harsh environments at -10 to 50°C for the duration of transportation) 温度控制卡车的温度设定在维持15-25ºC (当在恶劣的环境下-10到50ºC，运输一个成组装运设备经过验证符合内部产品要求)	No (for reefer truck): The truck safeguards ambient temperature of the ULD if needed. The ULD preserves the product's status. 不是(对于冷库车)：如果需要，卡车仅保护成组装运设备的环境温度。成组装运设备保护内部产品状态。	N/A 不适用	Low 低	Does not require a uniform, stable temperature in a tight range that would justify thermal mapping of the truck's temperature control system. Depending on season and ULD capability, the truck might not need temperature control at all. 不需要在一个严格的范围一个均匀、稳定的温度，卡车热分布图其证明卡车的控制系统。取决于季节与成组装运设备能力，也许卡车完全不需要温度控制。	Demonstrate process control 证明过程控制

4.0 Qualification of Active Temperature-Controlled Transportation Systems
第四章：有源式温度控制运输系统确认

Before the description below of the elements and procedures that are specific to each of the four active temperature-controlled transportation systems covered by this guidance (truck/trailers, ocean containers, active ULDs, and walk-in stores), a discussion of the qualification process for active systems is in order. Most but not all of the elements of the qualification process are common to all four active systems. The elements that are not the same for all four types of transportation systems are described in the sections on each of those systems (5).

在描述四个有源式温度控制运输系统(卡车/拖车、远洋运输集装、有源成组装运设备与大的冷库)的部件和程序之前，先来依次讨论一下有源系统的确认过程。大多数但并不是所有确认过程的要素在所有这四个有源式系统都有。对那些与所有四个类型运输系统不相似的要素，在本章节每个系统的章节中描述(5)。

For all four types of active transportation systems, the general approach is to verify that the active system has been commissioned to the appropriate criteria (6). Next, a thermal mapping and independent monitoring process verifies that the active system is operating properly. Following initial qualification, the system is monitored during ongoing operations to determine whether it requires requalification. For some systems, a regular requalification routine might be appropriate if performance history or product risk factors dictate such a schedule.

对于所有四种有源式运输系统来说，一般方式是确证有源系统是否已经按照恰当标准进行调试。接下来，使用一个温度分布与独立监测过程来确证有源系统正在正常运行。接下来最初确认，在持续运行对系统进行检测来判断是否需要重新确认。对于一些系统，如果性能历史或产品风险因素能够显示明显的周期规律，那么一个周期性的重新确认也许是很适合的。

4.1 Approach: Protocol Development
第 4.1 节：方式：方案开发

Before any temperature mapping or qualification is conducted, both the product requirements and transportation process capabilities and risks should be assessed to develop a protocol for assessing their potential impact on product quality.

If the assessment determines that a system's components or processes will have a direct impact on product or material quality, then a system qualification is required and a VMP (also known as a quality assurance plan) that integrates the objectives and methods chosen for DQ, IQ, OQ, and PQ should be developed. Temperature control design for long-term storage is also based on the registered label requirements and stability data. Shipping and distribution temperature control is based on the complete stability profile as guided by the regulatory filing.

在温度分布或确认实施之前，应评估产品要求与运输过程能力及风险，来开发一个评估其潜在对产品质量的影响方案。如果评估确定系统的部件或过程对产品或物料质量有直接影响，那么就需要开发一个整合目标与选择设计确认、安装确认、运行确认及性能确认方法的系统确认以及验证总计划(也就是质量保证计划)。对于长期储藏的温度控制设计也基于注册标签要求及稳定性数据。运输与流通温度控制是基于按照药政文件编辑的完整的稳定性概况。

A number of factors should be considered when developing a qualification protocol. Primarily, the level of testing should be based on the quality requirements of the products being transported or stored. In addition to the product requirements, the risk assessment can address the following issues:

当开发确认方案时应考虑很多因素。主要的，测试水平应基于所运输或储存产品的质量要求。在产品要求以外，风险评估也应考虑以下几个方面：

- Quality systems associated with the process or equipment, including loading/unloading operations
  与过程或设备相关的质量体系，包括装载/卸载操作
- Available drug product supply and ability to replace that supply
  药品供应可行性及可替代这种供应的能力
- Business tolerance of risk of damage to individual shipments that requires remedial action or return/destruction
  在一次运输中需要一个补救措施、召回/销毁在商务上可承担损坏风险
- Manufacturer history and experience with its products
  与产品生产相关的生产历史与经验
- Preventive maintenance (PM) requirements
  预防性维护 (PM) 需求
- Calibration requirements for the system monitors and test monitors used

对于系统监测与所使用的测试监测的校准需求

- Product protective packaging plan to add a layer of temperature protection to the active system
  增加有源性系统保温层的产品保护性包装计划

When developing the qualification protocol for a group of several similar units, one should consider whether all units, a single unit, or a sample of units will be used in the qualification protocol. Using one or more units to represent the group is known as a family approach to qualification. Statistically based random sampling of units used for qualification testing is an accepted industry practice. The extent of the testing and the number of units tested depends on the organization's policy concerning risk management and qualification (4,7,8). Refer to Section 4.6.4 for more details on the family approach.

当为一组相似单元开发确认方案时，应考虑从所有的单元中选择一个单元，或在确认方案中使用一个单元样本。使用一个单元或多个单元来代表整个组，被认为是一种族方式的确认。在行业惯例中接受确认测试中对所用的单元基于统计学上的随机取样。测试深度与测试单元数量取决于组织有关风险管理与确认的方针(4,7,8)。有关族方式更详细的信息请参阅第4.6.4节。

In addition to regulatory compliance, qualification:

药政符合性与确认其它方面:

- Reduces the risk of failure during transportation/storage
  减少在运输和储藏期间失败的风险
- Defines the optimal location for temperature monitoring
  为温度监测确定最理想的位置
- Provides a correlation of internal ambient temperature with product temperature
  提供一个内部环境温度和产品温度的相关性
- Verifies other concerns beyond temperature control and uniformity
  确证在温度控制与均匀性上的其它方面
- Ensures that other functional and user requirements are met
  确保符合其它功能与用户需求
- Provides a record of the system's condition and configuration
  提供一个系统条件与配置记录
- Ensures that all other required systems are in place to support continued equipment operation
  确保已经有所有其它所需系统来支持设备持续运行

4.2 Design Qualification

第 4.2 节：设计确认

Design qualification (DQ) is typically the first stage of qualifying any process or equipment and determines the design's suitability for the intended process. DQ can include physical testing or mathematical modeling. The DQ ensures that functional requirements can be met by the proposed process or equipment. The process parameters evaluated can include:

典型的，设计确认是过程或设备以及设计适用与其过程的第一步。设计确认可包括物理测试或数学模型。设计确认确保需求功能可有所建议的过程或设备满足。所评价过程参数包括:

- Process duration
  过程持续时间
- Ambient temperature (including extremes in actual conditions)
  环境温度(包括在实际条件中的极端)
- Insulation (type of insulating material/air conditioning system)
  保温(保温材料类型/空调系统)
- Quantity and locations of TCU cooling and/or heating systems
  温度控制单元制冷，和/或，加热系统数量与位置

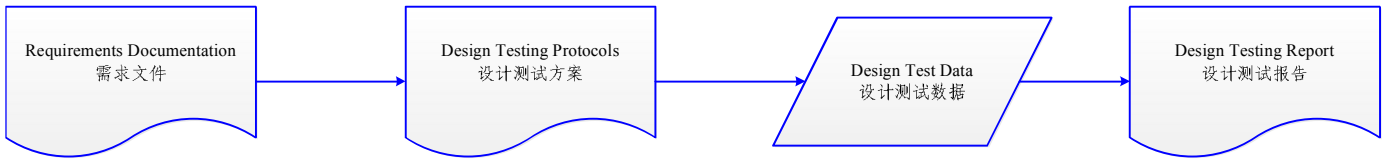
- Match between TCU's heat exchange capacity and CES volume
  温度控制单元热交换能力与受控环境空间体积匹配
- Volume and velocity of air produced by the TCU
  由温度控制单元产生的风量与风速
- Airflow in product shipping configuration
  在产品运输中气流形式
- Minimum and maximum thermal mass of the anticipated preconditioned load
  预计装载产品最小与最大热质量
- Monitoring systems (including locations of temperature measuring probes)
  监测系统(包括温度测量探头位置)
- Alarms settings, notification systems, and response procedures
  报警设置、通知系统与响应规程

The outcome of a successful DQ is a high level of confidence that the OQ results of a specific process or equipment will be positive. The results of DQ should be formally documented in a report. The components of a DQ are illustrated in Figure 4.2-1.

一个成功的设计确认的输出是即将肯定特定过程或设备运行确认结果高度信心。设计确认的结果应在报告当中正式记录。设计确认构成在图4.2-1中说明。

Figure 4.2-1 Design Qualification Steps

图4.2-1：设计确认步骤



1. Shipping temperature
   运输温度
2. Shipping Duration
   运输期间
3. Primary package
   内包装
4. Secondary and other packaging
   外包装与其它包装

1. Temp. mapping
   温度分布
2. Thermal test profile
   温度测试概况
3. Air/product relationship
   空气/产品关系
4. Duration
   期间
5. Develop specifications
   开发规格标准

1. Product temp. vs. time
   产品温度与时间
2. Ambient temp vs. time
   环境温度与时间

1. Product temp. evaluated against acceptance criteria
   已经评价的产品温度与接受标准
2. Temperature mapping of system
   系统温度分布

Although design qualification, sometimes referred to as commissioning, should be performed prior to qualification testing, it is not a required component of the overall qualification package (5).

尽管设计确认，某些时候也涉及调试，应在确认测试前实施，但其不是一个完整确认包所必须的部分(5)。

4.3 Installation Qualification

第 4.3 节：安装确认

The purpose of installation qualification (IQ) is to verify that a temperature control system has been installed in accordance with the design, manufacturer's specification, and/or requirements for the intended use and that other systems are in place to support the continued operation of the process or equipment. IQ can be accomplished by the equipment vendor or the user.

安装确认的目的是为了确证温度受控系统已经按照设计、生产商规范，和/或，预期使用要求安装，并且已经有其它系统来支持过程设备的持续运行。安装确认可由设备供应商或用户来完成。

Specific requirements and acceptance criteria should be established in a written protocol and approved prior to their execution. The IQ process should be part of a quality systems audit to qualify a vendor.

在书面方案中应建立特定要求与接受标准，并在实施前批准。安装确认过程应是审核一个有资质供应商质量体系的一部分。

A system description (with boundaries) is included in each IQ protocol. An IQ protocol can include cleaning records, system specifications, and operating instructions. Some form of installation verification should be conducted at storage facilities to ensure that they have the necessary external electrical power and physical support. For example, if a container will need to be recharged at its destination, the destination warehouse should be checked to ensure that it has the necessary electrical power connections (plug type), voltage, and amperes to meet the requirements of the container(s).

在每个安装确认方案中包括系统描述(带有边界)。一个安装确认方案可包括清洁记录、系统规范和操作指示。应在储存设施实施一些安装表格确证，来确保其具有所必须的外部电源和物理支持。例如，如果一个集装箱需要在其目的地进行充电，那么应核实目的地的仓库来确保其具有必须符合集装箱要求的电源连接点(包括插座类型)、电压和电流。

The following types of verifications described below might be performed as part of the IQ.

在后面描述的以下类型确证可能作为安装确认的一部分来实施。

4.3.1 Document Verification

第 4.3.1 节：文件确证

Much of the IQ process involves collecting relevant documentation for the temperature control system. During this exercise, documents provided by the vendor (including operation and maintenance manuals, spare parts lists, calibration and cleaning procedures, drawings, and certificates) are verified to ensure that they are current and available. In later phases of the equipment's lifecycle, this information becomes invaluable for ongoing maintenance and/or modification of the temperature control system via change control. Documents that should be verified during the documentation verification process could include user and functional requirement specifications (if included in the equipment's lifecycle), manuals for the system, system layout in the form of as-built ("red-lined") drawings, and component specifications.

多数安装确认过程包含收集相应的温度受控系统文件。在实际过程中，应对由供应商提供文件(包括操作与维护手册、零件清单、校准与清洁规程、图纸与证书)进行确证，来确保其是现行并有效的。在设备生命周期的晚期，对于持续维护，和/或，通过变更控制对温度控制系统进行修改来说，这些信息变得毫无价值。应在文件确证认过程中进行确证的文件可包括用户与功能需求规范(如果包括在设备生命周期内)、系统手册、竣工(红线)系统平面图，及不见规范。

4.3.2 Equipment Installation Verification

第 4.3.2 节：设备安装确证

The temperature monitoring equipment must be physically and visually inspected during the IQ process. During this phase of IQ, the equipment should be verified to ensure that it conforms with intended purpose / design as derived from upstream specifications / quotations / purchasing agreements. The equipment should also be verified to ensure that it has been constructed or installed suitably. Aspects that might be verified during this phase include:

在安装确认过程期间，必须对温度监测设备进行物理或目测检查。在安装确认阶段，应对设备进行确证，来确保其符合预期目的/来自上游设计/引用/采购协议。设备确证同样确保设备已经恰当建造或安装。在这一阶段，可能确证方面包括:

- Manufacturer name, serial number, and model number
  生产企业名称、序列号、型号
- Construction material and quality
  建造材料与质量
- Insulation thickness and density
  保温厚度与密度
- Dimensions
  尺寸
- Construction quality of the mounted components, if any
  如果有，已经安装部件建造质量
- Other equipment-specific information for each major system component and subsystem

每个主系统部件与分系统的特定信息

4.3.3 Preventative Maintenance

第 4.3.3 节：预防性维护

After the IQ exercise is completed, a required operational process to ensure that the temperature control system is maintained in its "qualified' or "validated" state is the performance of PM on the system at regular intervals. A PM regime should be developed by "experts" in the system (i.e., mechanics familiar with the system's operations) or based on recommendations from the equipment vendor/ manufacturer. Historical failure data can be captured to plan and schedule future maintenance before failures occur. Furthermore, this PM regime should be established as part of a mandated schedule to ensure that it is performed on a regular basis. This schedule can be driven by SOPs and documented using a paper-based recording system or an electronic or computer-based system, such as those provided by a computerized maintenance management system.

在安装确认完成后，确保温度受控系统维持在"已经确认"或"已经验证"状态下需要操作性过程，是系统定期间隔的预防性维护绩效。应由在系统内的"专家"或基于来自设备供应企业/生产企业的推荐开发预防性维护制度。此外，应建立预防性维护制度作为规定日程表的一部分来确保其在定期的基础上实施。这个日程表可来自用纸质记录系统，或诸如计算机化维护管理系统所提供的电子的，或基于计算机系统的标准操作规程(SOP)与文件。

Although it is not required, the PM verification should also include a verification of other materials required to provide ongoing equipment support. This can include ensuring that critical spare parts are on hand or are list of these parts is available so that they are more readily available in the event of failure. This step might also include determining whether a list is available of other materials, such as refrigerants and lubricants, used as part of the systems history file or engineering turnover package.

虽然不是必须，但预防性维护确证应包括提供设备持续支持需要的其它材料确证。这可包括确保关键部件在手，或有这些部件清单，一边在失败事件发生时能便利获得。这个步骤可能同样包括判断是否有其它材料清单，例如，制冷剂、润滑剂，作为系统历史文件或工程移交包的一个部分。

4.3.4 Calibration Verification

第 4.3.4 节：校准确证

As with PM verification, critical instruments should be entered into a calibration program to ensure that they are calibrated within recommended intervals. Recommended intervals can be derived from vendor recommendations or historical data for the components of a temperature monitoring process or piece of equipment.

和预防性维护确证一样，关键引起应进入校准程序来确保其在推荐期间内经过校准。推荐期间可来自供应商推荐，或温度受控过程不见或设备部件的历史数据。

Critical instrumentation can be assessed during qualification or be defined in an upstream design document. The operator should be careful to define which temperature monitoring instruments are critical and which are within the system's or process's boundaries. For example, a system or process might utilize two (or more) instruments that monitor and control temperature conditions separately. If the monitoring instrument is the instrument of record (providing the product conditions record), it is the critical instrument and must be calibrated.

关键仪器可在确认期间进行评估，或在之前的设计文件规定。操作者应小心规定哪个温度监测仪器是关键的，以及哪个处于系统或过程边界。例如，一个系统或过程可能使用两个(或更多)仪器来分别监测与控制温度条件。如果监测仪器是记录仪器(提供产品条件记录)，其就是关键仪器并必须经过校准。

4.4 Operational Qualification

第 4.4 节：运行确认

To ensure successful operational qualification, the temperature control process or equipment should have undergone a successful IQ and risk analysis. The OQ's purpose is to verify that the process or equipment operates as specified and meets the predetermined requirements for control of design operating parameters. Ideally, the OQ follows the completion and approval of IQ activities and is satisfactorily executed and approved before the PQ starts. The IQ and OQ might be part of the same document. However, these activities may begin before the previous qualification has been approved, provided that the previous qualification has been executed and any deviations have been addressed. This approach must be approved by quality management and any other appropriate personnel within the organization.

为了保证成功运行确认，温度控制过程或设备应经过成功的安装确认与风险分析。运行确认的目的是为了确证过程或设备按照特定运行，并符合预先设定的设计操作参数的控制。理想的，运行确认在安装确认活动完成并批准后并在性能确认开始前成功实施并批准。安装确认与运行确认可作为同一个文件的一部分。然而，这些活动在先前的确认已经批准证明先前的确认已经实施，并任何偏差已经解决后才能开始。这个方式必须得到质量管理部门或在组织内其他恰当人员的批准。

OQ testing is designed to demonstrate operational conformance to design specifications. Appropriate source documentation can either be copied or referenced in the executed protocol. Factory acceptance testing results may be used if they have been properly

preapproved and documented. Specific testing requirements and acceptance criteria are defined in the preapproved protocol. Deviations must be investigated and closed as separate entities and included in the summary report for the protocol. The implementation of any action plan resulting from a deviation can be approved as part of the summary report.

运行确认设计用来证明运行性能符合设计规范。可复制哦或参考在实施方案中的恰当来源文件。如果已经恰当地预先批准并 记录，可使用工厂验收测试结果。在预先批准的方案中规定特定的测试要求以及验收标准。对偏差必须进行调查并及作为一个独立的项目关闭，并包括在方案的汇总报告内。任何一个行动计划实施导致的偏差可作为汇总报告的一部分进行批准。

All qualification testing equipment utilized during OQ execution must be calibrated against National Institute of Standards and Technology (NIST) or comparable international standards and be documented in accordance with a facility calibration plan.

在运行 确认实施期间，所有确认测试仪器都应按照美国国家标准及技术研究所(NIST)校准，或与国际标准比较，并按照设施的校准方案进行记录。

All activity related to the execution of OQ should be formally documented in a protocol.

所有与实施运行确认的相关活动都应正式地记录在一个方案中。

The test method(s) used should have relevant justification. Test results should be comparable and reproducible based on the agreed-on temperature profile of the environment outside the active transportation system, including exposure to the climate. When any testing is involved in this activity, it should be adequate to show reproducible results. It is recommended that the acceptance criteria developed for any given transportation system establish a high degree of confidence that the system is effective and reliable. Acceptance criteria for an OQ are typically developed around the process's or equipment's operational range; however, the intended use might require more stringent acceptance criteria. Typical elements specific to the four individual types of active transportation systems addressed in this guidance are discussed in the OQ sections for each system.

