FREE PREVIEW

OPERATIONAL GUIDE

COLD CHAIN

CONTROLLED TEMPERATURE SYSTEMS

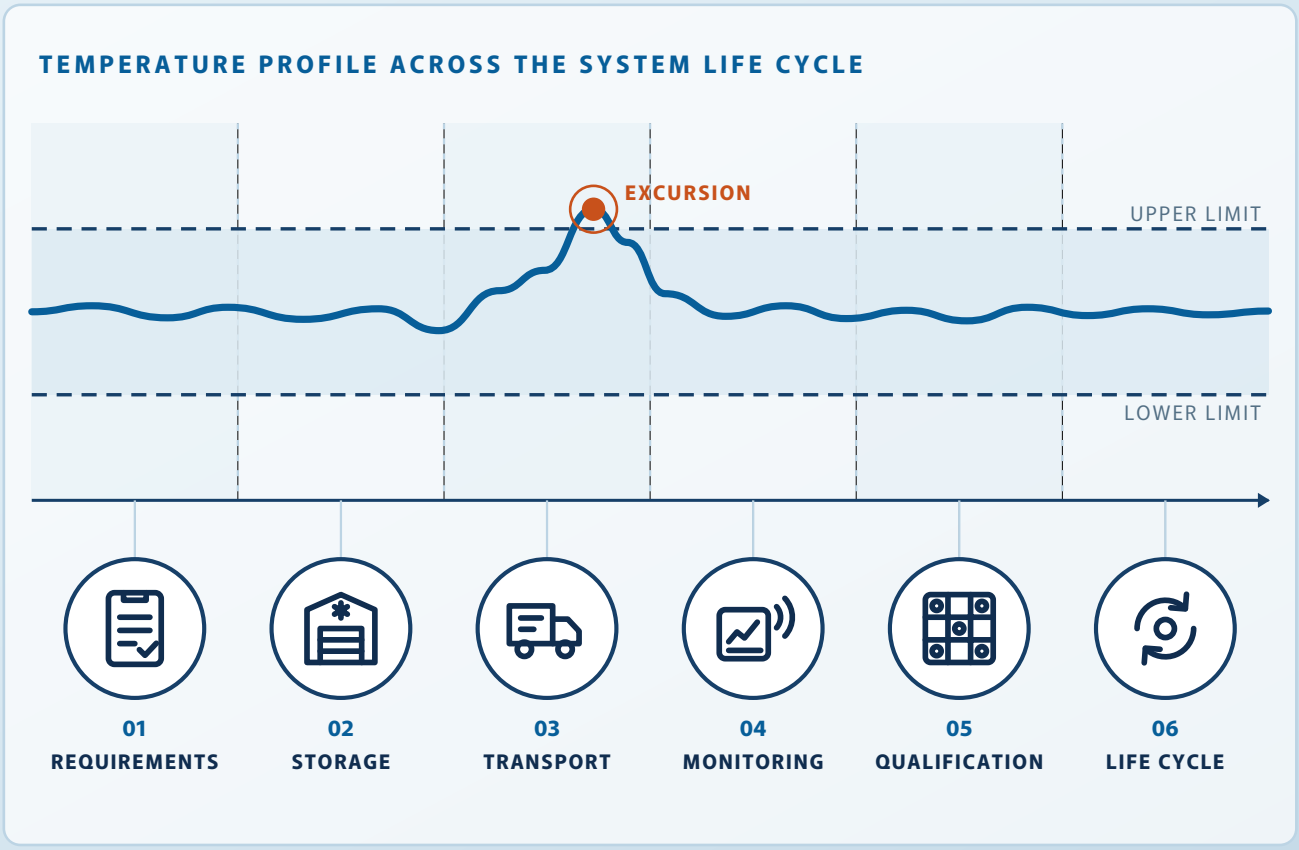
IN GMP/GDP

Storage, Transport, Temperature Mapping, Qualification, Monitoring and Lifecycle Control

275 PAGES · PDF A4 · 24 WORD + EXCEL TOOLS · ENG EDITION

FROM PRODUCT CONDITIONS TO A SYSTEM UNDER CONTROL

FIRST EDITION · SEPTEMBER 2026 · V1.0 · REGULATORY VERIFICATION 28/09/2026



About this guide

The guide supports those who design, qualify and govern the temperature-controlled systems of a pharmaceutical company — cold rooms, refrigerators, freezers and ULTs, active and passive shipments, monitoring and alarm systems — from the product's temperature profile to the evidence that holds up in an inspection. For every point it says which text governs it, with what force and in which jurisdiction, which value it gives (or does not give) and of what nature, what the company has to decide and where the decision is recorded. No universal values: conditions, thresholds, delays, sensors, durations and frequencies remain company decisions, taken with a written criterion.

This extract contains, exactly as they appear in the full edition: how the book is built and its label system; the complete table of contents; a technical extract from Chapter 18 with its example; Case A from Chapter 24; real pages of four toolkit tools; the list of what the purchase contains. First edition, September 2026, v1.0; regulatory verification date 28/09/2026.

How this guide is built

Six parts named after the areas of the Cold Chain hub: Requirements & Temperature Strategy (Chapters 1–4); Storage Systems & Equipment (5–8); Transport & Distribution (9–12); Monitoring & Alarm Management (13–16); Qualification & Temperature Mapping (17–20); Lifecycle & Procurement (21–24). Appendices A–F: glossary, sources, chapters–toolkit–articles matrix, toolkit instructions, assumptions and limitations, revision.

Chapters 2–23 share fourteen fixed sections: the problem and the decision; scope and boundaries; data to collect; technical principles; requirements and sources; reasoned procedure; alternatives and trade-offs; evidence; example; errors to avoid; chapter checklist; toolkit tools and related articles; the decisions this chapter produces; chapter sources. The reasoning always follows the same chain: product and authorised condition → real system → risk → text governing the point, with its status and force → value with its nature, or silence of the text → company decision → test → record → evidence.

