

Use of MenAfriVac™ (meningitis A vaccine) in a controlled temperature chain (CTC) during campaigns

**Guidance for immunization
programme decision-makers
and managers**

Immunization, Vaccines and Biologicals



**World Health
Organization**

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**The Department of Immunization, Vaccines and Biologicals
thanks the donors whose unspecified financial support
has made the production of this document possible.**

This document was produced by the
Expanded Programme on Immunization (EPI)
of the Department of Immunization, Vaccines and Biologicals

This document forms part 1 of 3 parts of the training guide for
the Use of MenAfriVac™ (meningitis A vaccine) in a
controlled temperature chain (CTC) during campaigns

Ordering code: WHO/IVB/13.04
Printed: July 2013

This publication is available on the Internet at:
www.who.int/vaccines-documents/

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Printed by the WHO Document Production Services, Geneva, Switzerland

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Abbreviations and acronyms

AEFI	adverse event following immunization
CTC	controlled temperature chain
EPI	Expanded Programme on Immunization
HIV	human immunodeficiency virus
HPV	human papillomavirus
ICC	Inter-agency Coordinating Committee
IPAC	Immunization Practices Advisory Committee (WHO)
MVP	Meningitis Vaccine Project
MOH	ministry of health
NIDS	National Immunization Days
NITAG	National Immunization Technical Advisory Group
NRA	national regulatory authority
PATH	Program for Appropriate Technology in Health
PQS	Performance, Quality and Safety
UNICEF	United Nations Children's Fund
VVM	vaccine vial monitor
WHO	World Health Organization

Acknowledgements

This document was developed through a working group of the Immunization Practices Advisory Committee whose membership included: Diana Chang-Blanc, Modibo Dicko, Francois Gasse, Thierry Gastineau, David Hipgrave, Debra Kristensen, Julie Milstien, Olivier Ronveaux, Jane Soepardi, Michel Zaffran and Simona Zipursky. The initial draft of the training materials were completed by Karin Bergstrom. Technical and review inputs were provided by Mamoudou Harouna Djingarey and Andrew Garnett.

Pilot testing was conducted in collaboration with the Ministry of Health in the Republic of Benin, WHO Regional Office for Africa, the Benin - WHO Country Office and the Meningitis Vaccine Project (MVP).

Support for this work was provided through Optimize — a WHO-PATH collaboration funded by the Bill & Melinda Gates Foundation.

Preface

The need to keep vaccines in a 2°C to 8°C cold chain is a constraining factor for many immunization campaigns due to limited storage capacity and/or limited ice pack freezing capacity; supplementary immunization activities planned across sub-Saharan Africa are a good example.

In 2012, the license for the Serum Institute of India's meningitis A vaccine, MenAfriVac™, was changed based on a thorough review of scientific data by regulatory authorities and the World Health Organization (WHO) to allow for the use of the vaccine for a period of up to four days at temperatures of up to 40°C in a controlled temperature chain (CTC). This document provides countries with guidance on when and how to take advantage of this flexibility.

What is a controlled temperature chain (CTC)?

A CTC allows vaccines, for which there is on-label guidance, to be stored and transported at temperatures outside the traditional 2°C to 8°C cold chain for limited periods of time, under monitored and controlled conditions.

Using a CTC, the MenAfriVac® meningitis A vaccine and its diluent can be removed from the 2°C to 8°C cold chain, immediately before use, for a single period of time not exceeding four days. During this period it can be stored, transported and administered at temperatures up to 40°C. In order to monitor temperatures during CTC, vaccinators and health-care workers must use a peak threshold indicator card, placed inside the vaccine carrier; this indicator will inform teams and staff if the peak temperature of 40°C has been reached.

This document provides guidance as follows:

- 1) For decision-makers: how to decide if a CTC is the right approach for your country.
- 2) For district/zone coordinators: how to plan and implement a CTC campaign.

It is important to note that this is not a stand-alone document and it should be used as a complement to the CTC vaccinator training guide and accompanying facilitator's guide. These documents provide guidance on 'how to' implement CTC practices and, together with the WHO's existing Immunization in Practice guidance series, provide general immunization session planning information.

Countries should only consider a CTC when ALL the following conditions apply:

- A MenAfriVac® vaccination campaign is being planned.
- Ambient temperatures in the CTC area during the campaign time are below 40°C.
- There are at least two months before the campaign start date.
- Cold-chain storage capacity and maintenance is challenging.
- Ice-pack production and/or storage capacity is insufficient to meet campaign needs.
- Outreach forms a key component of the activities.
- It is difficult or impossible to reach the entire target population if vaccine is kept in the 2°C to 8°C cold chain.
- There is interest in the CTC approach and the necessary commitment from district medical officer(s) to implement it. This will ensure that proper training, supervision and monitoring are in place.

1. Introduction

In 2012, based on a thorough review of scientific data by regulatory authorities and the World Health Organization (WHO), the licence for the Serum Institute of India's meningitis A vaccine, MenAfriVac™, was changed so as to allow for the use of the vaccine for a period of up to four days at temperatures of up to 40°C in a controlled temperature chain (CTC). This document is designed to provide countries with guidance on when and how to take advantage of this new flexibility.

The new label for MenAfriVac™, prequalified by WHO in 2012, states the following:

MenAfriVac™ can be stored at up to 40°C for not more than four days immediately prior to administration, provided that the vaccine has not reached its expiry date and the vaccine vial monitor is still valid. Unopened vaccine should be discarded at the end of the four days at up to 40°C. Reconstituted vaccine should be discarded within six hours. when stored at 40°C.

This information can be found in the package insert for MenAfriVac™ and is reflected in the WHO Performance, Quality and Safety (PQS) website¹ as well as on the manufacturer's website².

¹ http://www.who.int/immunization_standards/vaccine_quality/PQ_197_MenAconjugate_10dose_SII/en/index.html.

² https://www.seruminstitute.com/content/products/product_menafriyac_e.htm.