所使用的测试方法应有有关证实。基于已经批准的有源式运输系统外环境温度概况，包括暴露的气候，测试结果应可比较、可重复。在该活动中所涉及到的任何活动，应恰当显示可重复结果。对于一个给定的运输系统，推荐开发一个高置信程度的可接受标准，来证明系统的有效性和可靠性。通常，一个典型的运行确认可接受标准都围绕过程或设备运行范围；然而，预期使用可能需要一个更严格的可接受标准。在本指南所关注的四种独立类型的有源式传输系统典型考量要素将在运行确认章节对每种系统进行讨论。

The transportation system's ability to control temperature should be tested. Typically, the system is required to respond to changes in setpoint and then stabilize and maintain a uniform temperature around that setpoint. Temperature mapping is the typical method used to demonstrate a system's ability to control temperature.

应测试运输系统的控制温度能力。典型的，要求系统根据设置温度点变更而响应，然后在围绕在设点稳定并维持均匀的温度。温度分布是一个用来证明一个系统控制温度能力的典型方法。

4.4.1 Power Failure Recovery Testing

第 4.4.1 节：断电恢复测试

Once the transportation system has reached the desired temperature, the electrical power is turned off to simulate a power failure and determine how long the system's backup generator takes to react to the condition or, if there is no backup generator, how long the unit can hold the desired temperature before it reaches an out-of-tolerance temperature. The power failure recovery test should be performed concurrently with temperature mapping studies and, ideally, using an empty storage unit to simulate the worst case because there will be no thermal mass load to influence the unit's temperature. Once an out-of-tolerance temperature is attained, power is restored and the time required for the system to return to the operational temperature range is determined. This information is helpful for such activities as discrepancy analysis and creation of disaster recovery SOPs.

一旦运输系统达到所需要的温度，切断电源来模拟断电并确定多长时间系统的备用发电机对条件开始反应，或在没有备用发电机时，系统该单元在达到超出可接受温度前可在多长时间保持所需要的温度。断电恢复测试应与温度分布研究同时进行，理想的，使用一个空存储空间来模拟最差情况，因为这样就没有装载热质量影响单元温度。一旦达到超出可接受温度，恢复电源，从而确定了系统恢复运行温度范围所需要的时间。该信息对于诸如不符合项分析及生成灾难恢复标准操作规程等工作是有帮助的。

4.4.2 Alarm Testing

第 4.4.2 节：报警测试

The intent of alarm testing is to demonstrate that the system will effectively emit an alarm when the temperature in the transportation system reaches an alarm condition. The test method used should be consistent with and similar to that used in OQ temperature control testing. It is reasonable to combine alarm testing with power failure recovery and open door testing in which the power failure recovery and open door temperature excursions serve as alarm conditions

报警测试目的是为了证明当运输系统达到一个报警条件时，该系统将有效地发送一个报警。所使用的测试方法应与在运行确认对使用的温度控制测试一致或类似。可合理的将报警测试与断电恢复及开门测试合并，将断电恢复与开门温

度超出作为报警条件。

4.4.3 SOP Verification

第 4.4.3 节：标准操作规程确证

The SOPs used during the temperature control process or equipment operation should be approved prior to releasing the equipment for normal operational use.

在放行给设备正常使用之前，在温度控制过程或设备运行阶段所使用的标准操作规程应经过批准。

SOPs for operation ensure that the equipment or process is operated consistently with every use and can include:

运行标准操作规程每次使用的确保设备或过程一致运行，并可包括:

- Process or equipment operation, including startup
  过程或设备运行，包括启动
- checks and preconditioning procedures
  核实并初始条件过程
- Loading of product
  产品装载
- Alarm and contingency management
  报警或异常管理
- Cleaning consistent with other GMP systems within the facility (if applicable)
  符合在设施内的其它药品生产质量管理规范系统的清洁 (如果可能)
- Calibration and PM programs
  校准与预防性维护程序

Loading and unloading have similar risks when these activities are conducted in an area that is exposed to uncontrolled, external weather. Loading of product is also critical to ensure that the required clearances are maintained to ensure proper airflow and that circulation and extended open door times are limited. Ideally, the qualification also ensures that systems operators are trained in the applicable SOPs. Training is especially important when a manual action is a part of the process. Training might also prevent actions that might be inappropriate for some products and not others (e.g., turning off a unit under cold ambient conditions as a cost saving measure based on the assumption that the temperature-sensitive product is robust or has been tested at very cold temperatures).

当在一个暴露在不受控的外部区域，外部天气实施这些活动时，装载与卸载有相似的风险。产品装载对于确保保持要求的空场来确保恰当的气流同样是关键的，并且周期及延展开门时间是受到限制的。理想的，确认同样确保系统操作人员已经经过恰当的标准操作规程培训。当手动措施是过程的一个部分时，培训特别重要。培训可同样预防可能对于一些产品不恰当并没有其它措施(比如，出于节省成本措施，基于温度敏感产品是耐受的假设，或已经在非常冷的温度进行测试，在冷环境下关闭单元)。

4.4.4 Temperature Controls Verification

第 4.4.4 节：温度控制确证

Whether temperature controls operate within the manufacturer’s recommended range should be verified. During OQ, the range of a temperature control system’s performance can be determined based on intended product requirements (e.g., a system’s ability to cool an environment to -20°C and maintain that temperature might not be tested if the system will never operate at that temperature, but this range might have been tested as part of IQ). It is recommended that tests on the temperature controls during IQ and OQ be performed prior to the full unit mapping described below during PQ to minimize set-up time and related costs. These tests can be conducted in conjunction with temperature mapping studies, but doing so is normally less efficient.

应确证是否温度运行在生产企业推荐的范围之内。在运行确认期间，基于所与其的产品需要(例如，一个系统可将环境冷却-20°C，并维持在这个温度，如果系统从来不在该温度下运行，可能不需要测试，但这个范围可能作为安装确认的一个部分进行了测试)，可判断温度控制系统的性能。推荐在安装确认与运行确认期间，在后面即将描述的在性能确认期间即将开始实施整个单元温度分布测试之前对温度控制进行测试，这样就可减少设置时间和相应的成本。这些测试可联合温度分布研究进行，但一般来说这么做效率较低。

A test that modifies a setpoint so as to observe the temperature control system’s response to the change beneficial. This test introduces an artificial load by causing increased cooling or increased heating in the system, and, subsequently, the system’s

stability characteristics can be observed.

有一个修订一个设定值测试来观察温度控制系统对这种变更响应是有益处的。这个测试通过增加系统制冷或增加加热引入一个人工负载，并在后续观察系统稳定性特性。

Modification of system setpoints or even startup can also be used as an opportunity to assess the system's ability to achieve a steady state temperature. This data can then be used as a basis for cold room/refrigerator/ freezer or standalone unit preconditioning times mandated in material and product-specific storage SOPs.

同样可修改系统设定值或初始状态作为评估系统达到一个稳定状态温度能力机会。这些数据可作为冷库、冰箱、冷冻室或单体单元的在物料与产品特定储存标准操作规程中所需要的预设时间。

Criteria for this testing depend on the control system. Fundamentally, the system should demonstrate a response to a change in temperature above or below the setpoint and maintain the temperature at that setpoint.

这些测试的标准基于控制系统。基本上，系统应证明一个对高于或低于设定值的温度变更的响应并维持温度在这个设定值上。

4.4.5 Configurable Parameter Verification

第 4.4.5 节：重构性参数确证

The configuration of a temperature control system is recorded for several reasons, including that the system might have been designed and configured for a specific application, and for the intended use, the vendor has recommended the use of a set of parameters. To ensure equivalent performance in future, parameters similar to those used during the qualification should be employed. Typically, configurable parameters are associated with automated temperature control systems. For TCUs, parameters to be verified are probably related to the temperature control or monitoring system (e.g., piping and instrument diagram control parameters and alarm settings).

记录到的温度控制系统重构有多个原因，包括系统可能已经为了一个特定的应用进行了设计与重构，对于与其使用，供应商已经推荐了一组使用参数。为了确保将来性能等效，在确认期间应 使用那些相似的参数。典型的，重构参数与自动温度控制系统相关联。对于温度控制单元，即将确证的参数可能与温度控制或监测系统(例如，管路和仪器图表控制参数以及报警设置)相关。

4.4.6 Repeatability and Consistency Considerations

第 4.4.6 节：复现性和一致性考量

During the qualification process, the principles of repeatability and consistency established in the master validation plan apply to the operational qualification design concept when the methodology for testing active containers (including the number of tests, types of tests, and types of equipment) is determined. Because active temperature-controlled containers have electrically powered cooling units, the OQ design can incorporate aspects of the qualification of passive temperature control solutions. It might not be necessary to perform a complete triplicate series of summer and winter tests as would be done with passive containers; however, multiple tests performed on one ambient temperature profile should show repeatability, control, and overall performance.

在确认过程中，当测试有源集装箱的方法(包括测试数量、测试形式、设备类型)决定后，在验证主计划中建立的复现性和一致性基本原则应用于运行确认设计概念。因为有源式温度控制集装箱有电能制冷单元，确认设计可整合无源温度空解决方案确认方面。也许不需要完成就像无源集装箱一个一式三份连续夏天和冬天测试，然而，在一个环境温度概况下完成的多种测试应显示重现性、控制、整体性能。

4.4.7 Acceptance Criteria

第 4.4.7 节：接受标准

Acceptance criteria for OQ include:

运行确认的接受标准包括:

- Testing demonstrates that the temperature control system/process performs as intended.
  通过测试证明温度控制系统/过程按照预期实施。
- Executed and approved IQs and OQs are available for the system.
  系统已经实施并批准的安装确认与运行确认。
- Any pertinent SOPs are listed.
  已经开列所有相关的标准操作规程。
- All critical and non-critical instruments have been calibrated, as required.
  如果需要，对所有关键与非关键仪器已经进行了校准。

- Calibration of temperature sensors supports the qualification study's temperature conditions (e.g., when thermocouples are used, a study that varies the temperature from 0°C to 40°C must use temperature sensors calibrated over a range that brackets the operating range, a full loop calibration is necessary to ensure measurement accuracy.)

  温度传感器校准支持确认研究的温度状况(例如，当使用热点偶时，温度变化范围从0°C到40°C研究必须使用已经覆盖整个最大与最小操作范围校准的温度传感器，需要一个全闭环校准来确保测量准确度)。

- Approved SOPs for measurement systems (e.g., thermocouples) require calibration before use and calibration checks after use.

  测量系统(例如，热点偶)需要在使用前进行校准并在检查后进行校准核实的已经批准的标准操作规程。

- Equipment is within its calibration period.

  设备在校准期间内。

Consideration should be given to the fact that thermocouples and other temperature sensors occasionally malfunction, break, or fail after calibration. Strategies developed by industry to mitigate this risk include:

必须考虑到热电偶与其它温度传感器偶尔在校准后失灵、损坏、失效这样的实施。行业中为了减少这种风险而采取的策略包括:

- Specifying that at least 90% of the sensors must pass post use calibration tests. This strategy ensures that sufficient data are available to demonstrate temperature uniformity.

  至少90%的传感器应通过使用后校准测试。这个策略确保有足够的数据来证明温度均匀性。

- Placing primary and secondary probes in known critical locations, such as hot spots or adjacent to control probes. If the primary probe fails, the secondary probe can be used to evaluate system performance.

  在已知的关键位置放置主与次探头，诸如，热点或邻近控制传感器探头。如果主传探头失效，次探头可用于评价整个系统性能。

4.4.8 Reporting Criteria

第 4.4.8 节：报告接受标准

Criteria for reporting OQ results are as follows:

报告运行确认结果接受标准如下:

- All criteria are recorded, and original data cannot be altered and are available for review.

  记录所有接受标准，不能更改原始数据，并且有审核。

- A copy of the calibration data is included in the qualification package or report.

  在确认包或报告中应包括校准数据的复印件。

- Data are displayed with the minimum and maximum temperatures of each thermocouple or stand-alone recording device used during the study, the graphs are attached, and the data are within the specified range for the protocol.

  展示的数据包括在研究中所使用的每支热电偶或独立记录设备最小与最大温度，附上图表，并且数据在方案所特定的范围内。

4.5 Performance Qualification

第 4.5 节：性能确认

The purpose of performance qualification (PQ) is to verify that the transportation system functions consistently within the required process range of operation under expected loads in an operational environment as defined by user requirements and established in IQ and OQ. PQ may be executed as soon as all prerequisite IQ/OQ testing is successfully completed, reviewed, and approved. Specific testing requirements and acceptance criteria are defined in the preapproved protocol or relevant material specifications, SOPs, and regulatory guidance. PQ testing should be conducted according to the approved SOP, and consideration should be given to including extremes of empirically obtained (preferred) or published seasonal temperature variations.

性能确认目的是为了确证预期负载在一个已经由用户需求规定并已经在安装确认与运行确认中建立的运行环境，运输系统功能在要求的过程运行范围一致性。在安装确认与运行确认测试所有先决条件成功完成、审核、批准后，性能确认才可实施。在预先批准的方案或有关材料规格标准、标准操作规程、药政指南中规定特定的测试要求与接受标准。性能确认应按照已经批准的标准操作规程来实施，并应给出的包括凭借经验获得的(可取的)或公开的季节温度变化极端条件的考量。

Acceptance criteria for PQ should establish a high degree of confidence that temperature control process or equipment

performance is both effective and reproducible. All activities related to the execution of PQ should be formally documented.

应建立一个高置信度性能确认的接受标准，温度控制过程或设备性能既有效又可重复。应正式记录所有与实施性能确认相关活动。

All qualification testing equipment used during PQ should be calibrated against NIST or other traceable standards and documented in accordance with a facility calibration plan.

所有在性能确认中使用的确认测试设备应按照美国国家标准及技术研究所(NIST)或其它可追溯标准进行校准，并按照设施的校准计划进行记录。

A system description (with boundaries) should be either included or referenced in each PQ protocol. Typical PQ verifications can include product, load unit uniformity, or open door recovery tests.

在每个性能确认方案中应包括或参考系统描述(带有边界)。典型的性能确认确证可包括残品、装载单元均匀性，或开门回收测试。

4.5.1 Product Tests

第 4.5.1 节：产品测试

Production materials, simulated product, or “empty” containers can be used to test temperature control system performance.

可用生产材料、模拟产品，或“空”集装箱来测试温度控制系统性能。

4.5.2 Loaded Unit Temperature Uniformity

第 4.5.2 节：已装载单元温度均匀性

Loaded unit temperature uniformity should typically be tested with maximum use and/or individually specified tracking systems within the units and tested with wired probes or standalone recording devices to demonstrate acceptable system/process performance.

已经装载单元温度均匀性通常应针对最大使用，和/或，单元内的独立的特定追踪系统进行测试，通过有线探头或独立记录装置测试证明系统/过程性能可接受。

4.5.3 Open Door Recovery

第 4.5.3 节：开门恢复

All transportation systems experience interruptions in which the system’s integrity is broken (i.e., ambient air is allowed to enter) during, for example, loading/unloading of material or personnel entry via an open door. Testing should incorporate assessment of the system’s ability to recover from this condition. This testing should be geared to the system’s operation. The environment in which the doors might be open as well as how long the doors might be open and perhaps the frequency of door opening should be taken into consideration. Criteria for this test include that the system returns to the required temperature range within a reasonable timeframe (that, ideally, is supported by stability testing). Ideally, the open door recovery test is performed concurrently with temperature mapping studies to ensure that all areas in the system have recovered from the disturbance.

所有运输系统都会经历干扰，在诸如物料装卸或人员从打开的门进入期间，系统完整性被破坏(例如，环境空气进入)。测试应整合系统从这种条件恢复能力评估。该测试应与系统运行一致。应考虑门可能打开的环境、门打开多长时间、开门频次。该测试标准包括在合理的时间框架内系统恢复到所需要温度范围(理想的，应得到稳定测试的支持)。理想的，开门恢复测试应与温度分布研究同步实施，确保系统所有区域都能从干扰中恢复。

Open door testing can be performed in a variety of ways. One option is to test whether leaving a door open for a predetermined amount of time (established during engineering runs or during commissioning) does not cause the system’s contents to experience an excursive temperature. Another option might be to test the extent of an out-of-specification condition during an open door condition representing the worst-case ambient condition. Test criteria for this option are for the system’s temperature to return to the specified range within a period of time that is acceptable for the system’s contents. Such an approach would require input from the manufacturer regarding an acceptable time limit.

开门测试可不同的方式进行。一个选择是测试门在预设的一定的时间内开启时(在工程运行中或在调试期间建立)不会造成系统内的物料经历偏离的温度。另一个选择是测试在一个开门条件代表最差环境条件超出规格标准条件程度。该选择的测试标准是针对系统的温度在系统内物料接受的一个时间段内返回到特定范围。此方式将需要输入来自生产企业的一个有关可接受时间限度。

4.6 Additional Considerations

第 4.6 节：额外考量

4.6.1 Temperature Monitoring

第 4.6.1 节：温度监测

Temperature mapping studies for any CES can be performed as part of either or both OQ and PQ. These studies should be performed in an empty chamber to minimize any influences from conditioned or unconditioned thermal mass inside the CES. An empty CES map is normally developed during OQ. The data collected as part of these mapping activities can be used to help identify cold and warm spots within the unit and where best to locate the unit's controlling or monitoring probe(s).

对于任何受控环境空间温度分布研究既可作为运行确认也可作为性能确认的一部分来实施。这些研究应是在空的腔体内进行，以减少在受控环境空间内已经过或未经过空调处理热质量影响。一个空的受控环境空间温度分布图一般在运行确认中开发。作为分布图活动的一个部分收集到的数据可帮助辨识在单元内冷点与热点，及单元控制或监测探头最佳位置。

Once the extremes of time, temperature, and mass/volume are defined, the products to be placed within the CES can be evaluated to see whether they fit the system's bracketed temperature and mass/ volume ranges. It is helpful to measure the mass and volume of the individual materials or products that comprise the payload to define the weight and density of the minimum and maximum payloads.

一旦确定极限时间、温度、质量/体积，可评估放置到受控环境空间内的产品，来看是否他们适合系统最大与最小的温度和质量/体积范围。测量单个物体或产品的质量与体积，包括规定有负载，来规定最小与最大有效载荷的重量与密度是非常有帮助的。

Once established, the bracketing can be applied to the payload, no matter what material is to be shipped, as long as it falls within those bracketed guidelines for temperature and mass/volume. The dimensions of the production material should be considered when the size of the CES desired for the transit lane or storage space is evaluated. Evaluation factors for various active temperature-controlled transportation systems include the desired minimum and maximum payload space; use of truck, ocean, and air cargo space; and optimization of dimensional weight.

一旦建立，该最大与最小数值可用与有效载荷，而无论运输的是什么物料，只要落在这些温度与质量/体积最大与最小数值指南中即可。当已经评价的运输航道或储存空间期望受控环境空间尺寸时，应当考虑生产物料尺寸。不同有源式温度受控运输系统评价因素包括期望最小与最大有效负载空间；卡车使用，海洋运与空运空间，及尺寸重量上的优化。

It is not a regulatory requirement to perform temperature mapping in both OQ and PQ, and, in practice, only one mapping is usually performed. The approach for temperature mapping studies can vary due to regulatory requirements, product requirements, and company policy. If external thermal stress poses a risk (e.g., the cold room is adjacent to exterior walls), then temperature mapping should account for the peak temperatures of summer and winter seasons to show that the unit can maintain the desired interior conditions for the desired product load size or range of sizes. The temperature map is a measurement to ensure that process or equipment operation meets the desired performance standard.