Thesis of the book	Text supporting it	Source
The product's condition is what must be ensured	EU GDP, §9.2; GDP Q&A No. 22	FS-01, FS-02
No universal values	WHO Supplement 8, Step 9: "There is no formal time limit for a mapping study."	FS-39
Qualification, mapping and monitoring are distinct	EU GDP, §3.2.1	FS-01
Alarm, excursion and decision are three events; missing data are not compliant data	WHO TRS 961 Annex 9, glossary and §8.2.2; EU GDP, §9.2	FS-30, FS-01
Every statement carries its nature and jurisdiction	GDP Q&A, disclaimer; PIC/S PE 011-1, introduction	FS-02, FS-50
The system is governed across its lifecycle	EU GMP Annex 15, §4.1; EU GDP, §3.3.2	FS-11, FS-01

The guide is sold as an Italian or an English edition, each with its own toolkit; the toolkit supplied with this edition is in English and has 24 editable tools (12 Word, 12 Excel; codes CC-TK-01…24; folders 00–08): list in Chapter 1, instructions in Appendix D. Every chapter closes with the coded decisions D-NN.n (Appendix D) and with "Chapter sources" (URLs in Appendix B where recorded at consultation; for the other entries title and code). Simulated case: Arvena Pharma is a fictitious company and the data are hypothetical. Arvena has a manufacturing site (Site ST), a distribution centre (Site DC), four products and four integrated cases A–D (Chapter 24). The twelve hub articles are the entry point (Appendix C).

The labels in this book

Four labels state the status of the document (at its first occurrence in each chapter), seven the nature of the statement and one marks the examples; the jurisdiction sits outside the brackets ("CURRENT in the EU").

Label	Example in this guide
CURRENT	EU GDP 2013/C 343/01 in the EU
DRAFT	2025 revision of EU GMP Annex 11
IN DEVELOPMENT	Revision of ISO 21973:2020
~~SUPERSEDED~~	USP ‹1118›, replaced by ‹1079.3›
REGULATORY REQUIREMENT	EU GDP §9.2 in the EU; 21 CFR 211.142(b) in the US
COMPENDIAL REQUIREMENT	Ph. Eur. General Notices
GUIDANCE	WHO Supplement 8; GDP Q&A No. 22
TECHNICAL STANDARD	EN 12830:2018
SCIENTIFIC PRINCIPLE	T90 = ln(10)·τ for a first-order sensor
GEP/QRM	Two-level alarm thresholds
GUIDEGXP RECOMMENDATION	Decision trees, checklists, guard band
DEMONSTRATION EXAMPLE	Cases and calculations of the book's fictitious company

The nature of a value is not a label: it is written in words next to the number and decides how the number may be used.

Nature of the value	Example (document and section)	Source
requirement	calibration in transport "at least once a year" (EU GDP, §9.2)	FS-01
recommended	calibration in storage at least annually unless otherwise justified: WHO recommendation GUIDANCE (WHO TRS 961 Annex 9, §4.10.1), not a regulatory requirement in the EU	FS-30
example	mapping repetition "for example, every three years" (WHO Supplement 8, §1.1)	FS-39
test criterion	never below 0 °C for more than 1 h in the prequalification of vaccine refrigerators (WHO PQS E003/RF03.7 CURRENT GUIDANCE, §3)	FS-49
interpretation	a manufacturer's acceptance of 2–25 °C for 6 h does not authorise transport outside the labelled limits (GDP Q&A No. 22)	FS-02
definition	"in a refrigerator: 2 °C to 8 °C" in analytical procedures (Ph. Eur. General Notices CURRENT COMPENDIAL REQUIREMENT in the States party to the European Pharmacopoeia Convention, §1.2; text verified on the 7th edition)	FS-52
draft	alarm limits and delays "appropriately justified" (draft EU GMP Annex 11, §8.2)	FS-13

Full edition — complete table of contents: the map of the manual

The full edition comprises 24 chapters in six parts, named after the six areas of the Cold Chain hub, plus six appendices, over 275 A4 pages. Chapters 2–23 follow the same fourteen-section path: the problem and the decision; scope and boundaries; data to collect; technical principles; requirements and sources; reasoned procedure; alternatives and trade-offs; evidence; example; errors to avoid; chapter checklist; toolkit tools and related articles; the decisions the chapter produces; chapter sources. Page numbers refer to the full edition, not to this preview.

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Technical extract — Planning a temperature mapping study

From Chapter 18, exactly as it appears in the full edition: the problem and the decision, the technical principles, the reasoned procedure for planning a mapping study — object and purpose, grid and justified points, loads, conditions and duration, acquisition, criteria fixed before the tests —, the calculated example, the errors to avoid and the checklist. In the full edition the chapter also covers scope and boundaries, data to collect, requirements and sources, alternatives, evidence and the D-18.n decisions; Chapters 17, 19 and 20 cover qualification strategy, execution and data analysis, report and release.

The problem and the decision

A temperature mapping study answers only the questions written down before it starts: which volume is to be used, which events make its temperature vary, where the critical points lie. A protocol that starts from a number of loggers and a duration borrowed from another site produces data that answer no question at all. The decision is the design of the study, or studies, that demonstrate the temperature distribution in the volume to be used: how many points and where, for how long, with which load, in which season, with which loggers and against which criteria. The design belongs to validation with engineering and the warehouse; QA approves the protocol and the criteria before the start (D-17.4, see Chapter 17).

Technical principles

Where variability arises. Cold air stratifies; colder zones form near the evaporator supply air, warmer zones near doors and exposed walls, dead zones behind full pallets SCIENTIFIC PRINCIPLE. When the fans restart after a defrost, very cold air sweeps the levels close to the evaporator. The plan places points where these phenomena act, in addition to the grid.

Air, product, simulant. The report always states what was measured (air, surface, product, simulant) and where; air temperature changes faster than product temperature and the difference depends on thermal mass and packaging. Mapping of cold rooms and areas is normally carried out in air, and this is declared; a simulant estimates what reaches the product.

Interval and synchronisation. The recording interval is chosen according to the duration of the events to be detected (door openings, defrost cycles, failures) and to memory capacity; within the same study all loggers have the same interval and the same start time. The number of readings per logger is the duration divided by the interval SCIENTIFIC PRINCIPLE: if memory is insufficient the study loses its final part, which may contain the weekend.

DEMONSTRATION EXAMPLE SCIENTIFIC PRINCIPLE A 5-min door opening takes the air near the door from 5.0 °C to 14.0 °C; a fast-response air probe reads a peak of 13.51 °C. With spot sampling every 15 min the recorded maximum may be 8.64 °C; with sampling every 30 min, 5.00 °C: the event disappears from the data. DEMONSTRATION EXAMPLE Hypothetical data, calculated only to illustrate the method: they are not acceptance criteria or data from a real product.

Empty and loaded; redundancy. Empty mapping shows the plant, loaded mapping the effect of obstructions and thermal mass (see Chapter 17). With two refrigeration units, behaviour may change depending on which unit is running: WHO Supplement 8 CURRENT GUIDANCE recommends mapping "over a period that includes the operation of both units running separately" (Step 9).