2. Why consider a CTC?

The need to keep vaccines in a 2°C to 8°C cold chain is a constraining factor for many immunization campaigns due to limited storage capacity and/or limited ice-pack freezing capacity. Supplementary immunization activities planned to introduce MenAfriVac™ across sub-Saharan Africa are a good example.

In MenAfriVac™ campaigns, implementing a CTC allows countries to transport and administer vaccines without requiring ice packs during the final legs of distribution and administration provided that correct CTC procedures are followed.

Depending on cold-chain constraints at the health-centre level and for last-mile transport, a CTC may alleviate some of the need for surge cold-chain capacity required to accommodate the campaign vaccine. It may also provide an alternative in places where the cold chain is a challenge or ice-pack production is a constraining factor during campaigns.

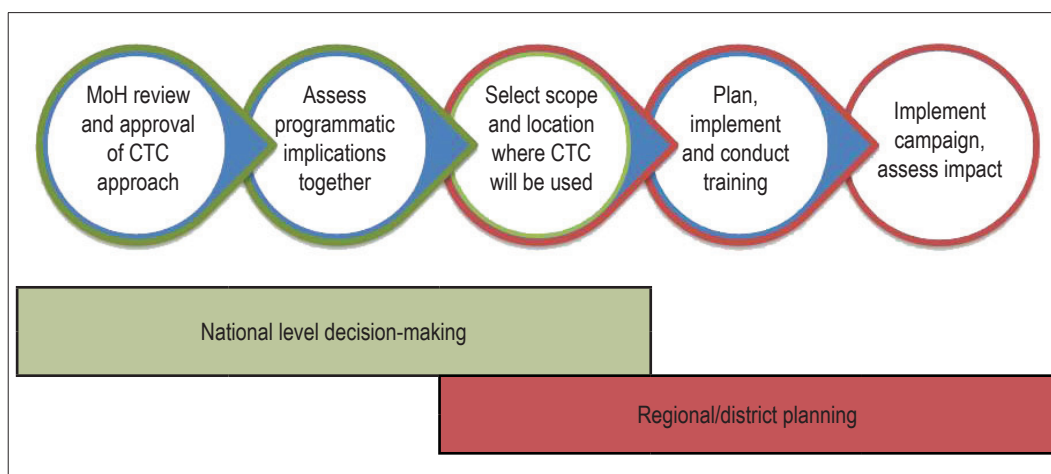
3. Where can a CTC be implemented?

The following factors are important to consider when evaluating where a CTC can be implemented. Additional information on these factors is provided throughout the document; please see p.6 “CTC implementation checklist” for a decision-making aid.

- **Geographic scope.** A CTC can be implemented nationally, or only in specific areas.
- **Cold-chain performance.** A CTC can have the most impact in targeted areas where cold-chain capacity or performance is insufficient or suboptimal.
- **Freeze capacity.** A CTC has significant benefits in areas where ice pack making and storing facilities are not available, or are limited or expensive.
- **Training can be implemented.** A CTC should only be implemented where there are sufficient properly trained health workers, able to safely implement and supervise the CTC protocol.
- **Peak ambient temperatures are below 40°C.** If the peak ambient temperature, in certain districts or during certain seasons, is likely to reach or exceed 40°C, storage and transport of MenAfriVac™ at ambient temperature cannot be safely done. The campaign will need to use cold chain in these districts, and/or during these seasons.
- **Integrated campaign activities.** If MenAfriVac™ is given along with other vaccines during the same campaign, CTC use needs to be carefully considered. Keeping MenAfriVac™ in a CTC while requiring that other campaign vaccines be kept in the traditional cold chain could lead to confusion, and is not recommended.

4. Implementing a CTC

The decision to implement a CTC approach for MenAfriVac™ campaigns requires careful consideration and planning. The following subsections provide guidance on factors to consider and some key steps for doing so.



5. National level decision-making

5.1 Ministry of Health and National Regulatory Authority review and approval

It is essential that the national immunization programme, Ministry of Health (MOH) and, if applicable, the National Regulatory Authority (NRA) agree to support a meningitis A vaccine campaign using a CTC approach.

Prior to further planning, it is important to ensure that MenAfriVac™ is approved for use in your country and that its registration includes the CTC storage conditions. For countries using the expedited pre-qualification process through WHO, the CTC storage conditions are already reflected in the product registration. The latest information for MenAfriVac™ licence and storage conditions from WHO is available online at http://www.who.int/immunization_standards/vaccine_quality/PQ_vaccine_list_en/en/index.html.

5.2 Assess the programmatic implications

5.2.1 Engage key decision-making bodies

Given that there are trade-offs to consider before selecting a CTC approach, it is important to consult with partner or technical coordination groups, such as the Inter-agency Coordinating Committee (ICC) and/or the National Immunization Technical Advisory Group (NITAG), before choosing to undertake a CTC strategy. These groups should be asked to advise on the issues described in Section 5.2.2 “Factors to consider when implementing a CTC”. The variety of viewpoints and expertise contained in these groups will help ensure all key considerations are fully examined.

If your country does not have an ICC and/or a NITAG, consider using an existing immunization technical working group, or setting up an ad hoc group to assess the CTC approach. When constituting the ad hoc group, all key immunization partners should be represented and the group should be led and chaired/managed by the MOH or the Expanded Programme on Immunization (EPI).

5.2.2 Factors to consider when implementing a CTC

- **Resource and time requirements.** A CTC is an innovative approach that, especially when first introduced, requires resources and time for training and the printing of guidelines, etc. If you have never conducted a campaign using CTC, and your campaign is less than two months away, there is unlikely to be enough time to plan properly for a CTC; a traditional cold chain approach should be used instead.
- **Human resources and training.** While CTC is well-liked by staff and supervisors, it is important to note that it is a new approach. Successful CTC implementation requires adequate numbers of motivated, trained and committed district and regional staff, who can supervise vaccinators effectively and are able to respond to questions during the campaign.
- **Assessing the trade-offs.** While there are clearly gains and benefits to using MenAfriVac™ in a CTC, there are also costs and risks associated with it. Table 1 summarizes the key pros and cons of implementing a CTC.