在运行确认与性能确认中都实施温度分布研究不是药政要求，而且在实践中，通常仅仅实施一个温度分布研究。温度分布研究的方法可因药政要求、产品要求以及公司方针不同而不同。如果外部热呈现一个风险(例如，冷库紧邻外墙)，那么温度分布验证应考虑夏天与冬天季节分度峰值，来显示该断垣能维持期望产品装载尺寸或尺寸范围所期望内部条件。温度分布是确保过程或设备运行符合多期望的性能标准的一个措施。

It is recommended that three-dimensional temperature profile assessments be conducted using an appropriate number of monitors that are spatially organized based on the CES's size and shape. The monitor's placement points (top to bottom, left to right, and front to back) should be in accordance with the product's placement within the normal useable area of the chamber or unit. This topic is further discussed in Section 8.2.2.

推荐基于控制环境空间的尺寸与形状，使用在空间组织恰当数量的监测器实施三维温度概况评估。监测器放置点(从上到下、从左到右、从前到后)应符合产品在腔或单元内正常使用区域的摆放位置。这一话题将会在第8.2.2节中进行讨论。

No definitive standard exists for the number of locations identified in any unit to map a three-dimensional space; however, the study must meet the original intent of demonstrating three-dimensional uniformity/compliance with product requirements. It is up to those responsible for conducting or executing the qualification exercises to prepare a justified approach and rationale for the study.

在研究任何单元三维空间温度分布辨识位置数量方面没有确定的标准；但是，该研究必须符合证明三维均匀性/符合产品需求的原有意图。到此， 实施或执行确认实践的责任是准备一个证明的方式以及该研究的基本原则。

For active temperature-controlled transportation systems, a single test is sufficient to establish acceptable temperature control functionality. Users can test multiple units or every unit based on the active system's design, its demonstrated consistency of operation, available process controls, and/or the product's needs. Temperature mapping should be performed for an adequate

length of time to demonstrate acceptable performance over the range of operating conditions. Consideration should be given to the amount of time required to cool the unit down to the predefined temperature range, defrost cycles, day-night cycles, or other factors relevant to proper system operation.

对于有源式温度受控运输系统，用一个测试已经足够建立可接受的温度受控功能。基于系统的设计，用户可测试多个单元或每个单元，其证明运行、过程控制，和/或，产品需求一致性。应在足够长的时间来实施温度分布研究，来证明整个运行环境范围其性能可接受。应考虑冷却单元到预定操作条件范围、除霜周期、日夜周期，或系统正确运行的其它因子所需要时间长度。

During the qualification process, the principles of repeatability and consistency established in the VMP apply to the operational qualification design concept when determining the number or frequency of requalification tests to perform. Differences in the qualification process between fixed installations and units used for transportation are addressed in the sections on each type of active transportation system below.

在确认期间，当确定即将实施的重新确认测试数量或频率时，在验证总计划中建立的重现性与一致性基本概念应用到运行确认设计概念。在后面每个有源运输系统的章节解决在确认过程与用来运输的固定安装以及单元之间的差异。

4.6.1.1 Bracketing Load Development

第 4.6.1.1 节：最大与最小装载开发

During qualification, temperature mapping studies can be performed under anticipated conditions that bracket pre-defined minimum and maximum loads based on actual use conditions (4). The following are generally true for any temperature-controlled space:

在确认期间，基于世纪书用条件，可在预先制订的最大与最小装载的预见条件下可实施温度分布研究(4)。任何的温度受控空间以下内容通常是正确的:

- Increased thermal mass has increased “thermal inertia” or temperature stability. Provided that loads are within the desired temperature range, increased or “full” loads represent a “best-case” scenario.

  增加热质量就增加“热惯性”或温度稳定性。在所期望的温度方位增加装载，增加的或“满”装载代表一个最佳情况。

- Conversely, the largest occupied volumetric space in the container can represent a worst-case scenario because the volume can disrupt airflows.

  相反，在集装箱内占据最大空间可代表一个最差状态，因为体积会阻挡气流。

When qualification of a range of load conditions is desired, CES mapping should be performed for both the minimum load (having the lowest thermal mass) and maximum load (having the maximal disruption of airflow) conditions. Minimum loads could consist of a minimum product load or, taken to the extreme, empty containers. Maximum loads should reflect anticipated maximal volumetric loads with mass that is equal to or less than the maximum intended product load. The minimum and maximum load conditions should be defined later in the SOPs so that operators do not exceed the qualified level.

当确认期望的装载条件范围时，应对受控环境空间实施最小装载(具有最低热质量)与最大装载(具有最大气流干扰)条件的温度分布研究。最小装载有可由最小产品装载，或采用极限状态，空箱。最大装载应反映预期最大体积装载体积，其热质量等于或小于最大预期产品装载。应在标准操作规程内规定最小与最大装载条件，以便操作者不会超过确认的水平。

4.6.1.2 Mapping Product Temperatures vs. Air Temperatures

第 4.6.1.2 节：产品温度分布与空气温度

Active transportation systems can be effectively mapped by measuring air temperature inside the CES as an indication of temperature control system operation. This information can then be applied to a flexible range of product loads. For a method that is specific to a particular product configuration, product temperatures should be mapped using either an actual or a simulated product load. This product load should have the same product thermal mass and packaging properties and quantity as the intended product’s load configuration. Air temperatures can be effectively mapped during either OQ or PQ. Product temperatures re most conveniently mapped during PQ.

通过测量受控环境空间作为温度受控系统运行指标的内部空气温度可有效地对有源式运输系统进行温度分布研究。这个信息可应用于产品装载的灵活范围。对于特定于特殊产品重构的方法，用使用一个实际或一个模拟的产品装载，对产品温度进行温度分布研究。这个产品装载需要有相同的产品热质量及包装特性，以及预期的产品重构。在运行确认或性能确认中，可对空气温度有效进行温度分布研究。在性能确认中，可对产品温度分布进行有效研究。

4.6.1.3 Locating Warm and Cold Spots

第 4.6.1.3 节：热点与冷点定位

Mapping studies can identify areas immediately around the product’s location that experience the greatest variation from the

setpoint, including the highest and lowest temperatures (the “warm” and “cold” spots) in the unit. An examination of the temperature map enables a determination of the best monitoring positions within the unit if the intent is to measure the CES’s air temperature during shipment or storage. The warm and cold spots established through empty chamber mapping can be used to determine where to monitor product temperatures. Periodic remapping can identify when the degradation of insulation over time causes a variation in the locations of warm or cold spots (see Section 3.2.1 above).

温度分布研究可辨识在单元类直接在产品周围在经验上与设定值最大变动位置，包括最高与最低温度(“热”点与“冷”点)。如果目的是测量在运输与储存期间受控温度空间的空气分布，一个温度分布测定能确定在单元内最佳监测点。已经通过空腔温度分布建立的热点与冷点可用来判断监测产品温度的位置。定期的重新温度分布研究可确定在一段时间后由于保温性降解而导致的热点和冷点位置改变(参见上述第3.2.1节)。

4.6.1.4 Duration of Mapping Studies

第 4.6.1.4 节：温度分布研究期间

Mapping studies should be performed over a period of time to demonstrate consistent performance. With active temperature - controlled transportation systems, monitoring performance over an extended period of time can be more useful repeating the tests. Mapping studies should also account for worst-case, seasonal, ambient temperatures. An example of a conservative approach for an active temperature-controlled container (truck/trailer, ULD, or multimodal container) is to map a container during transit using a worst-case route (season dependent) with actual product.

应在一个时间期间实施分布研究，来证明性能一致性。对于有源式温度受控运输系统，扩展监测性能时间期间可对重复测试更有帮助。温度分布研究也应考虑最差条件、季节性、环境温度。一个有源式温度受控集装箱(卡车/拖车、成组装运设备(ULD)，或多模联运集装箱)的保守做法例子是，用实际产品在最坏情况路线的运输途中来对集装箱进行温度分布研究。

A more aggressive approach using a stationary active temperature-controlled container could limit the mapping study to one or two days. It could be justified that within a 24- or 48-hour period, the container will have been subjected to the various conditions, such as compressor cycling, day-night cycles, and defrost mode. In addition, when a trailer is standing in the sun for a long time, the convection/airflow around the container is minimal and, thus, might have a bigger impact than when a trailer is moving. Test-to-failure studies of both high and low temperatures (e.g., performed either by the active system manufacturer or the user) would also indicate the extremes of ambient temperature that the active system can withstand.

一个更激进的方式是使用固定的有源式温度受控集装箱，将温度分布研究时间控制在1到2天。其可证明，在24或48小时的时间段内，集装箱经历多种条件，诸如压缩机周期、日-夜周期、除霜模式。此外，当拖车在日下停留长时间时，集装箱周围的对流/气流是最小的，可能有比拖车移动更大的影响。最高与最低温度“测试直至失败”研究(例如，由有源式系统生产商或由用户实施)将同样显示表示有源式系统可经受的极限环境温度。

4.6.2 Periodic Review of Qualifications

第 4.6.2 节：确认的定期审核

Since all processes and systems vary over time, periodic reviews are necessary to ensure that temperature control system performance remains within defined parameters. Periodic review activities can be based on historical performance as documented in system history files. If there is an indication that the system has changed its performance level, this should trigger an assessment, repair or replacement, and requalification process.

因为过程与系统在随着时间的不同而不同，需要定期地进行审核，来确保温度受控系统性能保持在已经规定的参数范围内。定期审核活动可基于在历史档案中记录的历史的性能数据。如果有数据表明系统性能水平变更，那么就启动评估、维修或更换，及重新确认过程。

The frequency of periodic reviews must be documented with a quality-approved rationale. The rationale must be based on predefined control parameters with specifications along with an ongoing data trend analysis that ensures that the temperature has been maintained within the specified parameters. In addition, risk assessments and historical performance data demonstrating that control parameters have been maintained for the intended use may be used to determine the frequency of periodic reviews.

定期审核的频率必须与质量部门批准的基本原则一道记录。该基本原则必须基于预先确定的带有规格标准的控制参数，及对持续数据趋势分析，来确保温度保持在特定的参数范围内。此外，证明控制参数已经保持在预期使用的风险评估和历史性能数据，可用来确定定期审核的频率。

Periodic review includes the following elements:

定期审核包括下列要素：

- Cumulative impact of all changes made during the review period to determine whether the qualified state has been affected

  在审核期间，所有变更做成的累计影响来确定是否已经确认的状态受到影响。

- Operational monitoring data to review trends in critical performance parameters to evaluate any impact on qualified state. For a CES, these data should include temperature monitoring data. Data to review include process monitoring reports and documentation from any applicable supporting systems.

  审核关键性能参数趋势运行监测数据，来评估对经过确认状态的影响。对于一个受控环境空间，这些数据应包括温度监测数据。审核的数据包括过程监测报告与任何恰当的辅助系统的文件。

- Report of discrepancy trend(s) that includes event types, assignable causes, trend assessments, and any corrective actions to address the trend. Discrepancy trend reports should be reviewed to assess the potential impact of discrepancy trends on the qualified state.

  不符合趋势报告，包括事件类型、相关原因、趋势评估，以及任何纠正措施，来解决趋势。应对审核不符合趋势报告，来评估不符合趋势对确认状态潜在影响。

The need for further action, including requalification, must be assessed when a periodic review or an alarm identifies adverse trends in performance at any time from monitoring the review elements. Such qualification studies should address the risk identified in the review. This can include any specific test that is typically part of OQ or PQ.

当定期审核或一个报警辨识任何时间来自检测评审要素性能上不良趋势，需要进一步措施，包括重新确认，必须进行评估。这样的确认研究应解决在审核中已经辨识的风险。这可包括一般作为运行确认或性能确认的一部分的特定测试。

When a periodic review confirms that the system is consistently producing results that meet its specifications and that no changes have been made to the qualified state, requalification is not required.

当定期审核确认该系统产生符合其规格标准一致结果，并没有作出对已经确认状态进行的变更，那么就不需要重新确认。

4.6.3 Leased Assets

第 4.6.3 节：租赁资产

The qualification of temperature-controlled shipping or storage spaces and processes that leverage leased assets presents a unique challenge to supply chain participants. Most active systems are owned by firms that are not subject to GMP or good distribution practice (GDP) regulations. This raises questions about how to adequately ensure product quality when leveraging these assets. Using a combination of vendor and process controls, it is possible to qualify shipping methods using leased assets in a manner that ensures patient safety, product quality, and regulatory compliance.

租赁资产方式的温度受控运输和存储空间与过程确认对供应链中的合作伙伴是一个唯一的挑战。大多数有源系统都属于不需要药品生产质量管理规范(GMP)或药品流通质量管理规范(GDP)规章所约束公司。这带来一个问题，当租赁这些资产时如何足够确保产品质量。使用供应商与过程控制的组合，以一个确保患者安全、产品质量，与药政符合性的方式来确认用租赁资产运输方法。

The general recommendation of this technical report is that processes be qualified with equal rigor regardless of whether the assets are owned or leased. Pharmaceutical manufacturers, wholesalers, or distributors may elect to participate in the qualification of leased assets, leverage the qualification of a service provider, and choose between individual equipment and family qualification strategies as described in Section 4.6.4.1 below. Whatever strategy is selected, firms must ensure that adequate controls are in place, which can include process monitoring, quality agreements, vendor audits, or other controls as appropriate.

本技术报告的一般推荐是，无论该资产是实际拥有还是租赁，即将确认的过程的严格程度是相同的。药品生产企业、批发企业，或流通企业可选择参与租赁资产确认、一个提供服务企业确认方式，并在下面的第4.6.4.1节中描述的单一设备或族确认策略中作出选择。不管选择哪种策略，公司必须确保有足够的控制，其中包括过程监测、质量协议，供应企业审计，或其它恰当控制。

4.6.4 A Family Approach

第 4.6.4 节：族方式

When risk assessment allows, a family approach to qualification can be appropriate for firms seeking to maximize operational flexibility.

当风险评估允许时，方式确认可能适合寻找最大运行灵活性公司。

4.6.4.1 Defining an Active System Family

第 4.6.4.1 节：定义一个有源系统族

As with any qualification approach, a family approach requires firms to identify the attributes that define the system being qualified. These attributes should be included in a service contract or quality agreement with the service provider. The family's attributes are typically confirmed during IQ, when a determination is made that the components are similar enough to be treated as a family. This ensures complete mutual understanding of the capabilities of the active temperature control system and service and

helps manage compliance with the service provider. This approach enables manufacturers to lease equipment in a clearly defined family from different suppliers at different times and still operate within the qualified process parameters.

With a properly defined equipment family and adequate controls, equipment within a defined family can be qualified by a strategy that includes OQ and/or PQ.

与任何一个确认方式一样，族方法需要企业辨识即将确认规定系统的属性。这些属性应包含在提供服务企业的服务合同或质量协议内。族的属性通常在安装确认过程中确认，当作出判断后，足够相似部件就像族一样来处理。这确保一个有源式温度受控系统、服务能力完整相互理解，并帮助管理与服务供应企业符合性。这个方法能够帮助生产企业从不同供应企业、不同时间在一个明确规定的族内租赁设备，并仍在已经确认的过程参数范围运行。拥有正确规定的设备族与足够的控制，在规定族内的设备就可在包括运行确认，和/或，性能确认策略所确认。

The technical details that define a family of leased equipment must ensure that product quality is maintained. Many factors drive system performance. Examples of the factors in truck systems that might be critical to product quality are listed in Table 4.6.4.1-1. It is recommended that firms use appropriate risk-assessment tools, product quality requirements, and technical specifications and studies to determine the appropriate definition of an equipment family.

订立一个租赁设备族的技术细节必须确保保持产品质量。许多因素影响系统性能。卡车系统对产品质量可能关键的因素例子在表4.6.4.1-1中开列。推荐企业使用恰当的风险评估工具、产品质量要求，及技术规范与研究来确认一个恰当的设备族。

Table 4.6.4.1-1 Examples of Critical Factors for Temperature-Controlled Truck Systems

表4.6.4.1-1：温度受控车系统关键因素例子

Type and quantity of insulation 保温的类型与数量
Critical dimensions (e.g., 53-foot-long trailer) 关键尺寸(例如，53英尺长拖车)
Cooling capacity (or excess cooling capacity at specified temperatures) 制冷能力(或在特定温度超出制冷能力)
Use of a calibrated temperature control system (re: ∫4.3.4, ∫4.4.7 above) 使用一个经过校准的温度控制系统(例如，上述第4.3.4节与第4.4.7节)
Grooved or flat deck, depending on airflow needs at the bottom of the load 沟槽或平台，取决于在装载底部所需要的气流
Air delivery chute to distribute air to the rear and sides of the trailer 空气输送来分布空气到拖车的后端与侧面
Maximum age of the trailer (e.g., due to insulation degradation over time) 拖车的最大年纪(例如，因为保温岁时间降解)
PM program in place (see Section 4.3.3 above) 有预防性维护程序(参见上述第4.3.3节)
Continuous or cycled airflow 连续或循环气流
Fan speed setting 风扇速度设定

After the family definition is complete, it is necessary to ensure that suppliers deliver the correct assets. Of primary concern is clear communication of expectations and proper documentation. Suppliers and service providers need to know what is expected to ensure that they can meet the requirements. Two common forms of documentation of these requirements are quality agreements and contracts that describe all of the technical requirements of the leased assets. Firms that lease equipment are encouraged to have legally enforceable documents to ensure adequate leverage in the event that incorrect equipment is delivered. In addition to technical requirements, firms might require suppliers to provide documentation upon the equipment's arrival at the shipping site for use in process control.

在完成对族的定义后，必须确保供应企业交付正确的资产。主要的考虑事务是对预期与正确文件明确沟通。供应企

业与提供服务的企业需要知道，期望其能确保符合要求是什么。这些需求的两个通常形式文件是质量协议与合约，其中描述了对租赁资产所有技术要求。鼓励租赁设备的公司有立法强制性文件，在交付不正确设备时有恰当的方式。除了技术需求，企业可能需要供应企业一旦设备到达运输点时提供过程控制所需要文件。

4.6.4.2 Process Controls

第 4.6.4.2 节：过程控制

Process controls for the use of leased assets are critical to ongoing success. Vendors might be called on to provide evidence of calibration, periodic maintenance of equipment, and technical data for the transportation equipment (e.g., cooling capacity). In addition, firms leasing equipment should consider which internal controls are necessary to ensure adequate shipping system performance. Table 4.6.4.2-1 identifies process controls that might be critical to protect product quality.