Reasoned procedure

1. **Questions of the study.** Input: URS, PTP. Action: volume to be qualified, loads, events, special tests. Record: CC-TK-18, §1.
2. **Points (D-18.1).** The number and position of mapping points are defined through a risk analysis of the area; the 5–10 m grid of WHO Supplement 8 is a recommended starting point, to be adapted to

layout, racking, air flows and actual storage locations. Action: starting grid, justified points added, points removed where nothing is stored. Record: CC-TK-18, §2 (ID, coordinates, type, justification).

3. **Duration and conditions (D-18.2).** The mapping duration must cover all cycles that generate variability (day/night, shifts and weekends, defrost cycles, switching of refrigeration units, loading and unloading); WHO Supplement 8 gives typical values, not a formal limit. Record: CC-TK-18, §4.

> `<to be defined>` (D-18.2) — **who decides:** validation with QA · **on what basis:** cycles that generate variability, external exposure, WHO Supplement 8 as a recommended reference · **where it is recorded:** CC-TK-18 (Mapping protocol §4)

1. **Seasons.** The need for seasonal studies is decided on the basis of the exposure of the area or vehicle to external variations and is documented; for temperature-controlled vehicles the EU GDP require seasonal variations to be taken into account. Q&A No. 8 (an interpretation) points to initial mapping in the extreme seasons; Supplement 8 does not normally consider seasonal studies necessary for cold rooms: the decision for each area cites both, together with the exposure data.
2. **Load (D-18.3).** Simulated load with thermal mass, arrangement and packaging comparable to the product; never empty boxes as the load. Record: CC-TK-18, §3.
3. **Loggers (D-18.4).** Measuring range, interval, same start time, memory sufficient for the duration, certificates valid until the end of the study. Record: CC-TK-18, §5; CC-TK-13.
4. **Criteria (D-18.5).** Product limits, acceptance zone with a guard band derived from the uncertainty budget (D-13.1, see Chapter 13), missing-data threshold (D-14.4), recovery criterion (D-07.3), data treatment method (D-19.1). Record: CC-TK-18, §6–§7; CC-TK-19, "Criteria".

> `<to be defined>` (D-18.5) — **who decides:** QA with validation · **on what basis:** PTP, logger uncertainty, use of the volume · **where it is recorded:** CC-TK-18, CC-TK-19 (Mapping protocol §6; Criteria)

1. **Special tests.** The door-opening recovery criterion is set in the protocol on the basis of actual door-opening behaviour and product sensitivity; the 30-minute value is an example in WHO Supplement 7 (return within limits after the door is closed) and a recommendation in WHO Supplement 8 (maximum time outside limits after the door opening, in studies that include door openings), to be justified in both cases. Power failure is planned as a separate test (see Chapter 17).
2. **Approval.** QA signs the protocol before the start (D-17.4). Record: CC-TK-18, Part A.

Starting grid GUIDEGXP RECOMMENDATION, a geometric reading of the 5–10 m grid recommended by Supplement 8 (Step 5), to be adapted with justified points: points on plan = (⌈L/pitch⌉ + 1) × (⌈W/pitch⌉ + 1); levels: three up to 3.6 m in height, a vertical array above that, following the Supplement 8 example.

Environment	Dimensions (m)	5 m pitch	10 m pitch
Cold room	12 × 8 × 4.5	4 × 3 points × 4 levels = 48	3 × 2 points × 4 levels = 24
Warehouse	60 × 40 × 10	13 × 9 points × 7 levels = 819	7 × 5 points × 7 levels = 245

DEMONSTRATION EXAMPLE Hypothetical data, calculated only to illustrate the method: they are not acceptance criteria or data from a real product.

Additional point	Why
Door, low and high level	Warm incoming air, recovery
Under the evaporators, top level	Cold spot, defrost
Next to the control probe	Offset between control and volume
Planned monitoring position	Verification of the choice
Corners and zones behind racking	Poor air recirculation
Outside	Boundary condition

Small equipment GUIDEGXP RECOMMENDATION. In refrigerators, freezers and ULTs the 5–10 m grid does not apply: points are chosen per shelf in use (warm and cold corners and centre), near the door, gasket and evaporator and next to the control probe, with a simulant next to the monitoring probe; the number is justified in the protocol (D-18.1). Arvena example: RQ-ULT01-25 on ULT-DC-01, 4 shelves in use × 3 points (two opposite corners and centre) = 12, plus 2 at the door gasket (top and bottom), 1 in front of the evaporator and 1 next to the control probe = 16 loggers in air, plus 1 logger with simulant next to TS-ULT01 = 17 DEMONSTRATION EXAMPLE.

Event to be covered	How it is covered
Day and night	At least one complete cycle, beyond stabilisation
Shifts and weekends	One period with activity and one without
Defrost cycles	At least one cycle per evaporator, including the fan restart
Refrigeration unit switchover	Each unit running on its own
Loading, unloading, picking	Working days with real activity
Door openings	Longest observed duration, recorded as an event

Tables GUIDEGXP RECOMMENDATION: the minimum duration of the study is the one that contains all the relevant rows.

▲ COMMON MISTAKE

WHO Supplement 8 states "There is no formal time limit for a mapping study": a protocol that sets "72 h mandatory" attributes to a text an obligation that the same text rules out, and may close the study before a defrost cycle or the weekend. The duration is derived from the events to be covered; the Supplement values are cited with their nature.

★ GUIDEGXP PRACTICAL TIP

Give the plan a "Justification" column for each logger (grid, door, evaporator, control probe, planned monitoring, outside): a logger without a justification is removed or explained before the start.

Example

DEMONSTRATION EXAMPLE Simulated case: Arvena Pharma is a fictitious company and the data are hypothetical.

Data. Cold room CR-DC-01 (Case A, see Chapter 24): interior 12.0 × 8.0 × 4.5 m = 432 m³; 2 rows × 10 bays × 3 levels = 60 pallet positions; high-speed sliding door with strip curtain; evaporators EV-1 (back wall side) and EV-2 (door side); control probe SR-CR01 in the EV-1 return air; refrigeration units GF-A and GF-B alternating weekly; scheduled defrost. ARV-410 "Store in a refrigerator (2 °C – 8 °C)" (demonstration condition invented for the example: it is not the condition of a real product or a reference value).

Rule or method. WHO Supplement 8, Steps 5, 7 and 9 as recommended references; Q&A No. 7; procedure of this chapter.

Calculation. 1. 5 m grid: 4 × 3 points × 4 levels = 48 loggers; 10 m grid: 3 × 2 × 4 = 24. 2. Choice: 10 m grid (24) plus 6 justified points (2 door, 2 evaporator supply air, 1 control probe, 1 planned monitoring position) = 30 internal loggers ML-01...ML-30, plus ML-31 outside = 31. 3. 5-min interval = 12 recordings/hour; 48 h = 576 readings; 168 h (7 days) = 2,016 readings per logger. 4. Acceptance zone: 2.0 + U; 8.0 − U, with U from the uncertainty budget of the ML loggers (certificates CERT-LT1-26-011... 041), which in the example is 0.21 °C, as for TS-CR01-01 (see Chapter 13): 2.21–7.79 °C.