The table that follows provides some factors for consideration when weighing trade-offs between a CTC approach and traditional cold chain.

Table 1: Gains and benefits compared to the costs and risks of implementing a CTC

Gains/benefits	Costs/risks
Infrastructure: Starting from the location in the supply chain where the CTC starts, there is no need to provide additional space in the cold chain for the MenAfriVac vaccine.	Risk of confusion: As CTC is a new practice, there is an increased risk of confusion.
Infrastructure: No additional freezer capacity is needed for ice packs.	Start-up costs: One peak threshold indicator per vaccine carrier or equivalent will be necessary. These are a low-cost paper card with a temperature-sensitive sticker costing under US\$ 1 each, depending on the quantities needed.
Vaccine wastage: There have been reports of unopened vaccines being discarded when the label becomes detached or unreadable after a day in a humid vaccine carrier. A CTC eliminates this problem because the air inside the vaccine carrier will be dry.	Vaccine wastage: Higher levels of closed-vaccine wastage may be seen if the vaccine needs to be discarded because the temperature has exceeded 40°C, or the 4-day time limit has been passed.
Operational: Savings of staff time —specifically around planning and managing extra cold-chain issues and ice-pack logistics. The time used for planning cold-chain space, freezing ice packs and managing the cold-chain equipment needed for transportation can be reallocated to other supervisory and field activities.	Operational: Additional time may need to be added to the training schedule to familiarize vaccinators and supervisors with this new approach.
Operational: Increased ease of vaccine transportation and reduced volume and weight burden for health-care workers to transport. Reduces the number of trips by health centres to the district level to pick up vaccines and/or ice packs.	
Operational: Increases the geographical access of the standard 2°C to 8°C cold-chain coverage area outside of hard-to-reach areas.	

CTC implementation checklist

DECISION-MAKING

Ensure government approval.

- If the EPI or NRA have concerns, or require further information, contact your local WHO office for technical support.

Assess the suitability of using a CTC approach.

- Is the cold chain a challenge? Are ambient temperatures likely to be below 40°C at the time of the campaign?

Assess the programmatic implications.

- Consult Table 1 and consider whether this is the right approach for your campaign (or part of your campaign)

Determine the geographic scope of having a CTC.

- Consider where a CTC can be of the most value. This will often be in areas where ice production is a challenge and outreach forms a major part of the strategy. Decide where you will use CTC — in one region? One district? The whole country?



If, after carefully reviewing these points, you have decided CTC is right for you, move on to the “factors to consider”.

FACTORS TO CONSIDER

Is there enough time?

- Two months are necessary to plan properly for a CTC campaign.

Do you have the necessary resources?

- These include human resources for training, supervision and the modification of training materials. These also include financial resources to conduct new trainings and procure peak threshold indicators.

Where will you implement CTC?

- See text box in section 6.1 for factors to consider.



After you have carefully considered the above factors, these key implementation steps will make the process move in the right direction.

KEY IMPLEMENTATION STEPS

Establish a working group with representatives from the MOH at the national level/participating regions, UNICEF, WHO and other immunization partners.

Develop a timeline.

Be sure to develop a timeline that includes adequate time for the sensitization of health-care workers at all levels and adequate time for vaccinator training.

Adapt training, supervision and adverse events following immunization (AEFI) materials to a CTC.

Sample training materials and forms are in the training guide. Please adapt them for local use and pre-test them with a few health-care workers and vaccinators to ensure that the message is clear.

6. Regional/district level decision-making

Once the decision has been made to proceed with using a CTC approach for the campaign, it is important to decide on the following:

- **Scope and locations.** Decide where, within the region or district, the CTC approach will be applied (e.g. across the entire campaign area or only in specific regions/districts).
 - Rather than having isolated districts implementing CTC, it may make sense to “group” districts into CTC areas, making supervision and training easier.
- **Moving the vaccines to a CTC.** When will the CTC practice begin e.g. the vaccine will stay in the standard 2°C to 8°C cold chain until the district level, or the most peripheral health facility, after which it will be managed in a CTC until administration.
 - For further suggestions on this topic see the scenarios in Section 7.

These decisions should be made in consultation with the ICC, NITAG, technical working groups and/or other advisory bodies.

Before making final decisions, it is important to conduct a mapping exercise to identify those parts of the country where the cold chain is currently a challenge. In addition, the peak ambient temperature during the time of the campaign must be considered. A good starting place for ambient temperatures is the World Meteorological Organization’s Africa Initiative at <http://www.acmad.org/> or sites such as <http://www.weatherbase.com/> or <http://www.wolframalpha.com/> (for WolframAlpha, please enter ‘climate <place name>’ to get a result. i.e. for the temperature in Nairobi, Kenya, you would need to enter: *climate Nairobi, Kenya*).

6.1 Selection of the scope and locations for CTC use

- CTC may be used across the country, or it may be applied only in specific districts.
- As a minimum, however, it is best to implement CTC throughout an entire district. Do not select specific areas or specific health centres within a district. Implementing CTC in only parts of a district may not be cost efficient and partial implementation carries the risk that health personnel will be confused.
- Consider how the CTC training and supervision will be conducted.

6.2 Resources to support the mapping and decision-making process

- **Previous campaign microplans and reports.** These will provide information from previous campaigns in target districts and health centres. They will be helpful in identifying areas where CTC could help address previous challenges or concerns—such as cold chain challenges—, and areas where outreach forms a large proportion of the vaccination strategy.
- **Cold-chain inventory.** If a recent cold-chain inventory is available, the data can be used to assess where cold chain capacity and ice pack freezing capacity is a problem. Cold-chain challenges are heightened during campaigns due to the surge capacity required and the large number of ice packs needed. In areas where cold-chain equipment is non-existent, not sufficient or nonfunctioning, CTC may offer significant advantages.
- **Energy issues/constraints.** If your cold-chain equipment uses gas or kerosene, and if shortages are occurring in any parts of the country, CTC may be a good solution to overcome these constraints. Similarly, if the majority of equipment is electricity based, and if there are supply problems or loadshedding measures in place, these areas may be priorities for CTC.
- **Peak ambient temperature in the country during the planned campaign dates.** A mapping of temperatures in each district, including highs and lows, during the planned campaign dates, is essential. Section 6 for sources to consultant for ambient temperature info. If the ambient temperature in certain districts is likely to reach or exceed 40°C, keeping the MenAfriVac™ vaccine at ambient temperature cannot be done safely and cold chain will need to be used for the campaign in these districts.