用于租赁资产的过程控对于持续成功是关键的。供应企业需要义不容辞地提供校准、设备定期维护，及运输设备技术数据(例如，制冷能力)证据。此外，企业租赁设备应考虑需要哪些内部控制来确保运输系统有足够的性能。表4.6.4.2-1辨识了对于保护产品质量可能是关键的过程控制。

Table 4.6.4.2-1 Critical Process Controls

表4.6.4.2-1：关键过程控制

Loading pattern (e.g., centerline, required minimum distance from the walls, cooling unit) 装载方式(例如，中心线，要求的距离墙壁、制冷单元最小距离
Product preconditioning requirements 产品预先处理要求
Shipping system preconditioning requirements (e.g., at setpoint prior to arrival) 运输系统预先处理要求(例如，到达前处于设定值)
Ensure loading within specified time limits 确保装载在特定时间限度内
Use of routine or periodic monitoring 使用常规的或定期监测
Ensure that loads do not exceed loading limits of equipment (e.g., maximum height in trailer) 确保装载不超出设备限度(例如，在拖车内最大高度)
Visual inspection of equipment prior to loading 在装载前对折本进行目测检查
Equipment used to secure the load (e.g., cargo straps and load bars) 确保装载安装所使用的设备(例如，货物绑扎带与装载条)
Equipment cleanliness 设备清洁性

4.6.4.3 Qualification of Active Temperature-Controlled Transportation System Families

第 4.6.4.3 节：有源式温度受控运输系统族确认

With a properly defined equipment family and adequate controls, equipment may be qualified by a strategy that includes OQ and/or PQ. It is advantageous to include PQ in the testing strategy of active systems due to the importance of process controls, such as product preconditioning and loading pattern. In addition, regulators often expect to PQ to be completed for shipping methods of significant importance, such as lot shipments by trailer, ocean container, or ULD.

随着正确定义设备族与足够控制，设备可通过包括运行确认，和/或，性能确认的策略来确认。由于过程控制的重要性，诸如产品预先处理与装载模式，在有源式系统测试策略中包括性能确认是优势。此外，药政部门经常希望为特别重要的运输方法，诸如，卡车运输，远洋运输或成组装运设备(ULD)进行性能确认。

Firms can perform concurrent PQ for active temperature-controlled transportation systems. Some active systems (e.g., trailers) are too large for typical temperature-controlled chambers, making laboratory testing impractical. Thus, it might be appropriate to conduct PQ during shipping. In such cases, firms must remain cognizant of regulatory expectations, thoughtfully assess product quality risk, and define the process controls needed to protect patient safety. Risk mitigation during concurrent PQ can include the

use of temperature monitoring equipment in each shipment to demonstrate adequate process control.

企业可对有源式温度受控运输系统实施同步性能确认。一些有源式系统(例如，拖车)对于典型的温度受控传输腔体来说太大了，实施实验室测试也不现实。那么，在运输期间实施性能确认也许比较合理。在这种情况下，企业必须保持对药政期望的认知，考虑评估产品质量风险，并规定保护患者安全所需要的过程控制。在同步性能确认期间风险减缓可包括在每次运输中使用温度监测设备，从而证明有足够的过程控制。

It is recommended that firms only conduct concurrent PQ if prior experience provides sufficient confidence that the PQ results will be positive. This can be achieved through documented process development studies in which surrogate materials are shipped and product mass and volume considerations are taken into account. For example, shipment of water-filled vials instead of product allows firms to prospectively evaluate a shipping method prior to committing resources to a formal qualification.

如果先前的经验提供性能确认的结果是肯定性的，推荐企业仅仅实施同步的性能确认。这可以通过已经记录的运输替代物料并已经考虑了产品质量与体积的过程开发研究来达到。例如，在提交正式确认资源前，运输灌装水的小瓶来代替产品，使企业前瞻性评价一个运输方法。

When a risk is found to be acceptable, the use of a family based qualification strategy can enable firms to increase operational flexibility while ensuring product quality, patient safety, and regulatory compliance. For this strategy to be effective, adequate vendor and process controls are necessary. Vendor controls can include audits, enforceable contracts, or other appropriate measures. Process controls can include equipment inspection on receipt, routine monitoring, or other defined activities. In this manner, firms can efficiently achieve business and GMP goals when shipping with leased equipment.

当已经发现的风险是可接受的，基于确认策略使用族方式可使企业增加运行的灵活度，同时确保产品质量、患者安全性，以及与药政法规符合性。对于这种高效的策略，需要足够的供应企业与过程控制。供应企业控制可包括审计、强制合同，或其它恰当措施。过程控制可包括设备在接收时检查、日常监测，或其它规定活动。在这个方式下，企业在使用租赁设备运输时，可高效地实现业务与药品生产质量管理规范目标。

4.7 Comparisons of Similarities/Differences of the Four Active Transportation Systems

第 4.7 节：四种有源运输系统相似性/不同点比较

Tables 4.7-1 and 4.7-2 compare the similarities/differences of the four active transportation systems.

表4.7-1与表4.7-2比较了四种有源运输系统的相似/不同点。

Table 4.7-1 Typical Properties of the Four Active Transportation Systems

表4.7-1：四种有源运输系统的典型特性

System 系统	Size 尺寸	Control Ranges (°C) 控制范围(°C)	Portability 适用性	Power Requirements 能源需求
ULD 成组装运设备	LD1 (92 × 60 × 60") to LD11(125 × 60 × 64") 从LD1(92英寸×60英寸×60英寸)到LD11(125英寸×60英寸×64英寸)	-20 to 25 -20°C到25°C	Via air, truck, rail, or ship 经空运、卡车、铁路、船舶	Battery independent or electric power 独立电池或电源
Temperature-controlled truck/trailer 温度受控卡车/拖车	20, 40, and 53 ft, on average, in North America and typically 13.6 m in EU, as small as 8 ft for specialized applications 在北美，平均20英尺、40英尺与53英尺；在欧洲，一般13.6米。在一些特殊场合，有8英尺的。	-30 to 23, on average, and up to 33 or more on specialized equipment 平均-30°C到23°C，对于一些特殊设备达到33°C或更高	Via truck, rail, or ship 经卡车、铁路、船舶	Diesel, self-contained generator, or electric supply from vehicle up to 240/60 柴油、自带发动机，车载电源240/60供电
Temperature-controlled ocean container 温度受控远洋集装箱	20' and 40' 20英尺和40英尺	-30 to 23, on average, and up to -40 to 55 on specialized equipment 平均-30-23°C，对于一些特殊设备温度范围为-40°C到50°C	Via truck, rail, or ship 经卡车、铁路、船舶	Self-contained diesel generator or electric supply from vehicle up to 240/60 自带柴油发动机，车载电源240/60供电
Cold storage unit 制冷存储单元	From 3 cu ft to more than 10,000 cu ft. 从3立方英尺到10,000立方英尺	From -80°C to +20°C Common setpoints: 从-80°C到20°C一般设置点 -70°C -20°C +5°C +20°C	Generally limited to facility or offsite locations with no movement of storage units 一般限于设施或厂区外现场非移动的储存单元	From 110/40 to 460/80 hard wired to main service at all times. Generator backup (either diesel or liquefied natural gas) can be hard wired to the units at specified power need. 在所有时间用来自110/40到460/80的硬连接电源线供电做主要服务。发动机(柴油或其它液化天然气)可在单元特殊能源需求时作为硬连接电源备用。

Table 4.7-2 Temperature Control Properties

表4.7-2：温度控制性质

System 系统	Accuracy 准确度	Ramp Rate 缓变率	Defrost Cycle Required 除霜周期要求
ULD 成组装运设备	+/-3°C average 平均+/-3°C	Varies 多种	Varies 多种
Temperature-controlled truck/trailer 温度受控卡车/拖车	+/-3°C average for subzero setpoints, up to 0.5°C for temperatures of 10°C to 30°C. 对于温度是零下的设置，平均+/-3°C，对于温度在10°C到30°C，到0.5°C	2°C to 4°C per minute, depending on test conditions 取决于测试条件，每分钟2°C到4°C	At setpoints below 0°C, the average defrost cycle is usually triggeredly startsof containers every four to six hours by a 20% increase in temperature from the setpoint and each cycle lasts up to 30 minutes. Alarm and operator input can increase the durations of these cycles to compensate for frequent door opening or extreme ambient conditions outside the container. 在设定值低于 0°C，平均除霜周期通常是由集装箱开始温度设定值触发，每四小时到六小时从设定值增加温度 20%并每个周期持续达 30 分钟。警报与操作人员输入可以增加该周期以弥补频繁开门或集装箱外极端环境条件。
Temperature-controlled ocean container 温度受控远洋集装箱	+/-3°C average for subzero setpoints 对于温度是零下的设置，平均+/-3°C	2°C to 4°C per minute, depending on test conditions 取决于测试条件，每分钟2°C到4°C	At setpoints below 0°C, the average defrost cycle is usually triggered every four to six hours by a 20% increase in temperature from the setpoint and lasts up to 30 minutes. Alarm and operator input can increase the durations of these cycles to compensate for frequent door opening or extreme ambient conditions outside the container. 在设定值低于0°C，平均除霜周期通常是由集装箱开始温度设定值触发，每四小时到六小时从设定值增加温度20%并每个周期持续达30分钟。警报与操作人员输入可以增加该周期以弥补频繁开门或集装箱外极端环境条件。
Cold storage unit 制冷储存单元	0.25°C to 3°C 0.25°C到3°C	1°C to 0.25°C per minute, depending on test conditions 取决于测试条件，每分钟1°C到0.25°C	At setpoints below 0°C, the average defrost cycle is usually triggered every four to six hours by a 20% increase in temperature from the setpoint and lasts up to 30 minutes. Alarm and operator input can increase the durations these cycles to compensate for frequent door opening or extreme ambient conditions outside the container. 在设定值低于0°C，平均除霜周期通常是由集装箱开始温度设定值触发，每四小时到六小时从设定值增加温度20%并每个周期持续达30分钟。警报与操作人员输入可以增加该周期以弥补频繁开门或集装箱外极端环境条件。

5.0 Temperature-Controlled Trucks and Trailers

第五章：温度受控卡车与拖车

Although refrigerated trucks and tractor trailers are similar in many ways to other vessels used to store or transport temperature-controlled materials, trucks face additional challenges because of the ambient, dynamic conditions that result from their exposure to changes in weather and the day-night cycle while in transit. Heat loads are much more dynamic because of greater convective heat loss/ gain due to motion. Product loading in the vehicle, including variances in payload size and placement within the vehicle, presents additional challenges. With a properly qualified and controlled shipping process, a truck can effectively protect product during transit, limiting the need for additional protective packaging.

虽然，冷藏卡车或拖车在很多方面与一些用来储存或运输温度受控物料罐相似，卡车面临因为在运输中导致暴露天气变化与日-夜周期环境、动态条件的其它挑战。由于移动热损失/获得更大的对流，热负载更加动态。在车辆中所装载的产品，包括在有效载荷大小与在车辆中的位置变动，都呈现了而外的挑战。在一个经过正确确认并控制的运输过程中，卡车能在运输期间有效地保护产品，有限地需要额外的保护性包装。

5.1 System Description

第 5.1 节：系统描述

The active systems employed for trucks consist of an attached cargo box (commonly called a “straight truck”) or a trailer pulled by the trucks that is equipped with a TCU mounted on the leading end of the truck’s cargo box or trailer. As described in Section 3.1 above, inside the CES, conditioned air flows through and around the product or other cargo. The air is cooled or heated to the required temperature in the TCU and then blown into the CES near the ceiling. Air in a truck or trailer is circulated from the front to the back and then returns to the TCU along the floor. Trailers sometimes have a slotted aluminum floor that facilitates the air movement’s return underneath the cargo. The temperature of this returning air is measured by the TCU to calculate the necessary input air temperature. The TCU setpoint and the temperature inside the CES are visible at all times on the display on a TCU’s external control unit or an independent data logger system.

一个货物箱构成卡车所使用的有源系统(一般称为“直线卡车”)，或由卡车牵引装备安装在卡车货物箱或拖车前端的一个温度控制单元的拖车。如上述第3.1节所描述，在口制环境空间内，空调气流通过并围绕在产品或其它货物。根据在温度控制单元温度需求，空气在温度控制单元内冷却或加热，并吹入到控制环境空间天花板。卡车或者拖车内的空气，从前往后进行循环，然后沿着地面回到温度控制单元。拖车有时候会有一道铝制槽的地板，其促进空气流动返回时进入到货物下部。返回空气的温度由温度控制单元测试，来计算输入所需要空气温度。温度控制系统的设定值与在控制环境空间内部温度在所有时间都可视，显示在一个温度控制单元的外部控制单元或一个独立的数据记录系统上。

To provide a more stable temperature environment in the CES, the TCU should be set on “continuous mode.” In continuous mode, the unit provides a constant supply of air to maintain the desired temperature range, resulting in a flat temperature profile. Alternative “fuel-saver” or “start-stop” settings turn off the compressor and fans until the temperature reaches the limit of the established acceptable temperature range before reacting with a surge of cold (or warm) air applied in one large, quick application to drive the temperature back toward the opposite temperature limit. In these alternative modes, the resulting temperature profile is full of spikes from one end of the temperature range to the other. The impact of defrost cycles to produce temperatures outside the desired temperature range is multiplied when defrost cycles are combined with one of these start-stop cycles. For this reason, normal operation and qualification testing should be done in continuous mode for pharmaceutical transport.

为了控制环境空间中提供更稳定的温度环境，温度控制单元应设定在“连续模式”。在连续模式中，该单元提供一个恒定空气供应，以便维持在期望的温度范围形成一个平坦的温度分布。替代的“节省燃料”或“启动-停止”设置关闭压缩机和风扇，直到温度达到已经建立的可接受温度范围限度，在与大量涌入空间的冷(或热)空气反应前，快速应用，驱使温度回到相反温度限制一端。在这样的选择性模式中，会导致温度概况从温度范围的一端到另一端充满钉点。当除霜周期与一个这样的“开始-停止”周期合并时，由除霜周期产生温度超出所期望温度范围的影响是多倍的。因为这样的原因，常规运行与确认测试应在药品运输中使用的连续模式中实施。

The cargo area in temperature-controlled straight trucks is normally between 12 and 24 ft long. This is short enough that the unassisted TCU fans can push air with sufficient speed and direction to reach from the front to the rear and the top to the bottom of the CES’s interior. Trailers up to 53 feet long often have a chute used to channel the air. In long trailers, the flexible chute focuses the airflow from the TCU, dispersing it gradually over the trailer’s full length to provide uniform temperature control throughout the entire space. The cargo must be stowed in the truck in such a way that the flow of air is not interrupted. Care must be taken to ensure that air can circulate across the top of the load and down the back and both sides and that the air has an unobstructed path along the floor to return to the TCU.

在温度受控直线卡车内的货物区域，一般长度在12英尺到24英尺之间。这样的长度足够短，那么温度控制单元不用辅助，风扇可推动足够风速与方向达到从前至后、从上至下吹入到控制环境空间内部。拖车达到53英尺长时，经常有一道用于空气引流的斜槽。在长的拖车里，灵活的斜槽关注温度控制单元气流，逐步分散到整部拖车的全部长度，来提供遍布整个空间的均匀温度控制。货物必须以不干扰气流的方式装载到卡车里。必须小心，确保空气可循环贯穿装载的上部与向下到后部和两侧，并且空气流经途径畅通无阻沿地面返回到温度控制单元中。

Truck temperature control systems are designed to operate optimally with cargo that is preconditioned to the desired shipping temperature. When preconditioning is incomplete or compromised during the shipping process, it is even more important to also position and secure the load in a way that allows air to flow within and between the boxes or pallets of cargo.

将卡车温度控制系统设计成为最佳货物运营，其是所需要的运输温度的前提。运输过程中，当先决条件不完全或是有欠缺时，以气流在箱或货物托盘内与间流动方式装载的位置与安全甚至更加重要。

Truck loads are subject to the forces of inertia and vibration as they travel over the road. Once a load is properly placed within a truck, it must also be secured sufficiently to avoid movements that would result in damage to the load or shifts in position that result in airflow blockage. A system of E-Track, E-Track shoring beams, and/or ratchet straps and floor rings can secure cargo against movement. Use of a two to four inch spacer made of almost any convenient material and laid along the side edge of the floor is a simple technique that can prevent shifting of cargo against the wall.

因为卡车是在公路运输，卡车装货必须考虑考惯性以及颠簸。一旦正确装载到卡车，必须充分确保安全，避免移位导致装载损坏，或者位置偏移导致空气阻塞。一种E-Track系统，这种系统有短梁，和/或，棘齿条及地形，这能够确保货物防止移动。利用一张2英寸到4英寸的几乎可用方便的材料制作垫片放置到地面的边沿，这是一个简单的技术但可避免货物位移靠墙。

5.2 Qualification

第 5.2 节：确认

This section highlights the differences between the qualification approach taken for trucks and the general approach for active systems discussed above.

这节强调的是卡车与上述讨论有源系统一般确认方式之间的区别。

Transportation of biopharmaceutical materials is generally performed by vehicles that are not owned by the pharmaceutical shipper. Section 4.6.3 describes considerations for developing approaches that are relevant to such assets. Guidance conveyed in the Agreement on the International Carriage of Perishable Foodstuffs and on the Special Equipment to be used for such Carriage supports the overall intent of qualifying these systems (9). This guidance is useful for creating a specification for units. But it should be understood that each vehicle performs differently, and serious consideration should be made before deciding whether it is acceptable to qualify trucks/trailers as families or as individual units. When sensitivity to temperature is high, testing to qualify individual vehicles is recommended.

生物药品物料的运输一般是由车辆运输，这些车辆不属于制药托运人。在第4.6.3节所描述是针对有关此类资产的开发方式考量。指南中传达了在国际易腐食品运输协定及对于此类运输使用支持确认这些系统的整体意图特殊装备(9)。该指南对于制作一份单元规范是有用的。但是应了解到，每一部车辆的工作不同，并在决定是否接受作为族方式或作为个体单元确认卡车/拖车之前应进行严肃地考量。当温度敏感度很高时，推荐对个体车辆测试进行确认。

5.2.1 Approach

第 5.2.1 节：方式

General approaches to qualification are discussed elsewhere in this report, including the family approach, and considerations for developing an approach to qualification for a specific transportation mode.

这份报告的其它地方已经讨论了确认的一般方式，包括族方式，及开发一个特定运输模式确认方式的考量。

5.2.2 Design Qualification/Vendor Selection

第 5.2.2 节：设计确认/卖方选择

The main challenge with formal DQ for temperature-controlled trucks is that, typically, carriers/operators are distinct businesses from the manufacturing company. The lifecycle's design and specification portion occurs outside a GMP environment. Furthermore, carriers supply transportation services to many different clients, including those outside the regulated industries. Therefore, a common risk profile for products and design requirements could be difficult to develop. For this reason, DQ in most cases cannot be reasonably performed for temperature-controlled trucks.

正式对温度受控卡车设计确认的主要挑战，典型地，承运人/运营企业与生产公司是不同的业务。生命周期的设计及规范部分发生在药品生产质量管理规范环境外。此外，承运人为很多不同用户提供运输服务，包括哪些在药政管制以外的行业。因此，产品的一个通用风险概况及设计需求对于发展来说是困难的。因为这样的原因，设计确认在多数情况下，对于温度受控卡车不能合理的实施。

In lieu of DQ, the manufacturer should assess the vendor's capabilities, technologies, and systems in the context of the product and GDP requirements, which might have been entered into the carrier agreements. These requirements should be formalized and provided to prospective vendors and should be included in the business and quality agreements between parties.

代替设计确认，生产企业应评估可能已经写入到承运人协议中的卖方在产品与药品生产质量管理规范要求环境的能力、技术及系统。这些要求应正式化并提供给预期的卖方，也应包括在业务与质量协议中。

5.3 Installation Qualification

第 5.3 节：安装确认

The approach for IQ for trucks is the same as that in Section 4.3 (IQ), with the following additional considerations.