Result. Protocol MPL-CR01: empty OQ of 48 h with GF-A; loaded PQ of 168 h (09/03/2026–16/03/2026) with a simulated load on 54 positions (simulant cases with thermal mass comparable to ARV-410 pallets; the 6 left empty are identified in the protocol and justified by the capacity required by the URS, with ML-22 and ML-27 in loaded positions), real picking, scheduled defrost cycles and switchover GF-A → GF-B on 12/03/2026 at 06:00; loggers calibrated by LAB-T1 at 0, 5 and 25 °C on 10/02/2026 (CERT-LT1-26-011...041), synchronised start. Criteria: loggers in the qualified volume within 2.21–7.79 °C for the whole duration; no missing data beyond 2 consecutive readings (D-14.4); valid certificates; door recovery within 20 min (D-07.3). Warehouse WH-DC-01 (60 × 40 × 10 m) has two seasonal studies, MAP-WH-25-S (14/07/2025–21/07/2025) and MAP-WH-26-W (13/01/2026–20/01/2026), with 96 loggers each against the 245 of the 10 m grid. The reduction is justified in the protocol with the risk-based approach that Step 5 of Supplement 8 allows: the racking forms homogeneous zones (same structure, same air distribution, no local source) mapped at a 20 m pitch, a pitch that note 10 of Step 5 allows for very large facilities, a WHO recommendation GUIDANCE (WHO Supplement 8, Step 5, note 10), not a regulatory requirement in the EU: 4 × 3 points × 7 levels = 84; 12 risk-justified points are added (4 loading bays, 4 under the roof along the south-facing wall at the highest level, 2 corners behind the racking with poor air recirculation, 2 next to the HVAC control probes) = 96 (D-18.1). Basis of the choice: ARV-440 has only an upper limit of 25 °C and the warehouse operating limits are 15–25 °C (D-02.4, see Chapter 2); the zone-based strategy does not extend to CR-DC-01.

Reading. The six added points sit where the door, evaporators and control act. The PQ includes a weekend, the defrost cycles and both units running separately. The qualified volume will come from the analysis (Chapter 19).

Arvena decision. D-18.1 (24 + 6 + 1 loggers), D-18.2 (48 h empty; 168 h loaded with switchover), D-18.3 (simulant), D-18.4 (5-min interval, synchronised start, LAB-T1 calibrations), D-18.5 (criteria with guard band); validation (VAL-01) with engineering (ENG-DC-01), QA approval (QA-CC-01); record MPL-CR01 (CC-TK-18, Part A).

DEMONSTRATION EXAMPLE Hypothetical data, calculated only to illustrate the method: they are not acceptance criteria or data from a real product.

Errors to avoid

1. **"One sensor every 5 m by law".** The grid is a Supplement 8 recommendation; the number is justified through the risk analysis (Q&A No. 7).

2. **"72 h by law" or "7 days mandatory".** There is no formal limit (Step 9): the duration comes from the events to be covered.
3. **Repetition "every year" or "every 3 years by law".** In the EU, mapping is repeated according to the outcome of a risk assessment or after significant modifications to the facility or the temperature-controlling equipment (EU GDP, §3.2.1); the three-year interval cited by WHO is an example.
4. **Seasons "always" or "never".** The decision is justified by the exposure of the premises; for vehicles the EU GDP require seasonal variations to be taken into account.
5. **"Recovery within 30 minutes under the GDP".** The GDP set no criterion; the Supplement value must be justified (D-07.3).
6. **Empty boxes as the load.** They reproduce neither thermal mass nor obstructions (D-18.3).
7. **A two-unit system mapped with only one unit running.** Behaviour with the other unit remains unknown (Step 9).
8. **Tables of "sensors per volume class" attributed to industry guides.** As of 28/09/2026 the numerical values of the ISPE guides on sensors per volume could not be verified on an official source.

Chapter checklist

No.	Check	Evidence (record)	Outcome
CL-18.1	The questions of the study are written down	CC-TK-18, §1	Y / N / NA
CL-18.2	The starting grid is calculated and declared as a starting point	CC-TK-18, §2	Y / N / NA
CL-18.3	Every mapping point has a written justification	Plan, "Justification" column	Y / N / NA
CL-18.4	Doors, evaporators, control probe and planned monitoring have dedicated points	CC-TK-18, §2	Y / N / NA
CL-18.5	The duration covers weekends, defrost cycles, switchover and real activities	CC-TK-18, §4	Y / N / NA
CL-18.6	The decision on seasons is justified	CC-TK-18, §4	Y / N / NA
CL-18.7	Simulated load and simulant are described	CC-TK-18, §3	Y / N / NA
CL-18.8	All loggers have the same interval and the same start time	Programming record	Y / N / NA
CL-18.9	Memory covers the duration at the chosen interval	CC-TK-18, §5	Y / N / NA
CL-18.10	Certificates are traceable and valid for the whole study	Certificates; CC-TK-13	Y / N / NA
CL-18.11	Criteria with guard band and the recovery criterion are signed before the start	CC-TK-18, §6	Y / N / NA
CL-18.12	The data treatment method is written down	CC-TK-18, §7	Y / N / NA

Applied example — Case A, the cold room

From Chapter 24, which holds four (A cold room, B passive shipment, C excursion, D ULT failure), all linked to the toolkit with the same identifiers. This one is reproduced in full. Arvena Pharma is a fictitious company: data, dates and codes are hypothetical.

Case A — The cold room

DEMONSTRATION EXAMPLE Scenario built for teaching purposes. Simulated case: Arvena Pharma is a fictitious company and the data are hypothetical.