The implementation of CTC is not safe without the use of a peak threshold indicator (see Section 7.3 for further information on peak threshold indicators).

6.3 Planning timeline

It is important to recognize that implementing a CTC-based campaign is a departure from the standard campaign practice. It is recommended that the decision to implement a CTC is made at least two months prior to the start of the campaign. This is important in order to allow proper time to:

National level

- select areas of the country where CTC will be conducted;
- decide what level to start the CTC;
- order peak threshold indicators;
- brief regional and district staff;

Regional/district level

- finalize areas where CTC will be implemented within the region;
- adapt training materials for the local context;
- develop appropriate microplans, including guidance on transportation and running an immunization session under a CTC;
- adapt supervision tools and forms for CTC use;
- train regional, district and health-care worker staff;

6.4 Training, education and information

CTC is a new practice, and currently only recommended by WHO for the MenAfriVac™ vaccine, and then only during campaigns. Accordingly it is important to train supervisors and health-care workers properly. In addition, it is important to ensure traditional and community leaders, as well as partner organizations, are informed and educated about CTC.

Questions can be expected from these groups, and it is important to be prepared in advance to offer clear, accurate and simple responses.

The first time CTC is used, it is important to plan for additional time to address these issues.

This includes explaining the following:

- MenAfriVac™ is stable for use outside the cold chain for a limited period of time.
- There have been many tests conducted in the laboratory to ensure MenAfriVac™ is still effective under these conditions.
- These tests have been validated by scientists at WHO and/or scientists in this country.³
- The condition of MenAfriVac™ is still being monitored at all times.
- Health-care workers have been specially trained on how to monitor MenAfriVac™ during the campaign in order to ensure it remains safe and potent to use before administering it.
- As part of the post-marketing and AEFI surveillance, the Ministry of Health with support from WHO are monitoring to see if there are any problems that we did not anticipate.
- This practice is only being used during this campaign, with MenAfriVac™. For all other immunization activities, the cold chain will still be used.

³ Scientists in this country refer to the NRA's testing, if applicable, and subsequent approval to use the vaccine in this manner.

The “Frequently Asked Questions” document, in the Supporting Documents section, provides further information *Immunization in Practice* gives the following suggestions for informing the community about immunization-related issues:

- Meet with key opinion leaders (politicians, traditional and religious leaders, community leaders, other health workers).
- Organize meetings at sites where the individuals/groups are comfortable and feel at ease to ask questions.
- If there is a national mass-media response, encourage your community members to watch and talk about it.
- React swiftly and adapt your ongoing activities to give a quick response.
- Develop strong relationships and trust with your community in advance (religious, social and media groups).
- Give clear and consistent messages.
- Take the time to deal with rumours. Doing so will benefit routine immunization, as well as campaigns.

7. Implementing a CTC

7.1 When to start a CTC

There are several scenarios which will enable you to make the best use of the CTC approach. Which of these you choose to use will depend on your existing cold chain and ice-making capacity at each level, as well as the transportation plans/infrastructure.

A careful planning exercise must then take place that takes into account the maximum time the vaccine is allowed to be kept in a CTC. Given that there is only a four-day window for a CTC, it is essential to ensure that you can carry out your planned CTC activities within that time.

Total time allowed in a CTC = transport and/or storage + vaccination

Figure 2, 3 and 4 below show three common scenarios for a CTC.

*Scenario 1 (see Figure 2 and Table 3) is best suited to situations where ice-making capacity at district level is limited, and distances between district and health centre involve less than a day of travel. **This scenario is suitable for health centres without functional cold chains** but requires more than one delivery from the district level to the health centre during the campaign.*