卡车的安装确认方式与在第4.3节(安装确认)中所描述相同，下述是额外的考虑。

5.3.1 Procedure Verification

第 5.3.1 节：规程确证

Procedures that might be specific to trucking processes include those that pertain to TCU operation, including startup checks and procedures and, especially, preconditioning procedures to ensure that the unit is at the required product temperature prior to loading. Verification that these procedures are in place should occur during IQ.

规程可能特定于卡车运输，包括那些属于温度控制单元运行，也包括启动检查与规程，尤其是预处理规程来确保在装载之前单元已经处在产品要求温度。应在安装确认期间确证有这些规程。

5.3.1.1 Trucks Used for Courier Routes

第 5.3.1.1 节：用于快递途径的卡车

Courier services or refrigerated vehicles used for pharmaceutical distribution to hospitals and pharmacies also face challenges. Refrigerated vans have the challenges of lower thermal mass and a potential bigger impact on warm air entering when doors are opened in warmer climates or during warmer seasons. Multiple door-open events and the time needed for the vehicle to recover from them can result in the inability to maintain a stable temperature in the desired range. When such vehicles are used as the primary temperature control method (instead of containers or packaging around the product, for example), procedures must be established to address this issue, and these procedures must be included in the qualification plan.

用来给医院与药房分发药品的快递服务或带有冷藏车也同样面临挑战。冷藏车面临低热质量的挑战，并且潜在更大的影响是在温暖气候或是温暖的季节开门时，热空气会涌进来。多个开门事件与车辆需要温度恢复的时间，可能导致不足以维持需求的稳定温度范围。当这些车辆用作主要温度控制方法时(例如，代替集装箱或产品周围的包装)，那么必须建立规程来解决这样问题，而且这些规程必须包括在确认计划内。

5.4 Operational Qualification

第 5.4 节：运行确认

The approach for OQ of trucks is the same as that in Section 4.4 (OQ), with the following additional considerations.

卡车运行确认方式与第4.4节一致，但还有以下进一步的考量。

5.4.1 Power Loss/Recovery and Redundant System Testing

第 5.4.1 节：断电/恢复及冗余系统测试

Qualification of a truck should include testing system functionality following a loss of power or fuel or in the event of a system malfunction. Testing should include a simple loss of power and restart. Testing criteria should require the system to startup under normal procedures (either automatically or by a predeveloped SOP that the operator follows).

卡车确认应包括在断电，或断燃料，或系统故障事件时测试系统功能。测试应包括简单的断电与重新启动测试。测试标准应在常规规程要求下要求系统启动(自动或操作人员遵守预先开发的标准操作规程)。

Other uses for a power loss test are to verify backup systems or identify the amount of time available for contingency intervention. If the truck incorporates a backup TCU, failure of the main unit should automatically lead to the startup of the backup unit. Ideally, this testing occurs concurrently with temperature mapping studies to evaluate the backup system’s performance from a stability/uniformity standpoint. This test can also be used to measure the length of time that the unit can withstand external temperatures when the power is off, giving a parameter for the amount of time available for intervention/recovery plans to be implemented if power is lost during transport.

断电测试的其它用途是确证后备系统，或辨识偶然性事件下可维持时间。如果卡车与后备温度控制单元整合，主单元失效应导致启动备用单元。理想的来说，该测试与温度分布研究同步，从稳定性/均匀性方面评价备用系统的性能。该测试可用来测定单元在断电后经受外部温度时间长短，给出一个如果在运输中断电所即将实施的干扰/恢复计划可用的时间量参数。

5.5 Performance Qualification

第 5.5 节：性能确认

Aspects of PQ tests that are specific to transport trucks and trailers include the following.

运输车辆与拖车特定的性能确认方面测试包括下列方面。

5.5.1 Static vs. In-Transit Studies During Performance Qualification

第 5.5.1 节：性能确认期间的静止与运输途中研究

Testing is performed to demonstrate that the truck's performance is not affected by external conditions while in motion/transit. This does not necessarily suggest that "in-transit" tests must be performed because there are conditions that make stationary or in-motion studies suboptimal.

实施测试是为了证明卡车的性能在移动运/输途中不会受到外部环境的影响。不必要建议必须实施 "途中"测试，因为这样的环境下静态或是动态研究是最不理想的。

In-motion studies would potentially subject the vessels to the greatest variance in temperature over a short period of time. For example, an extreme climb and descent through a mountainous region could subject the vessel to vastly different climates. However, a truck in motion would be subject to minimal solar heat gain relative to a static truck because much of the heat gain would be lost from convective heat gain/loss. Therefore, while in motion, the truck would be almost entirely subject to ambient temperature heat gain/loss only.

动态研究对于船舶在短时间内剧烈温度变化而言，是一个潜在的课题。比如说，经过山区时，极速攀升和急速下降，对于船舶在极端不同的气候条件下，可能是一个课题。然而，卡车移动过程中获得的热量，相对于静态的卡车还要弱一点。因为已经获得的热量大部分可能在对流中获取/损耗。因此，移动过程中的卡车几乎完全是依靠环境温度获取/损耗热量的。

A simulated environment might be used in which a truck is subjected to a single worst-case temperature over the study's duration. However, if that worst-case temperature is 40°C or -40°C, it is extremely difficult and costly to develop a controlled environment large enough to house a 53'trailer, for example. Furthermore, such an approach would not necessarily demonstrate the possibility of solar heat gain (although this could be accounted for by a higher and/or rising temperature over time). Such an approach would also not necessarily recognize localized heating sources that are outside a transport vehicle (e.g., hot asphalt or rolling tires).

为了研究卡车在整个期间的单一最差温度条件，可使用一个模拟的环境。然而，如果最差温度为40°C到-40°C，那么开发一个足够大的房间来容纳如一辆53英尺的拖车的可控的环境是困难且昂贵的。此外，并不一定需要用这种方法去证明获取太阳热量的可能性(即使这种方式可能会在整个时间导致一个比较高的温度，和/或，使温度升高)。因为热源处于车辆运输外部(比如热柏油路面或者轮胎转动的热量)，所以这种方法也没有必要找寻出局部热源。

Therefore, it is generally not necessary to test specific lanes of transport if the specific lane's conditions (or the worst-case conditions of a set of lanes) are accounted for during testing (e.g., for ambient temperature extremes). This is because, as an actively controlled system, a truck simply reacts to temperature differences on a continuing basis and should continue to do so provided that there is sufficient energy or fuel to operate the TCU.

因此，如果已经在测试期间考虑了特定线路状况(例如，一组最差的线路) (例如，极端环境温度)，那么一般不需要测试运输中的特定线路。这是因为一个有源受控系统，一辆卡车对温度差异在连续的基础上)做出简单反应，并应连续进行来提供操控温度控制单元运行的充足能源和燃料。

Ultimately, the manufacturer and service provider must provide a suitable rationale for testing using the selected approach.

最后，生产企业与提供服务企业必须提供一个用所选择方式测试的适当理由。

NOTE: Consider also that the unit is plugged to electricity, when on ferry crossings or parking for example.

注：此外还应考虑到在例如，码头仓库或停车，设备已经连接到电源上。

6.0 Temperature-Controlled Ocean Containers

第六章：温度受控海洋集装箱

Temperature-controlled ocean containers are similar in many ways to other vessels used to store or transport temperature-controlled materials. Ocean containers face the same additional challenges faced by refrigerated trucks because of the ambient, dynamic conditions that result from exposure to changes in climate while in transit and variances in payload size and placement within the vessel.

温度受控海洋集装箱与其它用于存储与运输温度受控物料的船舶在很多方面都相似。因为在运输暴露到气候变更的环境、动态条件，在集装箱内负载大小变化，海洋集装箱面临与带有冷藏车同样的额外挑战。

The strategies described in Sections 4.0 and 5.0 above for conducting temperature mapping and qualification studies apply to temperature-controlled ocean containers. The main difference is that due to the practical difficulties associated with resourcing ocean containers, the qualification effort is most profitably focused on the family approach, with a strong emphasis on process control rather than on qualifying individual containers. A family approach to qualification is discussed in Section 4.6.4 above. Therefore, the emphasis in this section is on the implementation of approved and controlled processes and procedures supported by detailed agreements between the shipper, freight forwarder, and/or carrier (e.g., a service-level or quality agreement).

第四章与第五章中描述的实施温度分布与确认研究的策略适用于温度受控海洋集装箱。主要区别是由于海洋集装箱资源实际困难确认工作最好侧重于族方式，强调过程控制而非个体集装箱确认。在第4.6.4节中已经讨论了族确认方式。因此，本节的重点是通过托运人、货运代理，和/或，承运人之间的详细协议(例如，一个服务水平或质量协议)，来对已经批准与受控过程及规程进行支持。

6.1 How Intermodal Temperature-Controlled Containers Work

第 6.1 节：温度受控集装箱联合运输如何工作

Valuable, temperature-sensitive, or hazardous cargo often requires the utmost system reliability. A temperature-controlled ocean container consists of a standard ISO container (i.e., intermodal container) and an integral refrigeration unit. The refrigeration unit is mounted on one end of the container. Air is cooled/heated to the required temperature in the condenser unit and then blown into the container and flows through and around the goods.

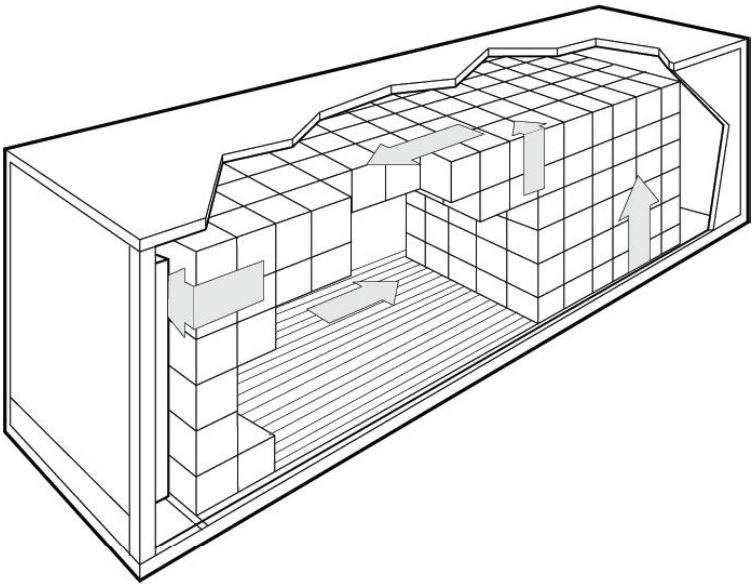
贵重的、温度敏感的，或危险品货物经常需要系统极其可靠性。一个温度受控海洋集装箱由一个标准国际标准化组织(ISO)集装箱(例如，联合运输集装箱)与一套冷藏联合单元构成。冷藏单元通常安放在集装箱的尾端。空气在冷凝单元冷却/加热到需要的温度，然后吹入集装箱并且流经货物周围。

In temperature-controlled ocean containers, the air flows through the container from the bottom to the top. Often, these containers have a “T-bar” floor so that the air can move underneath the product. This air is blown in through the gratings in the floor and then drawn off again below the container ceiling. The circulating fans then force the air through the air cooler (which also acts as the evaporator in the cold circuit) and back through the gratings into the cargo area (Figure 6.1-1). There is a maximum load height marked on the side walls that allows the air to circulate over the product. The temperature inside the refrigerated shipping container is displayed on an external control unit so that it can be checked at any time.

在温度受控海洋运输集装箱内，空气从集装箱的底部吹向顶部。这些集装箱经常带有一个 “T条” 地板，所以空气可从在地面通过栅栏吹入，然后再返回吹到集装箱的天花板隔层。循环风扇强制空气通过空气冷却器(也就是在冷循环中起到蒸发器的作用)，然后气体通过栅栏回到货物区域(图：6.1-1)。墙上有允许空气围绕产品进行循环最大负载高度标注。在冷藏运输集装箱内部的温度显示在在外部控制单元，以便任何时候都可检查。

Figure 6.1-1 Airflow in an Integral Refrigerated Container

图6.1-1：在内部制冷集装箱内的气流



For precooled cargo, air only has to flow around the goods because no heat has to be dissipated from the cargo itself. Only the heat that penetrates the insulation from outside has to be dissipated. To ensure that air can flow around the cargo, the container's inner walls normally feature corrugations. Then, even if the goods are stacked directly against the wall, air still flows through these channels and heat penetrating from outside is dissipated. The goods must be stowed in the container in such a way that the airflow is not interrupted (e.g., by stowing the goods too far above the load limit line) and to avoid circulation bypasses (e.g., as a result of free space in front of the door). The air takes a path of least resistance. Therefore, if there is free space around the product, the air might not circulate around the entire container area. Thus, suitable measures must be taken to cover the entire floor area. A fully loaded container has more temperatures than a partly loaded unit.

对于预冷的货物，空气只能够吹入到货物的周围，因为货物自身没有热量需要驱散。只能驱散来自外部穿透保温热量。为了确保空气可吹到货物周围，集装箱内墙面有褶皱特征。这样，即使货物直接靠墙堆放，空气仍然可通过这些缝隙吹入，并且将从外部穿透的热量驱散。货物必须按照气流不会被阻断(例如，货物堆放的超过警戒线)并避免绕道循环(例如，导致门前的闲置区域)的方式装载。空气流将走一条阻力最小的通道。因此，如果产品周围有空闲区域，空气流将不会环绕整个集装箱区域。所以，必须采取适当的措施来覆盖整个地面区域。满负载的集装箱相比于部分负载的集装箱会有更高的温度。

6.1.1 Process Review and Qualification

第 6.1.1 节：过程审核与确认

The qualification process for intermodal temperature-controlled containers is essentially identical to that of a trailer or active temperature-controlled ULD. The qualification steps are covered in detail in Sections 3.0 and 4.0 above, so this section reviews the process steps in a supply chain using a temperature-controlled ocean container. Each process step is reviewed to highlight potential risks and processes to mitigate these risks.

联合运输温度受控集装箱的确认过程对于拖车或有源温度受控有源成组装运设备实质上是一致的。确认步骤已经在第三章与第四章进行了详细描述，所以本节审核在供应链中使用一个温度受控海洋集装箱的过程步骤。每一个步骤都有潜在高风险，每个步骤都需要降低这些风险。

A summary of the process steps in the supply chain using a temperature-controlled ocean container to move temperature-sensitive pharmaceutical products is shown in Figure 6.1.1-1 below.

在供应链中使用一个温度受控海洋集装箱来运输温度敏感药品过程步骤汇总在下面图6.1.1-1中展示。

The first and possibly most critical step in successful ocean shipping is planning prior to the shipment. It is crucial that a risk analysis/assessment be completed to ensure that this transportation mode is suitable for shipping the products in question.

在海洋运输中第一个并且最关键步骤是在运输前策划。完成风险分析/评估是确保运输模式使用提议的产品运输的关键。

The decision to review ocean transportation for a given lane might be made for a number of reasons, including the volume of product going through a particular lane or the increasing costs and availability of alternative transportation modes. Other considerations need to be taken into account, such as a product inventory analysis to assess how much additional stock would be required while the cargo is in transit.

审核给定海洋运输航线决定可能基于很多理由，包括通过的特殊航道产品体积或增加成本及可供选择的运输模式。需要对其它考量进行考虑，诸如，一个产品库存清单分析来评估在货物运输期间需要增加多少库存。

If the value of a product is high and/or the product is not supported by good stability data, it might be determined not to use this method of transportation because the product could be out of the shipper's control for several weeks and it might be deemed that the risks are too high. It might also be the case that the insurance liability limit is exceeded, and, therefore, the container can be only partially loaded. This presents other risks, such as reduced thermal performance due to the container's not being fully loaded and a higher risk of damage if the load is not properly secured. This would also result in higher shipping costs per unit dose because a full container load was not used.

如果一个产品价值高，和/或，产品没有得到好的稳定的数据支持，那么就可决定不使用这种方式进行运输，因为产品可能要有几个星期不在托运人的控制范围内，这样被视为风险过高。还有一种情况是超出保险责任限度，因此集装箱只能部分装载。这就存在其它风险，比如由于集装箱没有满载导致热性能降低，以及如果装载没有得到适合的安全保护造成更高的风险。因为未使用满载的集装箱，这可能导致每个单元较高运输成本。

Refer to the PDA Technical Report No. 58, Risk Management for Temperature-Controlled Distribution, for a detailed examination of the risks and benefits of ocean transport (3).

详细的风险判断，参考美国注射剂协会(PDA)第58号技术报告-温度受控流通风险管理，对海运有益处(3)。

If, after consideration, the use of temperature-controlled ocean containers is still a viable option, the first step is to select the right logistics service provider. Once in full operation, the shipper generally deals with a freight forwarder and not the carrier; however, in the initial stages, it would be beneficial to have direct contact with the carrier to ensure that all assessments are accurate and complete (see Section 4.6.3 above for more details).

如果在考量后，如果认为温度受控集装箱海洋运输仍然是切实可行的选择，第一步是选择正确的物流服务提供企业。一旦开始全面操作，托运人一般与代理公司打交道，而不是承运人打交道；然而，在最初阶段，直接与承运人打交道来确保所有评估是正确的并完整的有好处的(更详细描述，参见上述第4.6.3节)。

An assessment should be made regarding the availability and frequency of ocean carriers from the origin to the destination to ensure that sufficient capacity is available and to allow shipments to be executed routinely.

应进行一个关于从原产地到目的地海洋运输承运人可利用性于频率的评估，来确保有足够的能力并能常规实施运输。

Once suitable partners have been established, a review is necessary of the processes in the supply chain to identify areas of risk and assess the level of, and need to implement, risk mitigation measures. Each phase in the shipping lane must be reviewed to fully understand the process steps, infrastructure, and capabilities of the stakeholders involved.

一旦建立合作伙伴关系，必须对在供应链中的过程进行审核，来辨识风险领域并评估风险水平，以及需要，风险减缓措施。自运输航线中的每个阶段，必须充分了解航运线上的每一步，基础设施及所涉及到的利益相关方能力。

Figure 6.1.1-1 Ocean Shipping Transport Phases

图6.1.1-1：远洋运输阶段

6.2 Qualification of Technology

第 6.2 节：技术确认

Using the family approach (discussed in Section 4.6.4), the shipper should perform qualification testing on a sample container. The testing should evaluate extreme conditions to ensure that the technology can maintain acceptable temperature limits when placed under duress, such as extreme ambient temperatures (hot and cold) and increased humidity. This testing only proves thermal performance; the shipper might also wish to perform power failure and open door challenges to better understand system capabilities, as described in detail in Section 4.0.

用族方式(已经在第4.6.4节进行讨论)，托运人应进行在集装箱样本上进行确认测试。这个测试应评估极端条件，确保在放置期间，如极端环境温度(冷与热)及增加湿度，该技术能够维持在可接受的温度范围内。该测试仅仅证实热性能；正如上述第四章讨论的，托运人可能也希望实施断电及开门挑战，以便更好地了解系统能力。

The Air-Conditioning, Heating, and Refrigeration Institute (AHRI) has designed a certification program for transport refrigeration (AHRI Standard 1110) (10).

美国空调、供热及制冷工业协会(AHRI)已经设计了运输冷藏认证程序(AHRI第1110号标准)。

NOTE: The AHRI transport refrigeration unit (also known as a TCU) standard deals with the mechanical performance of TCUs and not the performance of active systems. Therefore, AHRI certification, by itself, should not be confused with certification that the active temperature control system provides the product contained in that system with an acceptable temperature profile during transport. Another example of certification programs is the ATO certification produced by Wageningen UR Food & BioBased Research (11).