Context. Site DC, a distributor subject to EU GDP 2013/C 343/01 CURRENT REGULATORY REQUIREMENT in the EU (status in Chapter 1), builds cold room CR-DC-01 (432 m³; 60 pallet positions) for ARV-410, "Store in a refrigerator (2 °C – 8 °C). Do not freeze." (demonstration condition invented for the example: it is not the condition of a real product or a reference value). **Problem.** Qualify the room and choose permanent probes and alarms on the basis of data. **Risk.** Cold spots under the evaporators for a product that must not freeze; door zone; capacity at peak. **Decisions.** Redundancy, margin, grid, guard band, restrictions, thresholds. **Activities and data.** Heat load 6,066 W × 1.20 = 7,279 W per unit against 8.0 kW (ratio 1.10). Grid from WHO Supplement 8 CURRENT GUIDANCE, WHO recommendation GUIDANCE (WHO Supplement 8, Step 5), not a regulatory requirement in the EU: 24 loggers at 10 m, plus 6 justified points and external ML-31. U (k = 2) = 0.21 °C → zone 2.21–7.79 °C. 168 h PQ: qualified volume between 2.9 °C and 7.6 °C; ML-22 at 1.9 °C after the fans restarted at the end of defrost, ML-27 at 9.1 °C in the door test → 54 positions out of 60 (90.0%), 6 free at the peak of 48. Alert at 6.5 °C with a 5-min delay: 160 − 85 = 75 min available against 5 + 2 + 15 + 30 = 52 up to arrival → 23 min before the transfer, whose time is not measured, with the test run with the warehouse at 16–17 °C instead of the 30 °C design condition: budget still to be demonstrated (Arvena minimum 20); the 7.0 °C / 10 min alternative gave −7 min already before the action.

Date and time	Event	Record	Who
10/03/2025	Project brief	PRJ-CC-25-01	QA-CC-01
28/04/2025	URS approved	URS-CR01 rev. 1	ENG-DC-01; QA-CC-01
30/06/2025	Bid evaluation; order placed with FOR-X on 15/07/2025	SEL-CR01	PRC-01
26/01/2026–06/02/2026	IQ	PQP-CR01	VAL-01
02/03/2026–05/03/2026	Empty OQ (48 h); power failure: 8.0 °C after 70 min	MAP-CR01-26-01/OQ	VAL-01
09/03/2026–17/03/2026	Loaded PQ (168 h), GF-A → GF-B changeover on 12/03/2026 at 06:00; door (recovery in 11 min); power failure: 8.0 °C after 160 min	MAP-CR01-26-01/PQ	VAL-01
31/03/2026	Report with restriction	QR-CR01-26-01	QA-CC-01
01/04/2026	Room in use	ALM-DC rev. 3	MON-01

Documents. URS-CR01, PQP-CR01, QR-CR01-26-01, DWG-CR01-VQ rev. 1, ALM-DC rev. 3. **Evidence.** Per-logger table; drawing of the qualified volume; time budget for each threshold. **Outcome as of 28/09/2026.** In use with 54 positions; periodic review PR-DC-26, planned after six months of use, carries four actions: a PCO-DC-01 transfer drill to close the time budget; a test at the design external condition; a control-failure cooling test for the low threshold; a repeat of the door test, because in the PQ a routine opening (11/03/2026, 15:30) gave the warm spot a higher peak than the test. **Three lessons.** The cold spot appears only under load and after defrost: the PQ includes the real events. The guard band narrows the limits. The delay is sized on the time measured under load, at the worst external condition, counting the action that protects the product as well. **D codes.** D-02.4, D-05.4, D-06.2, D-06.3, D-07.3, D-08.3, D-13.1, D-13.2, D-15.2, D-18.1, D-18.5, D-19.3, D-20.3. **Tools used.** CC-TK-02 → CC-TK-04 → CC-TK-07 → CC-TK-18 and CC-TK-19 → CC-TK-13 → CC-TK-15. DEMONSTRATION EXAMPLE Hypothetical data, calculated only to illustrate the method: they are not acceptance criteria or data from a real product.

◎ **INSPECTOR FOCUS**

In a GDP inspection — EU GDP §3.2.1 asks for monitoring devices "positioned in the areas that experience the extremes of fluctuations". The inspector compares TS-CR01-01 and TS-CR01-02 with ML-03 and ML-21 in QR-CR01-26-01 and asks why ML-22 and ML-27 are not monitored: the answer is the restriction of the six positions on the drawing.

The toolkit: real pages of four tools

The images are pages of the delivered files — Arvena filled-in examples from the 07_Examples folder, English edition — converted to PDF without retouching. In the clean templates of folders 01–06 the same sheets are empty: no operational value is preloaded.



CC-TK-18 · Rev. 1.0 · Temperature Mapping Protocol & Report · [DEMONSTRATION EXAMPLE]

5 Acquisition

Loggers from the sensor register (CC-TK-13): calibration, interval, same start time, expected readings and memory.

The recording interval is chosen according to the duration of the events to be detected (door openings, defrost cycles, failures) and to memory capacity; within the same study all loggers have the same interval and the same start time.

Specification of the mapping loggers: Arvena choice (D-18.4): 5 min interval, synchronised start; LAB-T1 calibration at 0, 5 and 25 °C of 10/02/2026 (CERT-LT1-26-011…041); 2,016 readings in 7 days, 576 in 48 h

6 Acceptance criteria to be defined and rationale

No logger tolerance is added to the limits: uncertainty narrows the zone. The criteria are signed before the tests (§7).

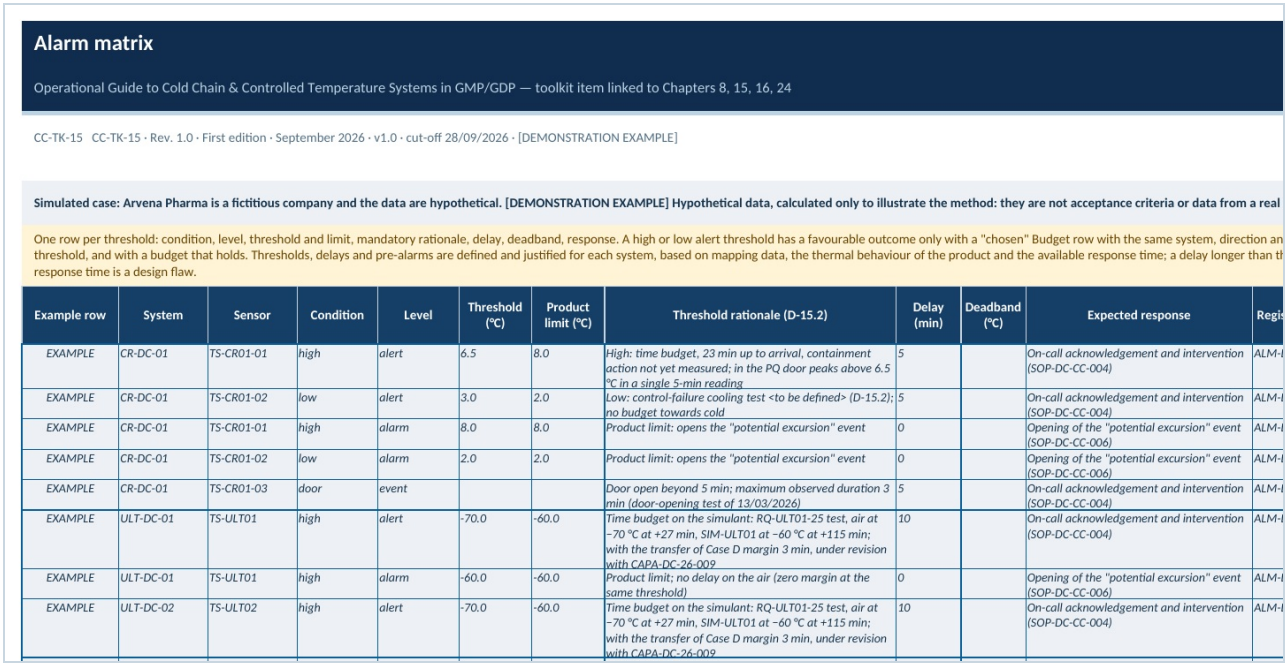
Criterion	Value (decision code)	Who decides	On what basis	Where it is recorded	Value adopted and rationale
Acceptance zone with guard band and duration	<to be defined> (D-18.5)	QA with validation	product limits and measurement uncertainty (D-13.1)	protocol §6; CC-TK-19, Criteria	
Door-opening recovery criterion	<to be defined> (D-07.3)	QA with validation	actual openings and product sensitivity	protocol §6; CC-TK-07	
Missing-data threshold	<to be defined> (D-14.4)	QA with validation	duration of the events to be detected	CC-TK-19	
Duration, events and seasons covered	<to be defined> (D-18.2)	Validation with QA	cycles that generate variability	protocol §4	