Figure 2:
CTC scenario 1: Implementing CTC, starting at the district level

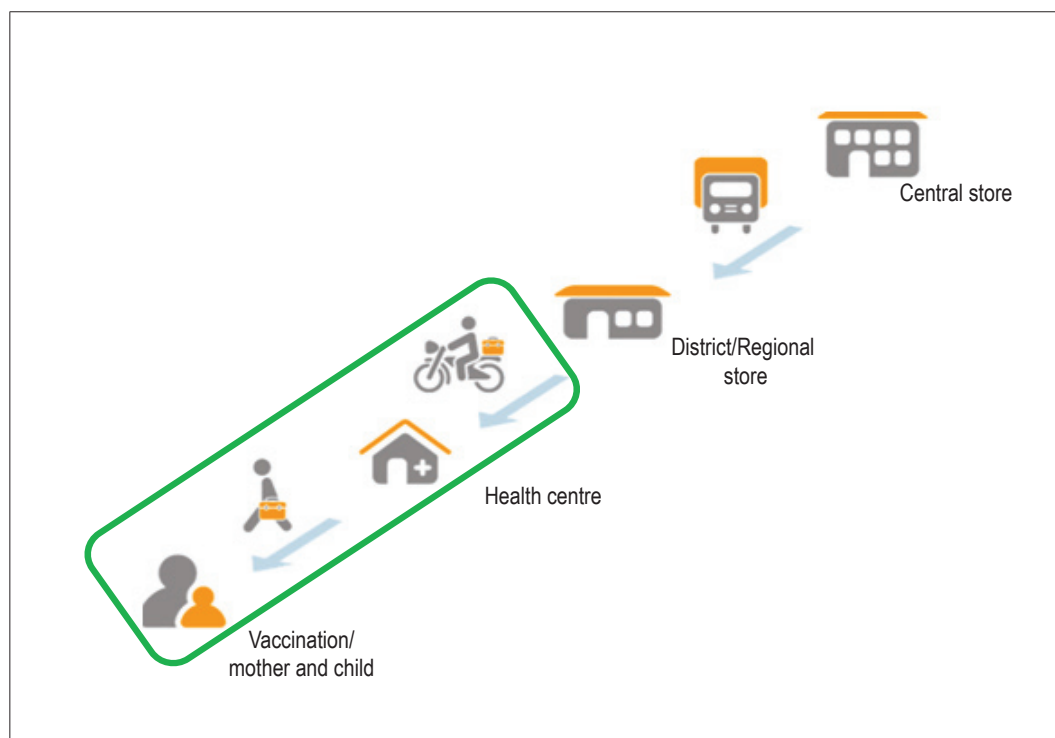


Table 3: Vaccine is removed from the cold chain *at the point of transport from the district level to the health centre* and is placed into a CTC with peak threshold indicators

Day 1	Vaccine is removed from the cold chain and transported to the health centre, without ice.
Days 2 to 3	<i>Option A:</i> Multiday overnight outreach (2 days/2 nights). <i>Option B:</i> Two days of outreach, each originating from the health centre each morning. Vaccine and diluents are stored overnight at ambient temperature.
Day 4	<i>Option A:</i> Travel back to health centre from multiday outreach (safety margin). <i>Option B:</i> Conduct another day of immunization using a CTC.

Scenario 2 (see Figure 3 and Table 4) is best suited to situations where ice-making capacity at the district level is sufficient and distances between the district and health centre are long, especially those requiring over a full day of travel. This scenario is also ideally suited to health centres that want to take advantage of the full CTC “window” for longer multiday outreach. This scenario is suitable for health centres without functional cold chains but requires more than one delivery from the district level to the health centre during the campaign

Figure 3:
CTC scenario 2: Implementing CTC, starting upon arrival at the health centre

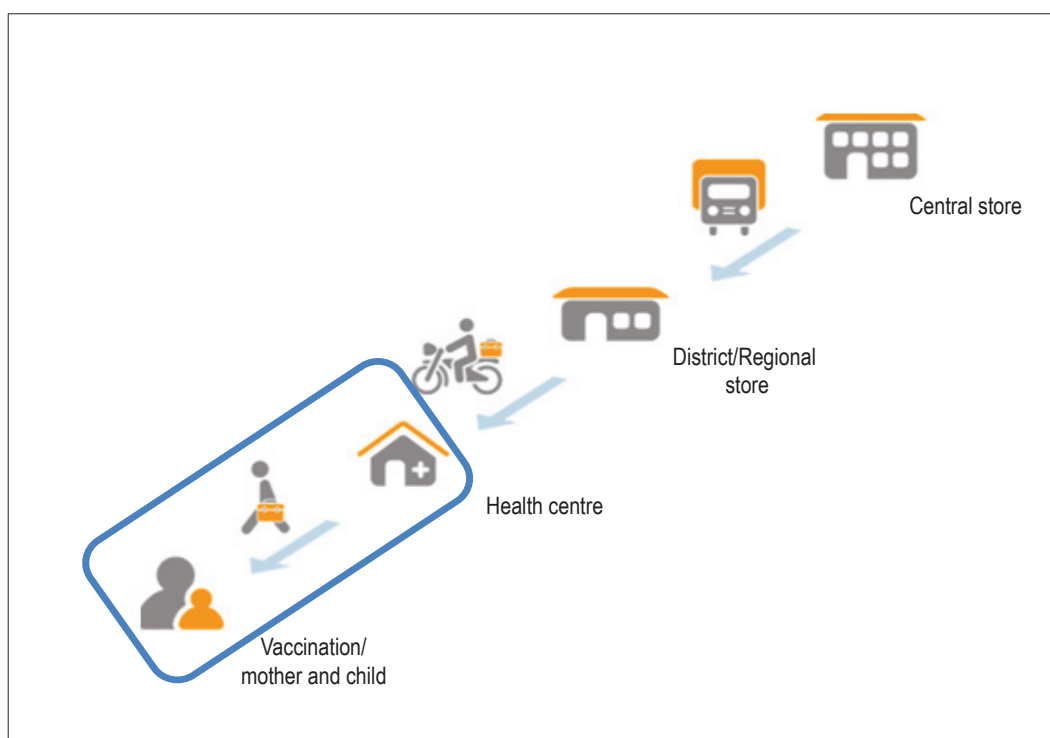


Table 4: Vaccine is removed from the cold chain *upon arrival at the health centre*

Day 1	Vaccine arrives at the health centre and is removed from the cold chain. Depending on time of arrival, immunization with the vaccines in a CTC may begin today.
Days 2 to 3	<i>Option A:</i> Multiday overnight outreach (2 days/2 nights). <i>Option B:</i> Two days of outreach, each originating from the health centre each morning. Vaccine and diluents are stored overnight at ambient temperature.
Day 4	<i>Option A:</i> Travel back to health centre from multiday outreach (safety margin). <i>Option B:</i> Conduct another day of immunization using CTC practice.

Scenario 3 (see Figure 4 and Table 5) is best suited to situations where health centres have a functional cold chain with adequate space for campaign vaccines. Option B of this scenario is ideally suited for health centres with nearby populations and limited ice-making capacity, and enables them to conduct day outreach using a CTC while storing vaccines in the cold chain at health-centre level.

Figure 4:
CTC scenario 3: Implementing CTC at the start of vaccination activities



Table 5. Vaccine is removed from the cold chain *on the day of vaccination/outreach*

Days 1 to 3	<p><i>Option A:</i> Multiday overnight outreach (3 days/3 nights).</p> <p><i>Option B:</i> Three days of outreach, each originating from the health centre each morning. Vaccine and diluents are stored overnight at ambient temperature.</p>
Day 4	<p><i>Option A:</i> Travel back to health centre from multiday outreach (safety margin).</p> <p><i>Option B:</i> Conduct another day of immunization using CTC practice.</p>

7.2 Developing new microplans

Microplans from previous campaigns will necessarily have taken into account the need to ensure adequate cold-chain capacity and the availability of ice packs.

