

Controlled Temperature Chain

The New Term for Out of the
Cold Chain

September 2009

Batiment Avant Centre
13 Chemin du Levant
01210 Ferney Voltaire
France

Phone: 33.450.28.00.49

Fax: 33.450.28.04.07

www.path.org

www.who.int

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Contact information:
Steve McCarney
Cold Chain Technologies Specialist
Batiment Avant Centre
13 Chemin du Levant
01210 Ferney Voltaire
France
smccarney@path.org

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The New Term for Out of the
Cold Chain (OCC)

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Overview

During the March 2009 meeting of the World Health Organization's (WHO's) Technology and Logistics Advisory Committee (TLAC), it was agreed that the term "out of the cold chain" (OCC)—used to mean storing vaccines outside of the standard 2° to 8°C range—was problematic. While the term OCC was intended to imply that vaccines can be stored out of the cold chain at temperatures outside the 2° to 8°C range but in controlled conditions, the term was not being interpreted as such. TLAC members and meeting attendees noted that the term seemed to contradict the current training messages and vaccine storage guidelines which stress the importance of storing vaccines in specific controlled temperatures. Further, the term was at times interpreted to mean "no cold chain" or "no need for vaccines to be stored at specific temperatures at all" resulting in concerns about the feasibility and appropriateness of the OCC concept due to a misinterpretation of the term.

It was therefore decided that alternate terminology should be sought in consultation with stakeholders. On August 26, 2009, Michel Zaffran started a discussion on TechNet (www.technet21.org) entitled *What's in a name? Selecting a term for storing and transporting vaccines outside of the 2° to 8°C range*. The TechNet post prompted no less than 26 replies, as of September 16, with a wide range of suggestions demonstrating the need to establish an accepted definition of storage conditions within immunization.

Key ideas

The recommendation is that the term OCC should be replaced with the term **controlled temperature chain (CTC)**. CTC is defined as storing and transporting vaccines in a controlled temperature chain within a temperature range appropriate to the particular vaccine's heat stability profile. The rationale for selecting this term follows within this report.

In summary, the basic premise of CTC is as follows: all vaccines should be kept in a controlled temperature chain. Traditionally this has been the 2° to 8°C range, known as the cold chain. However, several vaccines are quite heat stable and can be stored safely within other temperature ranges in a CTC appropriate to the vaccine's heat stability profile.

Summary of responses

Most of the suggestions received on TechNet involved changing the name of the term; several involved adding specific temperature conditions that would be associated with the suggested name. Thirty suggestions were proposed within the 26 posts. None of the respondents suggested eliminating the term "cold chain" and 16 of the suggestions retained the word "chain" as part of their proposed name.

Six contributors suggested "cool chain" or some variation of "cool." The only other suggested name that was repeated was "Flexible cold chain" or "Flex chain," and it was only repeated one time.

While “cool chain” was the most common suggestion, it was decided that the perception of the term “cool” could lead to a misunderstanding. One person stated that, “25°C is very close to cool” while the US Pharmacopeia (USP) definition for “cool” specifies 8° to 15°C. As the objective was to find a broad generic term for the concept, the term “cool” was eliminated as a potential option so as to avoid confusion with a pre-existing term that would be defined differently from our intended use of the term.

Six responses contained the word “control” or “controlled” within the suggested name. One person stated, “I think the other terms may have false implications of noncontrolled storage. This was exactly what happened with me when I first read about ‘out of cold chain’. I thought that the cold chain had failed and the product was spoiled.”

Another person suggested that no new name be added and that instead storage instructions should be added (e.g., “keep cool, do not freeze” for freeze-sensitive vaccines).

Suggested names

- Cool chain or Cool (6)
- Flexible cold chain or Flex chain (2)
- Easy cold chain
- Fast chain
- Hold chain
- Life chain
- Out of cold chain
- Safe chain
- Warm chain
- Controlled air conditioned storage
- Controlled ambience limited time
- Controlled ambient temperature storage
- Controlled room temperature
- Controlled temperature storage and transportation
- Vaccine control chain
- Briefcase vaccines
- Heat flexible vaccine storage and transport system
- Higher temperature storage
- RT (room temperature) stable
- Storage temperature below and above 2°/8°C range
- Storage temperature limit
- Thermostable vaccines
- Thermolabile vaccines
- Vaccine temperature limit

Review of existing terminology

Following the consultation with stakeholders on TechNet, we reviewed existing definitions used by other public bodies dealing with the storage of temperature-sensitive pharmaceutical products.