WHO Supplement 11, as an example, accepts readings up to 0.5 °C beyond the limits to allow for logger accuracy; a conservative criterion does the opposite and narrows the acceptance zone on the basis of measurement uncertainty.

The door-opening recovery criterion is set in the protocol on the basis of actual door-opening behaviour and product sensitivity; the 30-minute value is an example in WHO Supplement 7 (return within limits after the door is closed) and a recommendation in WHO Supplement 8 (maximum time outside limits after the door opening, in studies that include door openings), to be justified in both cases.

[DEMONSTRATION EXAMPLE] Simulated case: Arvena Pharma is a fictitious company and the data are hypothetical. — Signed criteria of MAP-CR01-26-01

CC-TK-18 — Temperature Mapping Protocol & Report (Word) · section 6, acceptance criteria to be defined and rationale



Alarm matrix

Operational Guide to Cold Chain & Controlled Temperature Systems in GMP/GDP — toolkit item linked to Chapters 8, 15, 16, 24

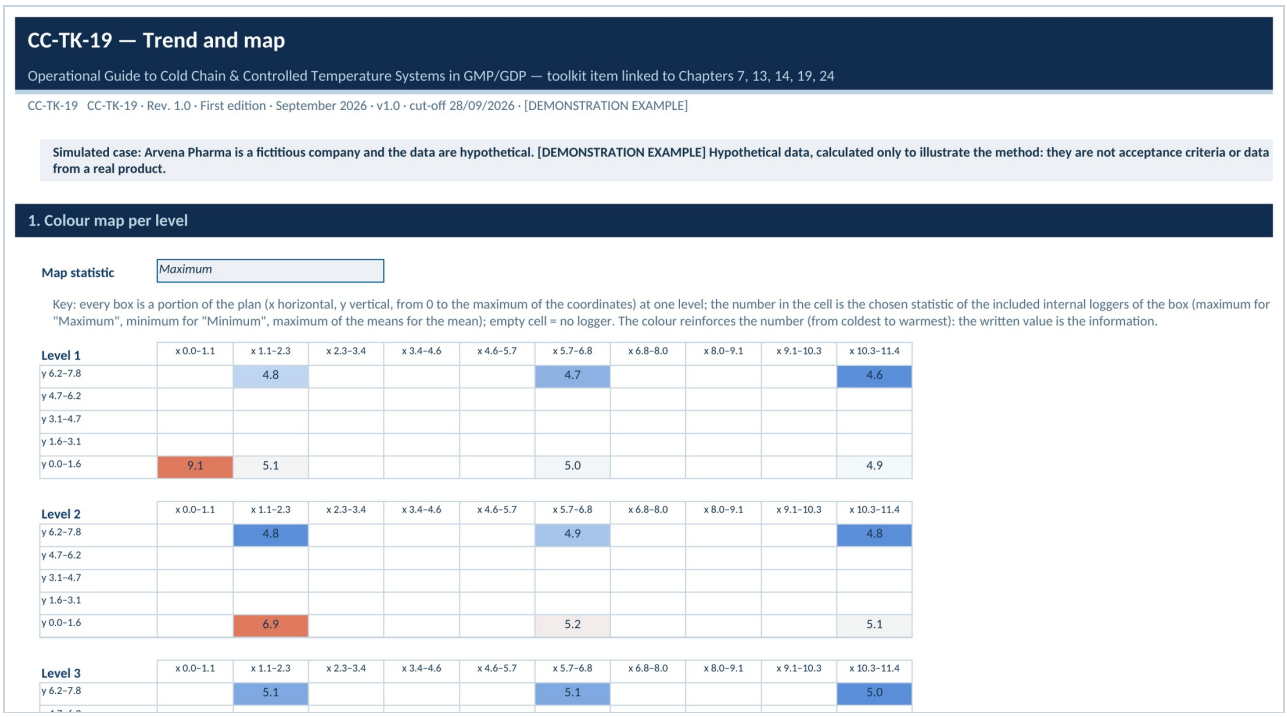
CC-TK-15 CC-TK-15 · Rev. 1.0 · First edition · September 2026 · v1.0 · cut-off 28/09/2026 · [DEMONSTRATION EXAMPLE]

Simulated case: Arvena Pharma is a fictitious company and the data are hypothetical. [DEMONSTRATION EXAMPLE] Hypothetical data, calculated only to illustrate the method: they are not acceptance criteria or data from a real

One row per threshold: condition, level, threshold and limit, mandatory rationale, delay, deadband, response. A high or low alert threshold has a favourable outcome only with a "chosen" Budget row with the same system, direction an threshold, and with a budget that holds. Thresholds, delays and pre-alarms are defined and justified for each system, based on mapping data, the thermal behaviour of the product and the available response time; a delay longer than th response time is a design flaw.