It is important to spend time developing new microplans that take full advantage of the flexibility offered through a CTC. In order to maximize CTC benefits you should do the following:


- Explore efficiencies in multi-day outreach trips; returning to a central point each night to collect ice for the next day will no longer be necessary.
- Now that there is no need for ice in the vaccine carrier, consider whether teams could vaccinate more people in one day by carrying extra vaccine.
- Now that there is no need to return for, or receive, an ice top-up during the day, consider which of the teams could travel further during the day in order to reach more remote populations.
- Explore the idea of packing vaccine carriers the night before to save time in the morning and to avoid errors resulting from the “morning rush”.

7.3 Peak threshold indicators

Most of the equipment needed for a CTC session is the same as that used in a regular campaign (e.g. auto-disable syringes, safety boxes, reconstitution syringes and vaccination cards). *However, the implementation of a CTC for MenAfriVac™ cannot be done safely without a tool to ensure that the maximum temperature of 40°C is not exceeded. It is, therefore, recommended that a peak threshold indicator be used at all times.*

7.3.1 What is a peak threshold indicator?



PEAK TEMPERATURE THRESHOLD INDICATOR



INSTRUCTIONS

Check the indicator as follows:

- When you **load the vaccines into the cold box**
- As you **remove each vial from the cold box**
- When the **last dose of vaccine for the day** is administered



Still good

Take action!

If the **INNER CIRCLE IS BLACK**,

DO NOT USE the vaccines and contact your supervisor

A peak threshold indicator is a small card that changes colour irreversibly when it is exposed to a peak temperature for a maximum period of time. It shows when the vaccine has been exposed to a peak temperature (i.e. a temperature over 40°C); the colour change indicates that the vaccine may no longer be effective and that it should not be used.

Note that peak threshold indicators do not replace vaccine vial monitors (VVMs). Threshold indicators measure **PEAK** exposure while VVMs measure **CUMULATIVE** exposure to heat.

7.3.2 When are peak threshold indicators used?

When implementing CTC, peak threshold indicators should be used **IMMEDIATELY** upon removal of the vaccines from the 2°C to 8°C range.

The indicators should be placed inside the vaccine carrier used for outreach activities or transport. If you are transporting the vaccine in its original cardboard-box packaging (tertiary packaging), a peak threshold indicator will need to be placed inside the box. There is no need to place a peak threshold indicator in the diluent boxes.

7.3.3 How many peak threshold indicators do I need?

As an estimate, one peak threshold indicator is needed per planned vaccination team, assuming each team will be using only one vaccine carrier. If additional vaccine carriers are to be used, additional indicators will need to be planned for.

A reserve stock of 50 percent is recommended, to deal with indicators that reach their end-point, damaged indicators and any changes to the number of teams.

7.3.4 Other temperature-monitoring technologies

WHO has a list of other prequalified temperature monitoring devices, including programmable electronic data loggers. Countries may wish to consider using these devices to help gather temperature data, especially when CTC is first being introduced. To consult the list of prequalified electronic temperature monitoring devices, please visit http://apps.who.int/immunization_standards/vaccine_quality/pqs_catalogue/categorypage.aspx?id_cat=35.

7.4 Vaccine carriers and cold boxes

A standard vaccine carrier or cold box is still the preferred option for transporting vaccines in a CTC. In addition, a standard vaccine carrier has the advantage that health-care workers and the community are very familiar with it and associate it with immunization activities. Its accompanying foam pad facilitates vaccine handling. There is no need to use ice packs when using a vaccine carrier or cold box in a CTC.

If you choose not to use vaccine carriers, it is important to ensure that you carry the vaccine in a container that is:

- well insulated;
- protects the vaccines from direct sunlight;
- keeps the vaccines and diluents safe from breakage;
- strongly constructed – do not use soft bags.

Vaccine carriers and containers should be dedicated specifically for vaccine transportation and not used to carry other equipment or supplies.

7.5 Transport under a CTC

ATTENTION!!

Special attention must be paid when transporting vaccines in a CTC as there is an increased risk of high temperature exposure.

Before deciding to transport vaccines in a CTC, it is important to ensure that you have properly planned your CTC timeline. CTC allows vaccines to be taken out of the cold and stored at a peak ambient temperature of up to 40°C for one period of four days immediately prior to use.

Once a vaccine is removed from the cold chain, its four day CTC life has started.

Monitoring temperatures during transportation can be challenging as the vaccines may be in the back of a car or motorcycle and thus out of sight. If vehicles are in direct sunlight for extended periods of time, the temperatures inside may rise higher than the outdoor ambient temperature.

Special attention and care must be taken when transporting vaccine in a CTC. If there are concerns that the 40°C may be surpassed, other options should be explored, including the use of cool water packs or transport in traditional cold chain.

7.6 Supervision

During a CTC campaign, supervisors should have more time to observe operations and provide guidance on immunization practices, because they do not need to spend time refreshing their teams' ice packs.

Prior to implementing a CTC it is important to ensure that all supervisors are properly trained on, and comfortable with, CTC practice, and that they are able to provide supportive supervision to vaccinators. In addition, supervisors should be trained to answer commonly-asked questions on CTC from the community.

CTC supervisors should be:

- Public-health experts. Able to answer questions on the CTC practice.
- Good communicators. Able to address concerns from vaccinators and the public clearly and articulately.
- Willing to travel. CTC supervision will often involve difficult travel to remote regions.

When supervising a CTC campaign, supervisors should pay special attention to the following questions:

- Are health-care workers able to explain the basic CTC principles?
 - Store vaccine and diluents for up to four days at up to 40°C.
 - Check the VVM, expiry date and peak threshold indicator before opening each vial.
 - Discard reconstituted vaccine after six hours.
- Are the vaccines and diluents being properly monitored for exposure to cumulative and peak temperature exposure?
 - Check for transportation, storage and utilization during the session.
- Are the vaccines and diluents stored in the shade?