注：美国空调、供热及制冷工业协会(AHRI)的运输冷藏单元(也称为温度控制单元(TCU))标准处理温度控制单元机械性能而不是有源系统性能。因此，美国空调、供热及制冷工业协会(AHRI)认证，其本身，不应与在运输中为在系统中的产品提供一个可接受的温度概况有源温度控制系统认证相混淆。另一个认证程序的例子是瓦赫宁根大学食品与生物研究所(Wageningen UR Food & BioBased Research)提供的ATO认证(11)。

Any TCU equipment that holds one of these certifications has been tested against set standards and therefore meets a prescribed performance level. If the shipper decides to use only containers fitted with TCUs that have this certification, it must do so after considering the quality requirements of the product and risk assessment. This might be an acceptable rationale for using the family approach and not conducting formal OQ on all containers.

任何一个温度控制单元设备都有这些证书中的一个，这些设备已经按照设定标准进行测试，因此满足预先描述的性能水平。如果托运人决定仅仅使用已经经过认证的带有温度受控集装箱，那么必须考虑产品质量要求及风险评估。使用族方式基本原则可能可以接受，并不是对所有集装箱都要正式实施运行确认。

6.3 Processes Affecting Container Performance

第 6.3 节：影响集装箱性能的过程

Because of the significant impact of the ocean shipping process on the operation of cargo containers, this section describes considerations for each phase within the shipping lane, as shown in Figure 6.1.1-1. The information within should form the basis for any agreement (e.g., service level agreement [SLA] or quality agreement) between the shipper and freight forwarding partner.

由于海洋运输过程对货运集装箱操作显著影响，本节的描述基于在图6.1.1-1描述的货运航线上每阶段考虑。本节的信息应形成托运人与货运代理之间任何协议(例如，服务水平协议[SLA]或者质量协议) 基础。

6.3.1 Pretrip Inspection

第 6.3.1 节：启运前检查

Before a container is used, ensuring that it is fit for purpose is critical. The pretrip inspection's purpose is to ensure that the container is in good working order and that there are no faulty components in the control and monitoring system or refrigeration plant. A diagnostics inspection is carried out on the control system to ensure that all readings are as expected and that there are no control faults. A visual inspection is carried out to ensure that there is no noticeable physical damage to mechanical components in the refrigeration plant or the container. The container's inside is then appropriately cleaned, possibly by steam cleaning, to ensure a high-quality cleaning and the removal of any odors. The container is then labeled to show that it is ready for use. This operation is the responsibility of the carrier as the unit's owner; however, the owner might issue a contract to a third-party organization to carry out this activity. It is important to ensure that such an organization is set up and operated at an appropriate level to ensure that only suitable containers are supplied for use. The processes and controls should be assessed to ensure that each container is inspected and prepared to the same standard.

在集装箱使用前，关键是确保适合于其目的。启运前检查的目的是取保集装箱是处于好的工作状态，并且在控制、监测系统、制冷设备中没有带有瑕疵部件。对控制系统实施诊断是为了确保所有读数已经如预期并且没有控制缺陷。实施肉眼检测是为了确保制冷设备或集装箱没有明显物理部件的损伤。集装箱里面应经过适当清洁，可能用蒸汽清洁，来确保高质量的清洁，并清除任何气味。将集装箱标记为“可用状态”。这样的操作是作为单元物主的承运人的责任；然而，该物主可能与第三方机构签署一份合同来实施这样的活动。确保该组织已经建立并在恰当水平上运行来确保运输仅仅使用合适的集装箱是非常重要的。应对该过程与控制进行评估，来确保每一个集装箱按照相同标准来检查与准备。

Because containers could be anywhere in the world, it is not possible to have a scheduled, planned, PM program in place. The pretrip inspection serves as a replacement for this because each container is examined before every use.

因为集装箱世界任何地方都有，但不可能有一个日程表、计划、预防性维护程序。启运前检查服务作为上述这些替代，因为每一个集装箱在使用前都会进行检查。

6.3.2 Loading and Transport to Sea Port

第 6.3.2 节：到海港的装运及运输

Once the container is ready, it should be fitted with a generator set (genset). This is a diesel generator unit that is attached to the container and powers the container's cooling system while it is in transit between the shipper's facility and the port. The genset should be fitted to the container and powered on, and the container should be preconditioned to the required product temperature range prior to its arrival at the shipper's location. The required parameters, including temperature range and alarm limits, should

be set here. This should be detailed in the Service Level Agreement A/Quality Agreement to ensure correct container operation.

一旦集装箱准备就绪，就应安装发电机组。当一个柴油发电机单元安装在集装箱上，并给集装箱的制冷系统提供电力，在到达托运人的地点前，该集装箱应预先处理到产品所需要的温度范围。所要求的参数，应在此设定包括温度范围与报警限度。其应在服务水平协议/质量协议中详细规定，以致确保集装箱正确的运行。

The container's size (20 ft or 40 ft) dictates how long the packing operation takes. If the container has to be opened and remains open for loading in an uncontrolled area or at a temperature range that is different from the desired product temperature, an assessment should be made of whether the temperature control system should remain on or be turned off during this operation. If the unit remains on, it will draw in ambient air from outside the container; however, it will work to maintain the setpoint temperature. If the unit is turned off, no air is drawn into the container but there is no cooling capacity. It might be necessary to simulate this operation during OQ testing to ascertain the most appropriate course of action during this process.

集装箱尺寸(20英尺或40英尺)表明包装操作有多长。如果在装载过程中集装箱在一个不受控的区域或者温度与产品需求温度范围不同区域打开或者保持打开状态，应进行一个评估，是否温度控制系统在给操作过程中仍然开启或关闭。如果单元保持开启，那么会将集装箱外部的空气吸入进来；然而，这将保持设定温度。如果单元关闭，没有空气进入集装箱，但也没有制冷能力了。这可能需要在运行确认测试期间模拟这样的运行，来确定在这个过程中一个最恰当的措施。

The freight forwarder might use a contract hauler to deliver the temperature-controlled ocean container and collect the cargo. It is essential to ensure that this contractor is fully trained and understands the genset's operation; however, the contractor should not need to change any of the TCU's settings. If the refrigeration plant is turned off during loading, appropriate SOPs should be in place with instructions for the correct operating procedures to reset the unit after loading.

货运代理合同运输人来发送海洋温度受控集装箱并收集货物。确保该合同人经过全面培训并理解发电机组运行是至关重要的；然而，合同人应不需要变更温度控制单元的任何设定。如果在装载过程中关闭了制冷设备，应当有恰当的标准操作规程，来说明在装载后正确的重新启动规程。

As with temperature-controlled trucks, to provide a more stable temperature environment in the CES of a temperature-controlled ocean container, the TCU should be set on continuous mode (see Section 5.1). In continuous mode, the unit provides a constant supply of air to maintain the desired temperature range, resulting in the flat temperature profile desired for transporting pharmaceuticals.

如同温度受控卡车，为了给温度受控海洋集装箱的受控环境空间内提供一个更稳定的温度环境，应设置温度控制单元在连续模式(参见第5.1节)。在连续模式中，该单元提供空气的恒定供应来供维持预期温度范围，导致为药品运输要求的平坦的温度概况。

It is important to avoid the presence of loose material or trash during loading and keep drains clear because obstructed drains can cause buildup of humid saturated air, leading to excess ice on the coil and water on the load.

在装载与保持排水过程中，避免物料松动或垃圾是非常重要，因为排水堵塞可能形成湿饱和空气，导致盘管过多结冰与装载物有水。

Once the product is loaded and the container is closed (this could include a security seal), a truck transports the container to the sea port of departure. Depending on the distance from the shipper's facility to the sea port, it might be necessary to preplan the journey route to minimize the travel time. This might be part of the SLA and could also include a backup route in case of an emergency.

一旦产品已经装载并且关闭集装箱(这包括安全铅封)，卡车运输该集装箱到启运港。根据托运人设施与海港的距离，有必要预先策划旅行线路使旅行时间最小。这可能是服务水平协议的一部分，并且也包括在紧急情况下的后背线路。

6.3.3 Unloading at the Sea Port, Staging and Customs Clearance

第 6.3.3 节：在海港卸货、转运与通关

Once the truck arrives at the port, the temperature-controlled ocean container must be offloaded from the truck and staged prior to being loaded onto the ocean vessel. In many cases, the minimum delivery time prior to loading is 24 hours. The genset is removed from the container before it is unloaded from the truck. Once the genset is unloaded, it is essential that the container be plugged into the electrical supply at the staging area until it is sent for loading onto the vessel. This process should not take long, and, therefore, the risk to the product's temperature should be low. However, if the container could be subjected to extreme ambient temperatures, the time without power should be controlled. The maximum allowable time for this operation might have been identified as a result of the testing carried out at OQ (as described in Section 4.4) during the power failure testing to determine how long the container can maintain acceptable temperature limits without power.

一旦卡车到达港口，在装载到远洋运输船舶前，温度受控海洋运输集装箱必须从卡车上卸下并转运。在许多情况下，在装载前至少24小时交付。温度受控海洋运输集装箱从卡车上卸载之前，发动机必须先行拆卸。一旦发动机卸下来，直至发送装载到船上，在暂存区域为集装箱连接上电源至关重要。这个过程不应花费太长的时间，因此，产品温度de 风险应是低的。然而，如果集装箱遇到极端环境温度，应控制断电时间。作为在实施运行确认测试中的断电测试确定集装箱能够在可接受温度维持多长时间的结果已经辨识这个运行最大的允许时间(如在4.4节描述)。

It is likely that the containers will not be connected to a central alarm control system. In many ports, the process is to walk around

all temperature-controlled ocean containers every 12 hours to ensure and document that there are no alarms. The port of departure and, therefore, the ambient conditions to which the container could be subjected will have a major impact on the amount of risk at this stage in the supply chain. If there is an alarm in the 12-hour period between alarm checks, sometime might elapse before the problem is responded to. Depending on the results of the power failure testing during OQ/PQ testing, additional steps might need to be implemented to safeguard the consignment.

可能集装箱没有连接到中央报警控制系统。在许多港口，每12小时巡视所有温度受控远洋运输集装箱，确保并记录没有报警。因此启运港，集装箱所经受环境条件将在供应链中的这个阶段风险数量有很大影响。如果在12小时内巡检过之间有警报，在作出反应前，一些时间可能已经过去了。按照运行确认/性能确认测试中的电测试结果，可能要实施额外的步骤来保卫装运货物的安全。

Once the ocean vessel is ready to be loaded, the temperature-controlled ocean container is unplugged from the staging area and transferred to the quayside for loading. During this time, the refrigeration plant and control system have no power supply and are therefore out of operation. This process could take more than two hours from unplugging at the staging area to being plugged in onboard the vessel. It must be ensured that the container can maintain acceptable product temperatures during this period, as identified in testing.

一旦远洋运输船舶准备装载，温度受控远洋运输集装箱从暂存区域电源桩上拔出，转运到码头周围等待装载。这时候，冷藏系统与控制系统没有电力供应，因此不能运行。从暂存区域电源桩拔出到插到船上电源桩，这个过程可能花费超过两个小时。必须确保该集装箱在这个在测试中已经辨识的期间可以保持可接受的产品温度。

Once the container is loaded onto the vessel, the ocean carrier is usually responsible for ensuring that the container is plugged in and the temperature setpoint has been checked and verified for normal operation during transit. This responsibility must be agreed and documented in the SLA.

一旦集装箱装载到船舶上，远洋运输承运人通常负责在确保集装箱插入电源桩及检查温度设定值并确证在运输期间正常运行。这种责任必须在服务水平协议中认可并记录。

6.3.4 In-Transit

第 6.3.4 节：运输中

Once the vessel has left the port of departure, the container is the ocean carrier's responsibility. As in the port, the container is not plugged in to a central alarm system unless this is specifically requested. If not, the container is checked for alarms every 12 hours. It is possible that an error with the container might not be reacted to for 12 hours, during which time the product might go out of specification. Appropriate procedures should be implemented to safeguard against such risks. Most vessels have a central alarm system and if this is required, it should be agreed with the carrier and documented in the SLA/QA. Depending on the product's temperature range, it is essential to ensure that the container does not default to freezing mode in the event of a system fault because this could result in total loss of a temperature-controlled product.

一旦船舶离开启运港，集装箱就是远洋运输承运人的职责了。正如在港口，除非有特殊要求，集装箱没有接入到中央报警系统。如果没有，每12个小时要检查一次集装箱报警。有可能对集装箱的一个错误不能在12个小时内做出反应，在这段时间内，产品可能会超出规格标准。应实施一个恰当的规程来保卫产品遭受该风险。多数船舶有中央报警系统，如果需要，其应经过承运人同意并记录在服务水平协议/质量保证协议上。根据产品的温度范围，在系统出现故障时，有必要确保集装箱没有默认冷冻模式，因为这可能导致温度受控产品全部损失。

Few faults that can occur with temperature-controlled ocean containers are not repairable. The ocean carrier's engineers should be trained and have sufficient spares to resolve most emergency situations.

少数故障发生在温度受控远洋运输集装箱上可能是不可够弥补的。远洋运输承运人的工程师应经过培训并有足够的备件解决常见的紧急情况。

In the unlikely event that a fault occurs that cannot be repaired and the container fails, the carrier contacts the freight forwarder, who, in turn, contacts the shipper about the issue. Nothing else can be done until the vessel arrives at the destination port, where the container can be unloaded for inspection and the internal temperatures can be reviewed. During this time, the freight forwarder is responsible for providing the shipper with details about the vessel in transit, such as route changes, including stops or diversions. The freight forwarder should also provide updates on estimated time of arrival and any other issues related to the vessel.

在不太可能的事件中，发生不能弥补的事件及集装箱故障，关于这个问题，承运人联系货运代理人、谁、依次，联系托运人。在船舶到达目的港集装箱可以卸载进行检查并审核内部温度之前，不能做任何事情。在这段时间里，货运代理人有责任提供给托运人关于船舶在运输中的细节，诸如，航线变更，包括停靠或者转移。货物运输代理人也应提供达最新的预计到达时间，以及其它任何与传播相关的事宜。

6.3.5 Port of Arrival - Unloading, Customs Clearance, and Delivery

第 6.3.5 节：到港-卸货、通关与交付

Once the vessel arrives at the destination port, the container is unplugged from the vessel's power supply, unloaded from the

vessel, and transported to the staging area to await customs clearance. Responsibility for the unplugging operation must be established and documented in the SLA/QA. This responsibility can vary between ocean carriers; some take responsibility and do not want the port operators boarding the vessel to carry out this function, whereas other carriers request that the port operators take responsibility for this task. Failure to capture this information could result in the container's being unloaded with the plug still attached to the vessel. The outcome could be the loss of the plug and the inability to restore power to the container once it has been unloaded.

一旦船舶抵达目的港，集装箱从船舶供电的电源桩上拔出，从船舶上卸载船舶，并运送至暂存区等待通关。在服务水平协议/质量协议中必须建立拔掉插头操作的责任记录。远洋运输承运人之间该责任可能不同；一些获得哲人并不想让港口操作人员登船来实施这个职能，然而其他承运人需要港口操作员负起这样的责任。不能捕捉这样信息可能导致即将卸载的集装箱插头仍插在电源桩上。结果就是插头损坏插头，集装箱卸载后不能够恢复供电。

The same processes are used as those for loading at the port of departure, and the maximum duration for unloading, alarm checks, and loading for transit to the final destination need to be controlled in accordance with the OQ testing results. Once the container is unloaded and has been plugged into the power supply at the staging area, sometime could elapse before the container is released by the local customs authority. The destination port's ambient conditions will determine the level of risk to which the product is subjected during this period.

相同的过程可用在启运港装载中，卸载的最长时间、报警检查及最终目的港的运输装载，都需要按照运行确认测试结果来进行控制。一旦集装箱卸载并在暂存区域已经插到电源供应桩上，在当地海关机构放行集装箱前，一些时间将流失。最终目的港的环境条件将决定这段时间内产品遭受的风险水平。

Once customs clearance has been granted, the container is delivered to its final destination. A truck with a genset might be used to deliver power to the container during transit. The principles used at the point of origin should be applied during this stage.

一旦通关，会将集装箱运送到最终目的地。将用带有发电机组的卡车在运输途中给集装箱供电。在原产地所使用的基本原则将应用在这个阶段上。

6.4 A Note on Insurance Liability and Security

第 6.4 节：保险责任与安全注意事项

Ensuring that the shipment is adequately insured against risk of loss or damage during transit must be part of the overall preshipment assessment process. In assessing the need for insurance, the carrier's liability limits should also be considered. Unless a service agreement/contract that includes increased liability terms and conditions has been negotiated between the shipper and the transportation carrier, the transportation company's liability is limited under the bill of lading's terms and conditions and applicable maritime law. For example, the transportation company's liability for an ocean shipment to or from the United States is, as of the writing of this report, limited to $500 USD per package under the Carriage of Goods by Sea Act (12). Liability insurance provided by the transportation company is normally limited to loss or damage arising from the carrier's negligence, and this negligence must be proven. In addition, loss or damage from spoilage, in particular, is not usually covered under the bill of lading issued by the transportation carrier. Coverage terms provided by first-party commercial cargo insurance carriers are typically much broader than the terms of the liability insurance policies commonly offered or provided by transportation carriers. Not only is the transportation carrier's liability limited, but that limit is typically far below the value of the goods being shipped. Therefore, it is extremely important for the shipper to ensure that adequate insurance is in place and commensurate with the value of the goods being shipped. This insurance policy should offer proper coverage for loss or damage due to spoilage.

取保已经按照在运输中损失或损坏的风险进行足够保险必须成为整个装运评估过程的一个部分。在保险需求评估时，应同样要考虑承运人责任限度。除非托运人与运输承运人之间已经商定了包括增加的责任条款的服务协议/合同，否则运输公司只限定在提单条款下及所适用的海商法中的责任。例如运输公司对一个到达或来自美国的远洋运输的责任是，按照本报告书面描述，在海上货物运输法之下仅仅限于每个包装500美元(12)。运输公司所提供的责任保险通常限于因承运人的过失造成的损失或损坏，而且这种过失必须经过证明。另外，因腐败导致的损失或损坏，通常并不在运输承运人签发的提单涵盖之下。由第一商业货物保险承运人所提供的条款范围通常比通一般提供给或由运输承运人提供的保险单责任条款明显宽泛。不仅有运输承运人的责任有限定，而且限度通常明显低于所运输货物的价值。因此，对于托运人来说确保有恰当保险并与所运输的货物价值相当非常重要。保险单应对由于腐败导致的损失于损坏提供恰当覆盖。

Security is a major concern for any mode of transportation when the shipper's product is outside its direct control. During the shipping of products in temperature-controlled ocean containers, the main security risks are at ports, where containers might be unattended for several days prior to shipping or while they are waiting for customs clearance. These risks should be assessed during the shipping lane's implementation, and appropriate procedures might need to be employed to limit this risk.