Example row	System	Sensor	Condition	Level	Threshold (°C)	Product limit (°C)	Threshold rationale (D-15.2)	Delay (min)	Deadband (°C)	Expected response	Regis
EXAMPLE	*CR-DC-01*	*TS-CR01-01*	*high*	*alert*	*6.5*	*8.0*	*High: time budget, 23 min up to arrival, containment action not yet measured; in the PQ door peaks above 6.5 °C in a single 5-min reading*	*5*		*On-call acknowledgement and intervention (SOP-DC-CC-004)*	*ALM-I*
EXAMPLE	*CR-DC-01*	*TS-CR01-02*	*low*	*alert*	*3.0*	*2.0*	*Low: control-failure cooling test <to be defined> (D-15.2); no budget towards cold*	*5*		*On-call acknowledgement and intervention (SOP-DC-CC-004)*	*ALM-I*
EXAMPLE	*CR-DC-01*	*TS-CR01-01*	*high*	*alarm*	*8.0*	*8.0*	*Product limit: opens the "potential excursion" event*	*0*		*Opening of the "potential excursion" event (SOP-DC-CC-006)*	*ALM-I*
EXAMPLE	*CR-DC-01*	*TS-CR01-02*	*low*	*alarm*	*2.0*	*2.0*	*Product limit: opens the "potential excursion" event*	*0*		*Opening of the "potential excursion" event (SOP-DC-CC-006)*	*ALM-I*
EXAMPLE	*CR-DC-01*	*TS-CR01-03*	*door*	*event*			*Door open beyond 5 min; maximum observed duration 3 min (door-opening test of 13/03/2026)*	*5*		*On-call acknowledgement and intervention (SOP-DC-CC-004)*	*ALM-I*
EXAMPLE	*ULT-DC-01*	*TS-ULT01*	*high*	*alert*	*-70.0*	*-60.0*	*Time budget on the simulant: RQ-ULT01-25 test, air at −70 °C at +27 min, SIM-ULT01 at −60 °C at +115 min; with the transfer of Case D margin 3 min, under revision with CAPA-DC-26-009*	*10*		*On-call acknowledgement and intervention (SOP-DC-CC-004)*	*ALM-I*
EXAMPLE	*ULT-DC-01*	*TS-ULT01*	*high*	*alarm*	*-60.0*	*-60.0*	*Product limit; no delay on the air (zero margin at the same threshold)*	*0*		*Opening of the "potential excursion" event (SOP-DC-CC-006)*	*ALM-I*
EXAMPLE	*ULT-DC-02*	*TS-ULT02*	*high*	*alert*	*-70.0*	*-60.0*	*Time budget on the simulant: RQ-ULT01-25 test, air at −70 °C at +27 min, SIM-ULT01 at −60 °C at +115 min; with the transfer of Case D margin 3 min, under revision with CAPA-DC-26-009*	*10*		*On-call acknowledgement and intervention (SOP-DC-CC-004)*	*ALM-I*

CC-TK-15 — Alarm Rationalisation & Escalation Matrix (Excel) · alarm matrix sheet



CC-TK-19 — Trend and map

Operational Guide to Cold Chain & Controlled Temperature Systems in GMP/GDP — toolkit item linked to Chapters 7, 13, 14, 19, 24

CC-TK-19 CC-TK-19 · Rev. 1.0 · First edition · September 2026 · v1.0 · cut-off 28/09/2026 · [DEMONSTRATION EXAMPLE]

Simulated case: Arvena Pharma is a fictitious company and the data are hypothetical. [DEMONSTRATION EXAMPLE] Hypothetical data, calculated only to illustrate the method: they are not acceptance criteria or data from a real product.

1. Colour map per level

Map statistic *Maximum*

Key: every box is a portion of the plan (x horizontal, y vertical, from 0 to the maximum of the coordinates) at one level; the number in the cell is the chosen statistic of the included internal loggers of the box (maximum for "Maximum", minimum for "Minimum", maximum of the means for the mean); empty cell = no logger. The colour reinforces the number (from coldest to warmest): the written value is the information.

Level 1

	x 0.0–1.1	x 1.1–2.3	x 2.3–3.4	x 3.4–4.6	x 4.6–5.7	x 5.7–6.8	x 6.8–8.0	x 8.0–9.1	x 9.1–10.3	x 10.3–11.4
y 6.2–7.8		4.8				4.7				4.6
y 4.7–6.2										
y 3.1–4.7										
y 1.6–3.1										
y 0.0–1.6	9.1	5.1				5.0				4.9

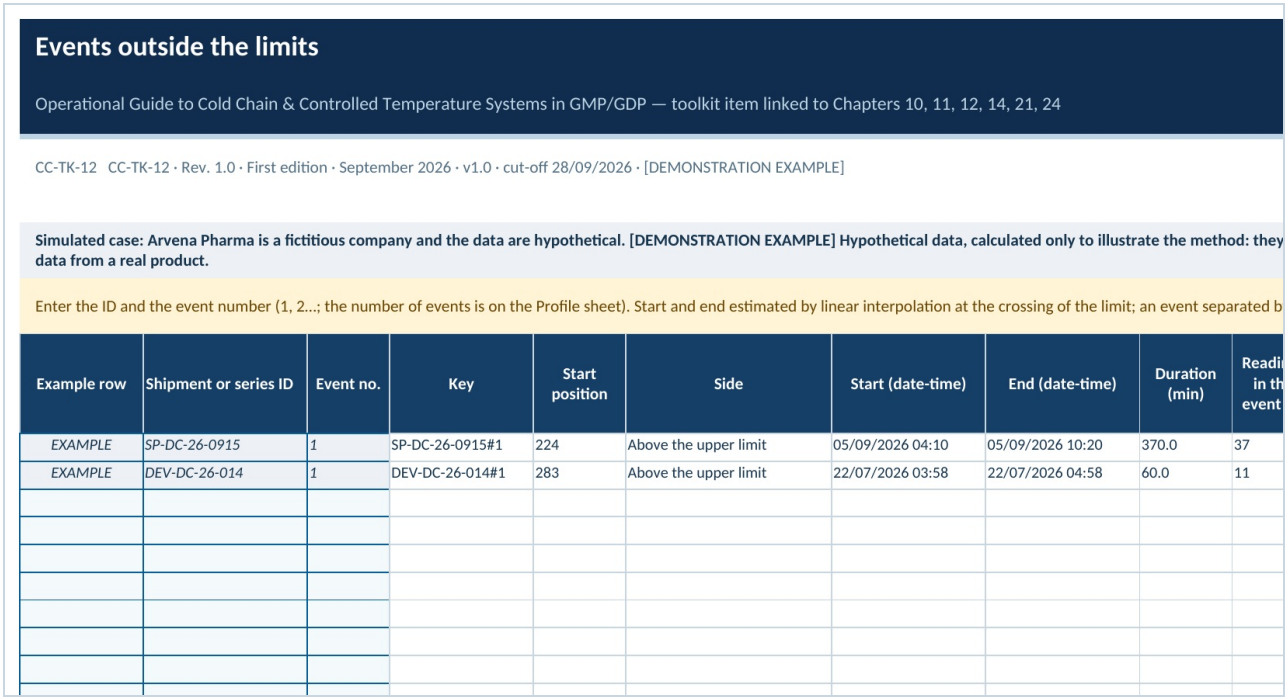
Level 2

	x 0.0–1.1	x 1.1–2.3	x 2.3–3.4	x 3.4–4.6	x 4.6–5.7	x 5.7–6.8	x 6.8–8.0	x 8.0–9.1	x 9.1–10.3	x 10.3–11.4
y 6.2–7.8		4.8				4.9				4.8
y 4.7–6.2										
y 3.1–4.7										
y 1.6–3.1										
y 0.0–1.6		6.9				5.2				5.1