-
- Are vaccinators able to explain the concept of CTC accurately?
 - Are vaccinators able to answer commonly-asked questions about CTC?
 - Do vaccinators understand what to do if the peak threshold indicator shows that the peak exposure has been reached?
 - Are any VVMs nearing their discard point, and if so are they being used first?
 - Is proper AEFI communication being given by vaccinators to caregivers?

As using CTC is a new practice, it is important to gather information on how the practice is affecting vaccinators and supervisors. This will help decision-makers assess whether or not they should replicate and/or expand the CTC practice in future campaigns.

The following is a guide to the types of observations and questions for supervisors. It is suggested to answer these questions following the first, middle and last day of the campaign. This will enable you to monitor how things change as the practice becomes more familiar.

Assess the impact of a CTC on immunization activities and your own supervision.

- Based on your experience, what differences do you observe between immunization sessions using CTC approach and regular campaign immunization sessions?
- Describe any differences you notice in your own supervision when supervising CTC practices versus regular campaign activities. Are you spending more or less time on certain topics? Are you covering more or fewer sites per day?

Assess the impact and perception of CTC practice for vaccinators.

- Ask vaccinators how they are finding the new practice. What benefits are they seeing, if any, and what challenges, if any?
- Ask vaccinators if they think the CTC practice is useful? Why, or alternatively, why not?
- Ask vaccinators to suggest things they think should be changed and/or improved, if the CTC practice is to be used again?
- Observe how the vaccinators' responses change between the first day, when practice is new, and the middle and end of the campaign — are there any differences?

7.7 Injection safety, AEFI monitoring and reporting

Injection safety is as important to a CTC as it is to regular campaigns. Table 6, which has been adapted from Immunization in Practice, lists the types of severe reactions that may arise if incorrect injection practices are used. The latest information and training on AEFIs is located at <http://www.vaccine-safety-training.org/getting-started.html>.

Table 6: Incorrect immunization practices and possible severe reactions following immunization

Incorrect practice	Examples	Possible severe reactions following immunization
Non-sterile injection	<ul style="list-style-type: none">Reuse of disposable syringe or needleImproperly sterilized syringe or needle	<ul style="list-style-type: none">Infection, such as local abscess at injection site, sepsis, toxic shock syndrome, or death
	<ul style="list-style-type: none">Contaminated vaccine or diluent	<ul style="list-style-type: none">Bloodborne infection transmitted, such as hepatitis or HIV
Reconstitution error	<ul style="list-style-type: none">Inadequate shaking of vaccine	<ul style="list-style-type: none">Local abscess
	<ul style="list-style-type: none">Reconstitution with incorrect diluents	<ul style="list-style-type: none">Vaccine ineffective
	<ul style="list-style-type: none">Drug substituted for vaccine or diluents	<ul style="list-style-type: none">Negative effect of drug (e.g. insulin, oxytocin, muscle relaxants)
	<ul style="list-style-type: none">Reuse of reconstituted vaccine at subsequent session	<ul style="list-style-type: none">Death
Vaccine transportation/storage incorrect	<ul style="list-style-type: none">VVM changed colour	<ul style="list-style-type: none">Vaccine ineffective
	<ul style="list-style-type: none">Peak threshold indicator indicates peak exposure has been reached (if used)	<ul style="list-style-type: none">Vaccine ineffective
	<ul style="list-style-type: none">Clumping of adsorbed vaccine	<ul style="list-style-type: none">Local reaction from frozen vaccine

AEFI surveillance is a key component of successful immunization activities. The same procedures used to monitor and track AEFIs during standard campaigns should be used by all health-care staff when implementing a CTC. These include, appropriate training of health centre, district and regional staff, along with the establishment of an AEFI committee with, if needed, the ability to rapidly investigate AEFIs across the campaign area. For further information, please reference the AEFI manual for MenAfriVac™ campaigns, available on request from the WHO Regional Office for Africa.

When implementing a CTC, AEFI reporting forms should be updated to allow vaccinators to indicate if the vaccine was administered in a district where CTC was used.

As with all campaigns, it is important to ensure that the committee tasked with reviewing and responding to AEFIs records whether or not the reported AEFIs occurred while the CTC was being used. An independent monitoring study conducted on the use of MenAfriVac™ in a CTC, concluded that the rate and severity of AEFIs is the same when the vaccine is used in a CTC as opposed to in a traditional cold chain.

8. Assessing the CTC practice

When CTC is first used, it is particularly important for the country to document and assess the benefits and challenges of the CTC approach, in order to inform future decision-making.

Countries should collect data on the following indicators, either as part of the existing campaign monitoring, or through a separate exercise.

In addition to existing monitoring requirements, which include things like the number of VVMs reaching their discard point, countries should consider monitoring:

- closed-vial wastage due to CTC;
- open-vial wastage;
- number of peak threshold indicators that have changed colour;
- number of people vaccinated per day by CTC teams, versus non-CTC teams.

9. Supporting documents

The following documents are appended to this guidance for your use. These include:

- 1) Frequently asked questions about MenAfriVac™ CTC.
- 2) Training materials for vaccinators, including:
 - a) exercises on route planning
 - b) threshold indicator sample and detailed guidance on its use
 - c) sample CTC monitoring form and CTC peak threshold indicator expiration form.
- 4) Facilitators' guide for vaccinators' training.
- 5) Adaptation guide for vaccinators' training.

10. Frequently-asked questions on the use of MenAfriVac™ in a CTC

- 1) **Vaccines usually need to be kept between 2°C to 8°C, yet the MenAfriVac™ vaccine can be distributed differently, in a “Controlled Temperature Chain”. What does this mean?**

Most vaccines need to be stored and transported at a temperature of between 2°C to 8°C in order to remain potent. It is difficult to maintain this temperature in many countries due to weak cold-chain infrastructure and limited ice pack production capacity. With a controlled temperature chain (CTC), we can safely use the MenAfriVac™ at temperatures beyond that range, for a specific period of time.