当托运人的产品不在其的控制时，任何运输方式的安全性是主要考虑的因素。用运输温度受控远洋运输集装箱运输产品期间，主要的安全风险在港口，运输前可能几天或等待通关时未被照顾到。在运输航线实施中，应评估这些风险，并可使用合适的规程来限制这些风险。

7.0 Active ULDs

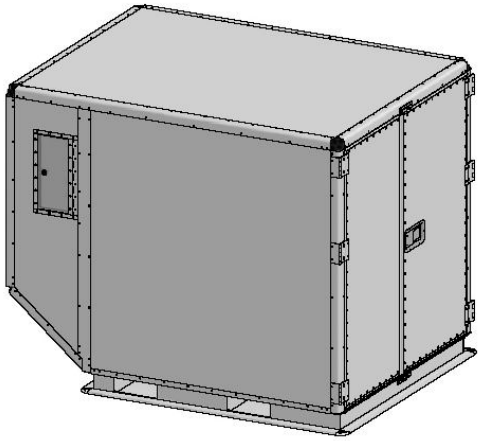
第七章：有源成组装运设备

Active temperature-controlled ULDs as defined in this report have heating and/or cooling capabilities (Figure 7.0-1). Active ULDs are typically operated from externally supplied AC power or internally stored and supplied DC power.

有源温度受控成组装运设备在本报告中定义为有加热，和/或，制冷能力(图7.0-1)。有源温度受控成组装运设备通常用外部供电的交流电或者内部储存与提供的直流电来运行。

Figure 7.0 -1 An Active ULD

图7.0 -1：一个有源成组装运设备



7.1 Design

第 7.1 节：设计

As with most temperature-controlled packaging systems, active ULDs are designed to maintain the product's preconditioned temperature as opposed to changing the product's temperature. Active ULDs accomplish this by distributing air within the cargo area, thereby insulating the freight from the effects of outside temperatures. Design considerations specific to active ULDs are noted below.

作为温度受控包装系统，有源成组装运设备设计成保持产品预处理的温度，而不是改变产品的温度。因此，有源成组装运设备通过分布在货物区域的空气达到这点，从而免除外部温度对货物的影响。有源成组装运设备的设计特定考量如下。

7.1.1 Thermal Integrity

第 7.1.1 节：热完整性

Items that can compromise an active ULD's thermal integrity include gaps around doors or walls, cracks in door seals, and inherent wall structure and insulation contained therein. Properly designed door closure systems and physical payload space securely isolate the cargo from the electrical and mechanical operating components. In many active ULDs, these areas are also isolated from one another.

一些会降低有源成组装运设备热完整性项目，包括门或墙周围的缝隙、门密封条上的裂缝、墙体的固有结构及其中的保温材料。正确设计的门密闭系统及实际载货容积，将电气与机械运行部件与货物安全隔离了。在许多有源成组装运设备中，这些区域与其它区域是隔离的。

7.1.2 Sufficient Heating/Cooling Capacity

第 7.1.2 节：充足的加热/制冷能力

Active ULDs must have sufficient capacity to add or remove the heat that is transferred into the cargo hold area from the external environment. The greater the difference in temperature between each container's setpoint and the external environment, the greater the amount of electric energy required. Since active ULDs are typically utilized for combination air and ground transport in a multitude of potentially extreme environments, their designs generally take temperature exposures into consideration.

有源成组装运设备必须有足够的能力来增加或是移除来自外部环境转移到货物放置区域的热。每个集装箱设定值和外部环境的温度差别越大，那么所需要的电能越大。因为有源成组装运设备典型地用在一个大量潜在极端环境空运与地面联合运输，所以有源成组装运设备设计一般要将外部温度暴露考虑在内。

7.1.3 Airflow

第 7.1.3 节：气流

Typical active ULDs are designed to distribute air with sufficient speed and direction to maintain a uniform temperature around the product and the interior of the cargo space (Figure 7.1.3-1). When the payload is too tall or positioned where airflow in the container is blocked, areas of stagnant air develop and adversely affect the container's ability to maintain both air and product temperatures uniformly. Payload volumes that are smaller than maximum design do not inhibit airflow and make for a more uniform temperature spread throughout the cargo area.

典型有源成组装运设备靠用足够的速度与方向分散空气来保持在产品周围及货物内部空间均匀的温度(图：7.1.3-1)。当有效负载太高或安置位置，当进入集装箱的气流被堵塞，形成空气滞留区域并对集装箱维持空气于产品温度均匀性的能力产生不良影响。有效荷载体积比最大设计的要就不会抑制气流并可使整个货物区域温度差更均匀。

Figure 7.1.3-1 Airflow within an Active ULD

图7.1.3-1：一个有源成组装运设备中气流

7.1.4 Temperature Control Accuracy

第 7.1.4 节：温度控制精度

Temperature control accuracy can be assessed by conducting a temperature mapping study. Ideally, temperatures are maintained within a variance that maintains the product temperature at ±3°C. Design parameters for interior temperature variance vary by ULD, depending on such factors as construction and insulation material, heating and cooling methodologies, numbers of interior fans, speed and placement, payload venting and recirculation, and control thermocouple location.

通过实施温度分布研究能够评估温度控制精密。理想的，温度维持在产品温度在±3℃波动。所设计的内在温度波动因成组装运设备不同而不同参数，其取决于诸如建造与保温材料、加热与制冷方法、内部风扇数量、速度与位置、有效载荷通风与再循环，以及控制热电偶的位置这些因素。

7.1.5 Monitoring and Alarming Capability

第 7.1.5 节：监测与报警能力

The cargo hold area of an active ULD should have ongoing temperature monitoring and out-of-specification alarm capabilities to notify users and reduce the risk of product temperature deviations. Alarm settings vary depending on ULD design and unit robustness.

有源成组装运设备的货物放置区应有持续温度监测及超出标准的报警能力来通知用户并降低产品温度波动的风险。报警设定根据成组装运设备的设计与单元耐用性的不同而不同。

7.1.6 Redundant Capability

第 7.1.6 节：过剩能力

Active ULDs might have redundant heating/cooling systems to serve as backups in the event of failure. System redundancies include backup compressor(s), heating elements, additional circulating fans, and electronic control system.

有源成组装运设备可能具有过剩的加热/制冷系统在故障情况下作为后备。系统过剩包括备用压缩机、加热要素、附加循环风扇及电力控制系统。

7.1.7 Power Loss and Open Door Recovery

第 7.1.7 节：断电与开门恢复

The intent of power loss and open door recovery testing is to demonstrate that an active ULD can recover effectively from a power loss or open door. Performing these tests under battery power, rather than while the active ULD is connected to AC power, also

indicates the performance capability of the active ULD while it is in transit.

断电与开门恢复测试的目的是证明一个有源成组装运设备能够从断电或者开门状态有效地恢复。这个测试是在电池供电状态下进行，而不是当有源成组装运设备已经连接到交流电状态下，这也表明有源成组装运设备在运输途中的性能能力。

It is also recommended to understand the container's holdover time after the batteries are depleted. A test should be conducted in which the batteries are fully discharged and the rate of change of the air and payload temperatures is recorded.

推荐清楚了解当电池耗尽后集装箱的续航时间。应在电池完全耗尽后实施测试，并记录空气及有效负载温度变动速率。

7.1.8 Alarms

第 7.1.8 节：报警

The intent of alarm testing is to demonstrate that the active ULD will effectively sound an alarm when the system reaches an alarm condition. It is reasonable to combine alarm testing with power loss and open door testing; in this test, power loss and open door temperature excursions serve as alarm conditions.

报警测试的目的是证明当系统满足报警条件时，有源成组装运设备将有效的进行音频报警。将断电与开门测试与报警测试相组合是合理的；在这个测试中，断电与开门后温度偏离是报警的先决条件。

7.2 Process Control of Active ULDs

第 7.2 节：有源成组装运设备过程控制

Refrigerants used for shipping temperature-sensitive products are designed to maintain these products at a specified temperature for a specified amount time based on the expected transportation schedule. A key advantage of active containers is that, if a power source is available, they can maintain products at a given temperature without time limits.

在温度敏感产品运输中所使用的制冷剂是为了在基于期望的运输预定时间计划的一个特定的时间段保持这些产品在一个特定的温度。有源集装箱的一个关键优势是，如果有电力供应，其可保持产品在一个给定的温度而没有时间限制。

The transportation process for active ULDs must be controlled within defined parameters, monitored closely, and have contingency plans in place. Steps to take when shipping an active ULD include the following:

有源成组装运设备运输过程必须控制在规定的参数范围，密切监测，并有对应意外发生的计划。在运输一个有源成组装运设备所采取的步骤包括以下所述：

- Precondition the container to the transport temperature before the container is loaded
  集装箱装载前，预先处理集装箱到运输温度
- Ensure that the product is preconditioned to the transport temperature before the container is loaded
  集装箱装载前，确保已经预先处理产品到运输温度
- Ensure that the container's control system is appropriately programmed for the current shipment, including its setpoint and alarm range
  确保集装箱控制系统已经为现行运输恰当地编程，包括设定值与报警范围
- Minimize the container's exposure to extreme ambient temperatures
  集装箱暴露在极端环境温度最小
- Ensure that the ULD size is compatible with available aircraft
  确保有源成组装运设备尺寸与飞机一致
- Check the battery voltage and container temperature at transit points
  在运输节点上，检查电池电压与集装箱温度
- Plan to charge the container at transit point(s) and during any delays
  在在运输节点与任何延迟期间为集装箱充电计划
- Determine the locations at which backup cold storage is available
  确定哪些可用备用冷库位置
- Define the actions to take with the service provider in case of container failure

规定万一集装箱失效时服务提供方采取的措施

8.0 Temperature-Controlled Storage Warehouses/Rooms

第八章：温度受控储存仓库/房间

This section applies to active temperature-controlled storage of pharmaceutical raw materials and/or products. Commonly referred to as cold rooms, refrigerators, or freezers, these rooms are CESs that can be designed to maintain temperatures around the stored material at whatever setpoint and range is required.

本章节应用于制药原料，和/或，产品的有源温度受控储存。通常是冷藏房间、冰柜、冷冻库，这些房间是控制环境空间，其用来保持所储存物料周围的温度在设定值于要求的范围内。

8.1 System Description

第 8.1 节：系统描述

This information regarding temperature-controlled storage rooms is applicable to a broad range of CESs designed to produce a stable environment at a specific temperature, including walk-in cold rooms, refrigerators, freezers, and room-temperature stores. Most commonly, walk-in cold rooms and refrigerators maintain a temperature uniformity range of 5 ± 3°C, whereas freezers typically have a range of -20 ± 5°C or -70 ± 10°C. In all cases, the range should be based on the temperature requirements of the material and/or product stored in the unit. These requirements should be based on the stability data of that material and/or product.

本节关于温度受控存储空间信息广泛地适用于用来在特定温度产生稳定环境控制环境空间，包括冷藏房间、冰柜、冷冻库和室温储存。最普遍的情况是，大型冷藏房间和冰柜保持温度均匀性范围在5 ± 3°C，而冷冻库典型温度范围是-20 ± 5°C或是-70 ± 10°C。在所有情况下，温度范围都应基于在其中储存的物料，和/或，产品要求。这些要求应基于物料，和/或，产品稳定性数据。

Four elements are required to maintain temperature. In designing a cold room, these factors should be considered, as noted in Section 3.0.

维持温度需要四种要素。在设计冷库时，如第三章描述的那样，这些因素应要考虑进去。

1. The construction should be of the type to maintain the temperature range required by the material and/or product stored within the cold room. Commonly, a modular construction with insulated double walls is used.

   建造应维持存放在冷藏房间的物料，和/或，产品的要求温度范围。一般来说，模块化建筑使用双层保温墙。

2. The temperature in the CES is usually controlled by a calibrated, solid-state, microprocessor based controller that constantly regulates air temperature. Simpler control systems employ an on/off temperature control system in which the unit's interior is only activated and deactivated at predetermined high and/or low temperatures (similar to thermostats in most homes). This type of simple system can sometimes save money, but the trade-off is that such systems provide less control over the range of temperatures in the CES.

   控制环境空间的温度通常通过校准的、固定状态，并带微处理器用不断调节空气温度的控制器的方式控制。更简便的控制系统是通过一个在单元内开关温度控制系统，通过预先设定的高，和/或，低温度(似于最常见的室内恒温调节器)来启动或停止。这种简单的系统有时候可节省金钱，但是权衡是，该系统在控制环境空间内只能够提供更少温度受控范围。

3. A walk-in cold room/refrigerator/freezer also employs some sort of recorder device. In some cases, this consists of a pen temperature recorder with a temperature alarm module. However, electronic recording systems connected to central servers or other electronic recording devices are becoming more common as technology advances. These types of electronic systems might offer more reliability, prompter alarms, and better and quicker analysis. To reduce business and product risk, alarm systems can be set to notify management prior to an out-of-specification condition within the unit. Alarms can be both local (at the source) and remote, such as to a security desk, or they can initiate a call to a predetermined telephone number. This monitoring should be continuous (24 hours a day, seven days a week).

   大型冷藏房间、冰柜、冷冻库也使用一些种类记录仪。在一些情况下，由带有温度报警模式的笔式记录温度仪构成。然而，作为先进技术，连接到中心服务器的电子记录仪或其它电子记录装置更常见。这些类型电子系统可提供更可靠、更即时警报、及更好更快速的分析。为了降低商业与产品风险，可以设定警报系统在在系统内条件超出标准前进行通知管理。警报可使本地(在发生地)或远程的，比如安全桌面，或他们可用电话联络预先设定的电话。这样的监测应是连续的(每天24小时，一周7天)。

   Assessments of the material and/or product can dictate the level of control accuracy required within the unit. Thermal mass of the material and/or product along with packaging that insulates the product can result in attenuation of the more rapid air temperature changes experienced by the conditioned air outside the material and/or product. Therefore, it is good to know not only what is going on around the packaging of the material and/or product but also to know what is happening within that packaging.

   对物料，和/或，产品的评估可显示在单元内要求控制精度的等级。物料，和/或，产品与保温该产品包装在一起

的热质量通过处理物料，和/或，产品外部空气，可以衰减导致的更快速的空气温度变化。因此，不仅仅知道在物料，和/或，产品包装周围将发生什么，而且知道在包装内正在发生什么情况是有益的。

4. Due to the extended nature of the storage activity, it is necessary to design sufficient redundant temperature control capacity into the system so that while TCUs are inoperative during maintenance or for other reasons, the CES's temperature stability is not compromised. A backup power source and duplicate control elements are also prudent.

鉴于存储活动延伸的性质，需要在系统内设计足够的过剩温度控制能力，以便在温度受控单元维护或其它原因不起作用时，不破坏控制环境空间的温度稳定性。备用电源与双套的控制要素也是慎重的。

Other elements of a walk-in cold room/refrigerator/freezer system that are important for storing pharmaceuticals include the following:

大型冷藏房间、冰柜、冷冻库系统对于储存药品重要的其它要素包括:

- Fire suppression system and alarms
  火灾扑救系统与警报
- Emergency and uninterrupted power supplies
  紧急与不间断电源供应
- Lighting and electrical receptacles
  照明与电插座
- Lightning protection
  雷电保护
- Temperature alarms
  温度报警
- Inventory control/organization systems
  库存控制/组织系统

TCUs are designed to maintain the internal air temperature within a desired range, thereby insulating the materials or products from outside influences and maintaining the interior conditions required for product storage and stability. To accomplish this, air must be able to move throughout the unit's interior. Thermal integrity, sufficient BTU capacity, and proper airflow and air movement are essential for this refrigeration process.

温度受控单元目的是维持内部空气温度在预期温度范围内，因此产品储存与稳定性要求物料与产品与来自外部影响保温并保持内部条件。为了完成达到这个目的，空气必须能进入单元内部。热完整性、足够热容量，及恰当气流欲空气流动对于冷藏过程是必要的。

8.2 Qualification

第 8.2 节：确认

8.2.1 Temperature Mapping

第 8.2.1 节：温度分布

Qualification of active temperature-controlled storage rooms includes a temperature mapping study, which temperature probes are placed in the three-dimensional space of the walk-in cold room/refrigerator and recorded over time and under various conditions, as described in Section 4.6.1. Temperature mapping in itself does not guarantee controlled conditions without verification of the systems that support the continued use of the temperature control system. Therefore, temperature mapping should generally be performed within a qualification study, such as OQ and/or PQ.

对于有源温度受控储存室的确认包括一个温度分布研究，温度探头安放在大型冷藏室/冰柜的三维空间内，按照第4.6.1节所描述，按照时间记录波动条件。没有对支持连续使用温度控制系统确证，温度分布自身不能保证受控条件。因此，温度分布通常应在确认研究中实施，比如运行确认，和/或，性能确认。

When determining the length of time for conducting the temperature mapping, the unit's external environmental conditions should be considered. If these conditions are stable, a shorter length of time might be appropriate. However, if the conditions are variable, more time might be required. Temperature mapping should be performed for an adequate length of time to capture any effects of the external environment on the chamber and establish the consistency and effect of defrosting within TCUs. It is generally accepted that capturing data over three or more complete defrost cycles is minimally sufficient. However, if the CES's exterior is exposed to outside weather, it is recommended that the temperature mapping not last less than 24 hours to capture these external

effects.

当决定实施温度分布的时间长度时，应考虑该单元外部环境条件。如果这些条件稳定，更短的时间跨度更为合适。然而，如果条件波动，就需要更长的时间。温度分布测试应在合适时间跨度上实施，用以捕捉任何外部环境对腔室的影响，并在温度受控单元内建立一致性与除霜影响。一般最低捕捉三个或更多的完整除霜周期数据是可以接受的。然而，如果控制环境空间外部暴露在外部气候里，建议温度分布持续不要小于24小时来捕捉这些来自外部的影响。

The three-dimensional temperature profile should be assessed by selecting points in at least three planes in each direction - top to bottom, left to right, and front to back - at which product will be present within the chamber or unit's normal storage area.

应当用至少在三个面上的每一个方向上，从上到下，从左到右，从前到后，在产品即将在腔内或单元的常规储存区域出现处，选择点来评估三维温度概况。

8.2.2 Load Used During Qualification

第 8.2.2 节：在确认中所用的负载

When there is not enough material to use a full load for qualification testing (e.g., 80% capacity) in a larger cold room/refrigerator/freezer unit, a step approach is recommended to achieve maximum capacity. This approach needs to be agreed on by the organization's quality unit and involves the validation of the cold room/refrigerator/freezer unit in increments of capacity over time. For example, when the unit reaches 25%, 50%, and then 75% capacity, a new mapping could take place.