Level 3

	x 0.0–1.1	x 1.1–2.3	x 2.3–3.4	x 3.4–4.6	x 4.6–5.7	x 5.7–6.8	x 6.8–8.0	x 8.0–9.1	x 9.1–10.3	x 10.3–11.4
y 6.2–7.8		5.1				5.1				5.0

CC-TK-19 — Temperature Mapping Data Analysis (Excel) · trend and map-by-level sheet



Events outside the limits

Operational Guide to Cold Chain & Controlled Temperature Systems in GMP/GDP — toolkit item linked to Chapters 10, 11, 12, 14, 21, 24

CC-TK-12 CC-TK-12 · Rev. 1.0 · First edition · September 2026 · v1.0 · cut-off 28/09/2026 · [DEMONSTRATION EXAMPLE]

Simulated case: Arvena Pharma is a fictitious company and the data are hypothetical. [DEMONSTRATION EXAMPLE] Hypothetical data, calculated only to illustrate the method: they data from a real product.

Enter the ID and the event number (1, 2...; the number of events is on the Profile sheet). Start and end estimated by linear interpolation at the crossing of the limit; an event separated b

Example row	Shipment or series ID	Event no.	Key	Start position	Side	Start (date-time)	End (date-time)	Duration (min)	Readi in th event
EXAMPLE	*SP-DC-26-0915*	*1*	SP-DC-26-0915#1	224	Above the upper limit	05/09/2026 04:10	05/09/2026 10:20	370.0	37
EXAMPLE	*DEV-DC-26-014*	*1*	DEV-DC-26-014#1	283	Above the upper limit	22/07/2026 03:58	22/07/2026 04:58	60.0	11

CC-TK-12 — Shipment Monitoring & Chain-of-Custody Log (Excel) · events beyond limits sheet

What the purchase contains

The purchase is digital: after payment you download a ZIP package with the guide and the toolkit in the language you chose. Choose one variant: **ITA - Italiano** or **ENG - English**; the two editions have the same structure, the same tools and the same codes.

- **The complete PDF guide** — 275 A4 pages, 24 chapters in six parts and six appendices (ITA/ENG glossary, source matrix, chapter–toolkit–article matrix, toolkit instructions, assumptions and limitations, revision); clickable table of contents and bookmarks.
- **24 editable tools** — 12 Word templates and 12 Excel workbooks, codes CC-TK-01…24, arranged in the six folders of the parts (list below).
- **24 filled-in examples** on the simulated Arvena Pharma case (folder 07_Examples) and demonstration datasets for mapping, shipments and ULTs.
- **Support files** — README, navigable toolkit index, field glossary, guide–toolkit–article matrix, Test Log of the Excel workbooks, file manifest.

Folder and group	Code	Tool	Format
01_Requirements · Requirements & Temperature Strategy	CC-TK-01	Cold Chain Project Brief & Responsibility Matrix	Word
01_Requirements · Requirements & Temperature Strategy	CC-TK-02	Cold Chain & Controlled Temperature URS	Word
01_Requirements · Requirements & Temperature Strategy	CC-TK-03	Product Temperature & Stability Register	Excel
01_Requirements · Requirements & Temperature Strategy	CC-TK-04	Cold Chain Risk Assessment	Excel
02_Storage · Storage Systems & Equipment	CC-TK-05	Storage Technology Selection Matrix	Excel
02_Storage · Storage Systems & Equipment	CC-TK-06	Storage Design Review Checklist	Word
02_Storage · Storage Systems & Equipment	CC-TK-07	Load Pattern & Recovery Challenge Matrix	Excel
02_Storage · Storage Systems & Equipment	CC-TK-08	Cold Chain Contingency Plan	Word
03_Transport · Transport & Distribution	CC-TK-09	Transport Lane Risk Assessment	Excel
03_Transport · Transport & Distribution	CC-TK-10	Thermal Packaging Qualification Protocol	Word
03_Transport · Transport & Distribution	CC-TK-11	Transport & Lane Qualification Protocol	Word
03_Transport · Transport & Distribution	CC-TK-12	Shipment Monitoring & Chain-of-Custody Log	Excel
04_Monitoring · Monitoring & Alarm Management	CC-TK-13	Sensor & Calibration Register	Excel
04_Monitoring · Monitoring & Alarm Management	CC-TK-14	Monitoring System & Data Lifecycle Specification	Word
04_Monitoring · Monitoring & Alarm Management	CC-TK-15	Alarm Rationalisation & Escalation Matrix	Excel
04_Monitoring · Monitoring & Alarm Management	CC-TK-16	Alarm & Failure Challenge Test Protocol	Word

Folder and group	Code	Tool	Format
05_Qualification · Qualification & Temperature Mapping	**CC-TK-17**	Qualification Plan & IQ-OQ-PQ Protocol Framework	Word
05_Qualification · Qualification & Temperature Mapping	**CC-TK-18**	Temperature Mapping Protocol & Report	Word
05_Qualification · Qualification & Temperature Mapping	**CC-TK-19**	Temperature Mapping Data Analysis	Excel
05_Qualification · Qualification & Temperature Mapping	**CC-TK-20**	Requirements Traceability Matrix	Excel
06_Lifecycle · Lifecycle & Procurement	**CC-TK-21**	Temperature Excursion Investigation & CAPA	Word
06_Lifecycle · Lifecycle & Procurement	**CC-TK-22**	Periodic Review, Maintenance & Requalification Planner	Excel
06_Lifecycle · Lifecycle & Procurement	**CC-TK-23**	Supplier RFP & Quality-Service Responsibilities Checklist	Word
06_Lifecycle · Lifecycle & Procurement	**CC-TK-24**	Technical Bid Evaluation & TCO	Excel

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STORAGE, TRANSPORT, TEMPERATURE MAPPING, QUALIFICATION, MONITORING AND LIFECYCLE CONTROL

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