Studies conducted by manufacturers and verified by independent laboratories show that all vaccines—even extremely heat-sensitive vaccines, such as the oral polio vaccine—can be kept at temperatures above 8°C for limited periods of time. However, so far, all vaccines have been licensed with the requirement that they be kept in the cold chain at all times (between 2°C and 8°C).

MenAfriVac™, which is a very heat-stable vaccine, has been shown to remain effective at temperatures of up to 40°C for a single period of up to four days. This has the potential to reduce the logistics burden for health-care workers across Africa and will help alleviate many of the obstacles to immunizing small villages, even in the most remote regions.

- 2) **What kind of data do you have to support the distribution of the MenAfriVac™ vaccine in a CTC, in terms of safety and efficacy?**

Safety and efficacy have been key considerations throughout the process of re-labelling MenAfriVac™ to allow for its use in a CTC. As a polysaccharide conjugate vaccine, MenAfriVac™ has specific characteristics (such as free polysaccharide and protein levels) that can be assessed and measured in the laboratory, that allow us to be extremely certain of how it will perform in the field. If these characteristics meet their required specifications, the vaccine will offer protection to those who receive it; if they do not, the vaccine’s efficacy may be compromised. MenAfriVac™ met all those conditions, even after four days at 40°C.

Regulatory authorities in India—where the vaccine is manufactured—and in Canada, as well as the vaccine prequalification team at WHO, reviewed all the available data on MenAfriVac™. This included data on more than 6000 vials—including vaccine vials that were at the very end of their shelf life. Studies were done looking at the vaccine in its lyophilized form, as well as after reconstitution while still at 40°C for the allowed 6 hour period. Using a “worst case scenario” methodology, the regulators reviewed the vaccine characteristics to ensure that,

even after CTC exposure in vials at the end of their shelf life, the vaccine would still provide the same level of efficacy, protection and safety as that provided by vaccines kept in a standard cold chain.

3) What impact will CTC have on public health/vaccination programmes in Africa?

Moving to a CTC approach will have a significant benefit for countries. Currently, MenAfriVac™ is one of several vaccines delivered across Africa, mainly through outreach campaigns. The population targeted is often huge. For example, the target population for MenAfriVac™ campaigns in Burkina Faso was 11 million people; in Nigeria it is 88 million people. Mounting the necessary logistics to reach this number of people in 7–10 days is a challenge anywhere, but it is especially so in many African countries. We know that there have been countries that have had to delay immunization activities, or use a “phased approach” to vaccinate their population, because the requirement to keep the vaccine between 2°C –8°C at all times posed too great a challenge. In 2011/2012, for example, at least one country suffered from outbreaks of meningitis A in regions where local authorities had been unable to introduce the vaccine because of such limitations. We hope the CTC approach will prevent that type of situation from occurring in the future.

4) What are the advantages of distributing MenAfriVac™ vaccine in CTC?

The CTC approach has the ability to reduce the logistics burden faced by health-care workers who often struggle to access reliable electricity to enable them to constantly keep the vaccine cold, as well as produce and store the necessary ice packs to enable the vaccine to be delivered through outreach services.

While the benefits will vary by country, depending on their existing cold-chain resources, as well as geographic challenges, preliminary studies indicate that the impact and cost savings are likely to come from the following.

1. Fewer ice pack logistics and transportation needs:

- No need to collect ice packs from facilities before the campaign in order to freeze them.
- Districts will not need to supply ice to sub-district/facility level.
- No need for ice top-ups to mobile teams.

2. Increased coverage:

- Overnight teams and mobile teams can deliver more vaccines in one trip and reach more people. Currently, the weight and limited capacity of vaccine carriers and the need to use ice-only cold boxes hinders delivery of vaccines to hard-to-reach populations.
- Speed of delivery, rather than access to ice, could determine the route for reaching a target population.

3. Reduction in storage space:

- Less space will be needed for storage at the facility level—especially important for countries introducing new vaccines into their routine immunization programme.

4. *Eliminate surge equipment needs:*

- Less stringent requirements for extensive investment in temporary cold-chain infrastructure; countries normally need this investment before they can implement immunization campaigns.

5. *Improved quality:*

- Fewer concerns regarding cold-chain related issues should mean that supervisors and vaccinators spend more time ensuring proper injection-safety procedures and learning to recognize and respond to any potential adverse events.

5) Do all future MenAfriVac™ introductions in Africa need to be done in CTC?

The WHO's Immunization Practices Advisory Committee (IPAC) has endorsed guidance and training materials to support countries interested in implementing a CTC approach.

However, using a CTC approach is not mandatory, nor is it recommended in all cases. For example, there may be situations where the temperature is likely to surpass 40°C.

The revision to the MenAfriVac™ label and the accompanying guidance from WHO provides countries with the scientific information on the actual stability of the vaccine, and this is particularly useful in countries where space limitations and a lack of capacity for freezing ice packs might prevent timely delivery of the vaccine.

6) To what other vaccine(s) could the CTC be specifically applied in Africa?

CTC can be applied to any vaccine. Currently, the immediate focus is on vaccines that, like MenAfriVac™, are delivered primarily through campaigns, or vaccines that are delivered at specific times to specific target age groups.

Two examples are: the vaccine against Hepatitis B which must be given within 24 hours of birth—a challenge in places where the majority of births do not take place in health facilities; and human papillomavirus (HPV), which is given largely through outreach activities at schools, and in communities, to girls aged 9–13. Currently, there are efforts underway to re-label other vaccines for CTC use. Among them are vaccines against yellow fever, Hepatitis B, HPV, rotavirus and pneumococcal disease.

We also hope that, in the future, manufacturers will build CTC studies into vaccine development so that new vaccines will come to market already licensed for use with CTC. Once that happens, we can start to envision a future where outreach throughout endemic regions can be done without needing to worry about (or carry the weight of) ice.

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