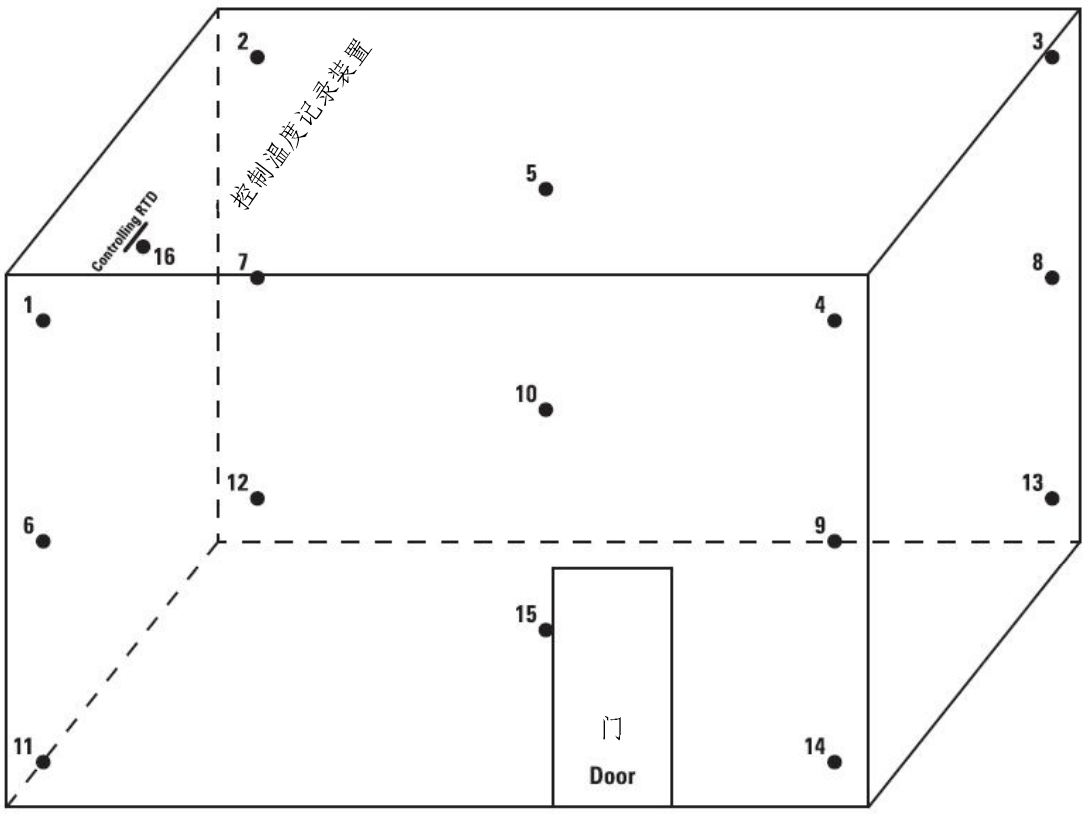
当较大的冷藏房间、冰柜、冷冻库确认测试中没有足够的物料用来满载（例如，80%能力）时，推荐一个分步方式来达到最大能力。这种方法需要由组织的质量部门同意，并涉及到冷藏房间、冰柜、冷冻单元随时间增加能力。例如，当单元达到25%、50%与75%的能力时间，进行新的温度分布测定。

In any case, walk-in cold rooms/refrigerators/freezers are typically first tested without loads (empty chamber uniformity) with thermocouple probes or standalone recording devices to determine their defrost cycle efficiencies and identify cold/warm spots. An illustration of an empty chamber mapping scheme and loaded chamber mapping scheme follow in Figures 8.2.2-1 and 8.2.5-1. Sample charts for tracking monitoring device location (Table 8.2.5-1) and documenting monitoring results (Table 8.2.5-2) are shown below.

在任何情况下，大型冷藏室、冰柜、冷冻库通常首先要进行无负载测试(空腔均匀性)，热电偶探头或独立的记录装置来测定除霜周期效率，并辨识冷/热点。空腔温度分布计划图及已经装载腔的温度分布计划图见下列图8.2.2-1与图8.2.5-1。追踪监测仪器位置图表样本（表8.2.5-1）与监测结果记录（表8.2.5-2）展示如下。

Figure 8.2.2-1 Cold Room Distribution Thermocouple or Stand-alone Recording Device Placement Diagram

图8.2.2-1：冷藏室热电偶或独立记录装置分布位置图



8.2.3 Controlling Devices

第 8.2.3 节：控制设备

The controlling recording temperature device (RTD) for temperature-controlled storage spaces should be identified through IQ and verified through OQ. Critical instruments should at least be defined and verified during OQ, and the calibration of these instruments should be verified during the system PQ. Based on the criticality of each instrument and vendor recommendations, critical instruments should be entered into a calibration program with intervals defined for recalibration that make sense for the system.

温度受控储存空间的温度控制记录装置(RTD)应通过安装确认进行辨识，并通过运行确认进行确证。在运行确认阶段，至少要规定并确证关键的仪器，这些仪器的校准应在系统性能确认阶段进行确证。基于每一个仪器的关键性与供应商的推荐，关键仪器应在规定的重新校准间隔启动对于系统敏感的校准程序。

8.2.4 SOPs and Training

第 8.2.4 节：标准操作规程与培训

SOPs can be verified at any time during qualification (IQ, OQ, or PQ). They must, however, exist in a final, approved format prior to the equipment's release to normal operational use. SOPs ensure that equipment is operated consistently with every use. Qualification also ensures that systems operators are trained in the applicable SOPs. Training is especially important when a manual action is a part of the process. Conversely, training can also prevent inadvertent actions that might be applicable to some products and not others.

在确认(安装确认、运行确认、性能确认)的任何时间都可以对标准操作规程进行确证。然而，其必须在设备放行到正常运行使用前，存在一个最后，批准的格式。标准操作规程确保设备在每次使用一致运行。确认也确保系统操作人员经过对恰当的标准操作规程的培训。在过程中有部分要手动操作时，培训尤其重要。相反的，培训也预防可能适合某些产品但不适合其它产品疏忽操作。

8.2.5 Summary

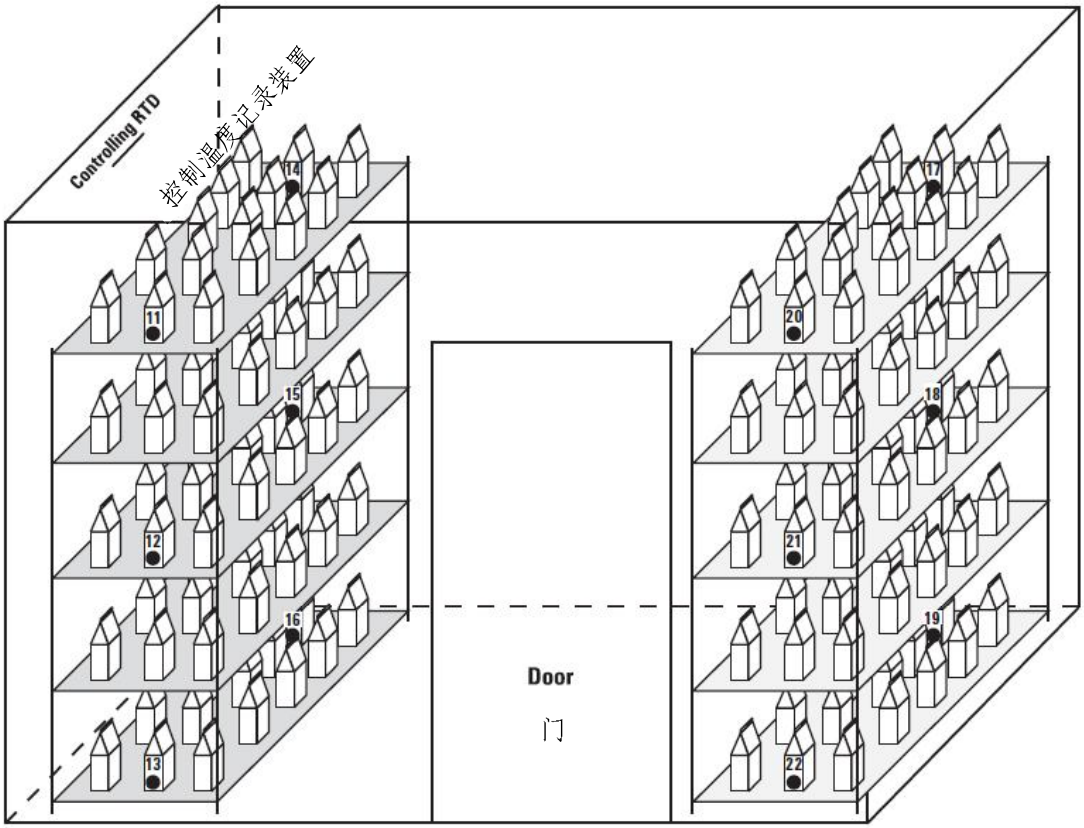
第 8.2.5 节：总结

Qualification is performed according to the procedures described in a protocol. This protocol identifies the steps required to perform and document the qualification activities. The need to map temperatures and the methodology used should be assessed based on the risk profiles established for each process and product. Ultimately, strategies for conducting qualification studies, including temperature mapping, should be based on knowledge of the product, including its stability profile; forced degradation studies; and temperature cycle studies.

确认按照在方案中已经描述的规程来实施。该方案辨识了需要实施的步骤及确认活动的文件。应基于每个过程与产品已经建立风险概况来评估对温度分布需求与所使用的方法。最后，实施包括温度分布的确认研究策略，应当基于包括其稳定性概况、强制降解研究，以及温度周期研究的产品知识。

Figure 8.2.5-1 Cold Room Penetration Thermocouple or Stand-alone Recording Device Placement Diagram

图8.2.5-1：冷藏室穿刺热电偶或独立记录设备放置图



NOTE: Thermocouples 1 through 10 are not shown; only the penetration thermocouples or stand-alone recording devices are illustrated.

注意：第1号到第10号热电偶没有显示，只说明了穿透型热电偶或独立记录装置。

Table 8.2.5-1Thermocouple or Stand-alone Recording Device Distribution List

表8.2.5-1：热电偶或独立记录装置分布目录

Location 位置	Thermocouple# 热电偶编号	Description 描述
1		Left, front, corner, top plane of CES 控制环境空间的左、前、角、顶盘
2		Left, rear, corner, top plane of CES 控制环境空间的左、后、角、顶盘
3		Right, rear, corner, top plane of CES 控制环境空间的右、后、角、顶盘
4		Right, front, corner, top plane of CES 控制环境空间的右、前、角、顶盘
5		Center, top plane of CES 控制环境空间的角、顶盘
6		Left, front, corner, middle plane of CES 控制环境空间的左、前、角、中盘
7		Left, rear, corner, middle plane of CES 控制环境空间的左、后、角、中盘
8		Right, rear, corner, middle plane of CES

		控制环境空间的左、后、角、中盘
9		Right, front, corner, middle plane of CES 控制环境空间的右、前、角、中盘
10		Center, middle plane, the chamber of CES 控制环境空间腔室中心、中盘
11		Left, rear, corner, bottom plane of CES 控制环境空间的左、后、角、底盘
12		Right, rear, corner, bottom plane of CES 控制环境空间的右、后、角、底盘
13		Right, front, corner, bottom plane of CES 控制环境空间的右、前、角、底盘
14		Left, front, corner, bottom plane of CES 控制环境空间的左、前、角、底盘
15		Center, bottom plane of CES 控制环境空间的中心、底盘
16		Next to controlling RTD 接近控制温度记录装置

Table 8.2.5-2 Penetration Thermocouple or Stand-alone Recording Device Data Worksheet

表8.2.5-2：穿刺型热电偶或独立记录装置数据工作表

Temperature Setpoint: _____℃

温度设置点：_____℃

Location 位置	Description 描述	Minimum 最低 (°C)	Maximum 最高 (°C)	Average 平均 (°C)	Pass/Fail? 通过/不通过 (2-8°C)	Initial/ Date 签字/日期
1	Left, front, top corner 左、前、上角					
2	Left, rear, top corner 左、后、上角					
3	Right, rear, top corner 右、后、上角					
4	Right, front, top corner 右、前、上角					
5	Left, front, bottom corner 左、前、下角					
6	Left, rear, bottom corner 左、后、下角					
7	Right, rear, bottom corner 右、后、下角					
8	Right, front, bottom corner					

	右、前、下角					
9	Center of the chamber 腔室中心					
10	Next to the controlling RTD 紧邻控制温度记录装置					
11	Left, front corner of the cold room, in the container, on the top shelf 冷藏室左、前角，集装箱顶层					
12	Left, front corner of the cold room, in the container, on the middle shelf 冷藏室左、前角，集装箱中层					
13	Left, front corner of the cold room, in the container, on the bottom shelf 冷藏室左、前角，集装箱底层					
14	Left, rear corner of the cold room, in the container, on the top shelf 冷藏室左、后角，集装箱顶层					
15	Left, rear corner of the cold room, in the container, on the middle shelf 冷藏室左、后角，集装箱中层					
16	Left, rear, corner of the cold room, in the container, on the bottom shelf 冷藏室左、后角，集装箱底层					
17	Right, rear, corner of the cold room, in the container, on the top shelf 冷藏室右、后角，集装箱顶层					
18	Right, rear corner of the cold room, in the container, on the middle shelf 冷藏室右、后角，集装箱中层					
19	Right, rear corner of the cold room, in the container, on the bottom shelf 冷藏室右、后角，集装箱底层					
20	Right, front corner of the cold room, in the container, on the top shelf 冷藏室右、前角，集装箱顶层					
21	Right, front corner of the cold room, in the container, on the middle shelf 冷藏室右、前角，集装箱中层					
22	Right, front corner of the cold room, in the container, on the bottom shelf 冷藏室右、前角，集装箱底层					
Comments: 意见:						

9.0 Conclusions
第九章：结论

Qualification for active temperature control systems typically involves DQ, IQ, OQ, and PQ. Periodic overviews of the qualification are required to assess variations in temperature-controlled systems over time. Some test elements may be omitted for various systems based on risk assessment results.

对于有源温度受控系统的确认通常设计到设计确认、安装确认、运行确认与性能确认。需要对确认进行定期审核来评估温度受控系统随时间的变化。个别系统基于风险评估结果可忽略一些测试要素。

Controls verification should be performed to verify that the temperature control equipment is performing within the recommended range. IQ's main purpose is to verify that the system complies with the proposed design or that it has been installed in accordance with the design. IQ includes document verification, equipment installation, PM, calibration, controls, and configurable parameters. IQ can be performed by the equipment vendor and/or user. Successful DQ and risk analysis ensure successful OQ. Ideally, OQ follows the completion and approval of IQ activities, and the OQ results should be approved prior to initiating PQ. Power failure activity, alarm testing, SOP verification, and temperature mapping are usually part of OQ. The purpose of PQ is to verify that the temperature control system functions consistently within the operation's required process range under expected loads and conditions.

应实施控制确证来确证温度受控设备在推荐的范围内运行。安装确认的主要目的是确证系统符合设计目的或已经按照设计进行安装。安装确认包含文件确证、设备安装、预防性维护、校准、控制、配置参数。安装确认可由设备供应商，和/或，用户来实施。成功设计确认与风险分析确保了运行确认的成功。理想的，运行确认在安装确认完成并批准后进行，并且应当在开始性能确认前批准运行确认结果。断电活动、报警测试、标准操作规程确证，与温度分布通常是运行确认的一个部分。性能确认的目的是确证温度受控系统功能在预期装载与条件下，在运行需要的过程范围内一致性。

Qualification must be performed for all four types of active systems: temperature-controlled trucks and trailers, temperature-controlled ocean containers, active ULDs, and cold storage warehouses/ rooms if a GMP/GDP environment is required.

如果要求药品生产质量管理规范/药品流通质量管理规范环境，必须对四种类型的有源式系统实施确认：温度受控卡车与拖车、温度受控远洋运输集装箱、有源成组装运设备，及冷藏储存仓库/室。

Temperature-controlled trucks and trailers face challenges due to the fact that their heat loads are more dynamic than those of other vessels due to their greater convective heat loss/gain as a result of motion and opening/closing of doors, particularly when these vessels must make multiple stops for loading or unloading along a route. Some considerations typical for trucks are as follows:

比那些因运动与门的开启/关闭，特别是当这些船只必须沿途多次停靠来装载或卸载由于其更大对流热损失/获得热负荷是更具动态，温度受控卡车与拖车面临挑战。一些典型对卡车考量如下：

- No common risk profiles are available for products because carriers supply different clients.
  承运人供应不同客户，对于产品没有通用的风险概况
- Tests should include loss of power and restart.
  测试必须包括断电与重新启动
- Simulated environments can be difficult and costly to develop.
  模拟环境可能非常难，也成本很高。

Temperature-controlled ocean containers are similar in many ways to other vessels in their ambient dynamic conditions due to climate conditions in transit and variances in payload size and placement within vehicles. The process of technology qualification includes pretrip inspection, loading and transportation to the sea port, unloading at the sea port, staging and customs clearance during transit and unloading, and delivery at the port of arrival.

由于在运输气候条件与在测量中有效负载波动及放置位子，温度受控远洋集装箱在许多方与其它在其环境动态条件下船只相似。技术确认过程包括启运前检查、装载并运输到港口、在港口卸货、在运输期间的转运与通关，及卸载，在目的港交付。

Active ULDs are typically operated with externally supplied AC power or internally stored and supplied DC power. Design considerations when selecting an active ULD are thermal integrity, sufficient heating/cooling capacity, airflow, temperature control accuracy, monitoring and alarming capability, redundant capability, power loss and open door recovery.

有源成组装运设备(ULD)通常由外部交流电供电或者内部直流电源供电运行。当选择有源成组装运设备时，设计考量是热完整性、足够的加热/制冷能力、气流、温度控制精密度、监测与报警能力，过剩能力、断电与开门恢复。

Temperature-controlled warehouses and rooms are most commonly walk-in cold rooms, refrigerators, or freezers that maintain a

temperature in the range of 5 ± 3°C, -20 ± 5°C, or -70 ± 10°C. The requirements to be considered are thermal integrity, sufficient BTU capacity, sufficient airflow, sufficient air movement, and a feedback control loop for adjusting CES temperature after a deviation. The operating characteristics of an active system, such as airflow, capacity for heat exchange, and temperature control accuracy, are essential and affect an active temperature control system's performance and qualifications.

温度受控仓库与室一般是一些大型冷藏室、冰箱或冷柜，其分别保持温度在5 ± 3°C、-20 ± 5°C, 或-70 ± 10°C。需要的考量是热完整性、足够热量、足够气流、足够流速，以及在一个偏差后调整受控环境空间温度反馈控制环。有源式系统的运行特性，诸如气流、热交换器能力、温度控制精密度非常重要，并影响有源式温度受控系统的性能与确认。

The methodology of the qualification studies should be risk based and determined by the business requirements, including product stability, regulation, transportation, and storage requirements. Other elements that can affect the methodology are the quality systems in place, PM and calibration requirements, loading and unloading operations, and protective packaging in addition to the active system.

确认研究方法应基于风险，并判断业务需求，包括产品稳定性、药政法规、运输，以及存储要求。其它能影响方法的因素是有质量体系、预防性维护与校准需求，装载与卸载操作，以及为有源系统提供另外的保护性包装。

The qualification of active systems has several benefits in that it:

对有源性系统进行确认有以下益处:

- Reduces the risk of failure during transport/storage
  减少运输/存储期间失败的风险
- Defines the optimal location for temperature monitoring
  规定温度监测最优化位置
- Provides a correlation between the internal ambient temperature and the product temperature
  提供内部环境温度与产品温度的相关性
- Verifies other concerns beyond temperature control and uniformity
  除了温度受控和均匀性确证其它有关项目
- Ensures that other functional and user requirements are met
  确保其它功能符合用户需求
- Provides a record of the system's condition and configuration
  提供系统条件与重构记录
- Ensures that all other systems are in place to support the equipment's continued operation
  确保所有其它系统都能支持设备持续运行

In conclusion, qualification for active temperature control systems gives a high level of confidence to quarantine, hold, or store raw materials, intermediates, or products at appropriate temperatures as supported by stability data.

综上所述，对有源温度受控系统的确认为在一个恰当的温度按照支持的稳定性数据对原料、中间体，或产品待检、留置或储存给出了高度的信心。

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