The United Nations Children's Fund (UNICEF) Supply Division provides an online catalogue that includes specific temperature requirements for the storage and transport of vaccines and pharmaceuticals. All vaccine descriptions include specific temperature conditions. Some vaccine descriptions also include advisories and other information such as time of temperature exposure and light exposure. Pharmaceutical descriptions may or may not include temperature requirements. Some pharmaceutical descriptions include the term **controlled temperature** usually followed by an indication (e.g., “no”).

The USP is an official public standards authority responsible for establishing standards for all prescription, over-the-counter medicines, and other health care products manufactured or sold in the United States. According to the USP, USP standards are recognized and used in more than 130 countries as well as by the WHO Expert Committee on Biological Standards. USP full definitions can be found at: www.usp.org or in the abbreviated summary in Annex 1.

USP definitions that would address potential OCC temperatures include **cool** (8° to 15°C), **Controlled room temperature** (20° to 25°C with allowance for some temperature deviations 15° to 30°C), **warm** (30° to 40°C), and **excessive heat** (any temperature above 40°C).

Controlled room temperature is a term used by the pharmaceutical industry, perishable-good transporters, and manufacturers of temperature indicators. Examples include the Temptime Corporation (with their vaccine vial monitors), GlaxoSmithKline (for the injectable drug Alkeran) and the International Air Transport Association (IATA)—included in their July 2009 IATA Perishable Cargo Regulations). The UNICEF Supply Division Catalogue uses an abbreviated and similar description for at least one drug stating, “where not specified room temperature is between 15° and 30°C.”

Cold chain temperature conditions are described in various WHO publications including those from WHO’s Performance, Quality and Safety (PQS) team where the “acceptable temperature range” for a vaccine refrigerator is defined as 2° to 8°C. This implies that outside the cold chain temperatures are greater than 8°C.

The current WHO PQS definition for the “acceptable temperature range” for vaccine storage in refrigerators also includes allowance for temperature excursions; this definition is similar to the temperature deviations noted in the USP “controlled room temperature” definition. The USP definition also recognizes that each manufacturer may establish the limits of temperature storage conditions (e.g. “controlled room temperature not to exceed 25°C”). This allows the flexibility to accommodate variations among vaccines.

Summary

There presently is no consistent interpretation or name for OCC. A single name with a clear definition would establish a basis for meaningful dialogue. To address the specific varying conditions encountered when using vaccines out of the cold chain, there is a set of already established and accepted definitions (USP terms) that could be adapted to specify temperature ranges. This set of definitions allows the term **cold chain** to be used as it is presently within immunization (i.e., between 2° to 8°C).

Recommendation

While the USP terminology provides useful guidance and detail, it is felt that at this point in time it is important to adopt a single overarching term to replace the concept of OCC with the adoption of the term **controlled temperature chain**.

Vaccine manufacturers and WHO will retain the flexibility to specify additional conditions for any definition—for example, a future vaccine description might include “transport and store at controlled temperature between 15° and 30°C.”

In order to support harmonizing immunization terminology with the pharmaceutical and perishable goods transport industries, it is also suggested that additional specificity and conditions be added to **controlled temperature chain** by referencing existing definitions and related temperature ranges established by USP; this will be a key step in standardizing language around products as we move to a more integrated health system environment.

Annex 1: USP definitions: Reprinted from the USP website

The following are storage definitions, as defined in the General Notices section of the United States Pharmacopoeia (USP) XXII-NF XVII, for recommended conditions commonly specified on product labels.

Freezer	A place in which the temperature is maintained thermostatically between -20° and -10°C (-4° to 14°F).
Cold	Any temperature not exceeding 8°C (46°F). A refrigerator is a cold place in which the temperature is maintained thermostatically between 2° and 8°C (36° to 46°F).
Cool	Any temperature between 8° and 15°C (46° to 59°F). An article that requires cool storage may be stored in a refrigerator, unless otherwise specified by the individual USP monograph.
Room Temperature	The temperature prevailing in the workplace.
Controlled Room Temperature	A temperature maintained thermostatically that encompasses the usual and customary working environment of 20° to 25°C (68° to 77°F) that allows for brief deviations between 15° and 30°C (59° to 86°F) that are experienced in pharmacies, hospitals, and warehouses. Articles may be labeled for storage at "controlled room temperature", at "up to 25°C", or other wording. An article for which storage at controlled room temperature is directed, may, alternatively, be stored in a cool place unless otherwise specified in the individual monograph or on the label. (See the entire revised definition of controlled room temperature in the Ninth Supplement to USP XXII-NF XVII.)
Warm	Any temperature between 30° and 40°C (86° to 104°F).

Excessive Heat

Any temperature above 40°C (104°F).

Protection from Freezing

Where, in addition to the risk of breakage of the container, freezing subjects an article to loss of strength or potency, or to destructive alteration of its characteristics, the container label must bear an appropriate instruction to protect the article from freezing.