



## 17th TechNet Conference

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Immunization Programmes That Leave No One Behind

[www.technet-21.org](http://www.technet-21.org)

# Update on thermostable and Controlled Temperature Chain (CTC qualified vaccines)

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VIPS

VACCINE  
INNOVATION  
PRIORITISATION  
STRATEGY



World Health  
Organization



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PATH  
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A global collaboration to prioritise and drive innovation to increase equitable vaccine coverage in low- and middle-income countries (LMICs)



# Outcomes of the VIPS prioritisation process in May 2020

## 3 Innovations have been prioritised...

VIPS has prioritised **3 innovations with the broadest public health benefits and broad applicability** that can help **better meet country needs & contribute to coverage and equity goals as well as global health security.**

**Microarray patches**



**Heat stable and CTC qualified vaccines**



**Barcodes on vaccine products**



**... and signaled to the market**

**Providing greater clarity to manufacturers and immunisation partners to make investment decisions**

# Both heat-stable and CTC qualified vaccines are part of the thermostability umbrella

## Heat-stable vaccines



- Refers to **improvement in long-term storage** of vaccines, including shelf-life, e.g., to the following stability targets:
  - From ultra cold-chain to  $-20^{\circ}\text{C}$  or  $2-8^{\circ}\text{C}$
  - From  $-20^{\circ}\text{C}$  to  $2-8^{\circ}\text{C}$
  - From VVM7 or VVM14 to VVM30
- Achieving these improvements may require reformulation and/or other novel or complex thermostabilisation technologies.**

## CTC qualified vaccines

A controlled temperature chain is an optional method of transporting and storing vaccines in carriers

**WITHOUT ICE PACKS** up to a specific number of days before the vaccines are administered.

It is only recommended for vaccines

**OFFICIALLY LABELED FOR THIS USE**

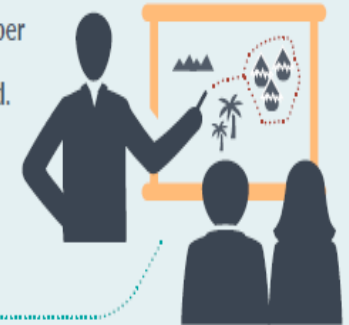
where a pronounced need is apparent and

**TRAINING AND SUPERVISION** are provided.

Vaccines carried in a CTC must be monitored

using a vaccine vial monitor (VVM) and peak temperature threshold indicator (PTTI)

to indicate exposure to heat.



# Heat-stable vaccines and CTC could become potential “game changers” for immunisation programmes



Opportunities for impact



Vaccine introductions and scale-up

Easier introduction of vaccines into programs **without** (CTC for last mile) **or with reduced need of cold-chain** (i.e., UCC/ freezers/ refrigerators for more heat-stable vaccines) especially at lower levels of health facilities



Reaching the unreached

Efficient for last-mile delivery with **less time/ costs/ logistics** for campaigns, outreach and special strategies, especially in areas with constraints to cold-chain. (CTC)



Programmatic and financial sustainability

**Lower vaccine wastage** as lack of vaccine thermostability leads to wastage when vaccines must be discarded after they have been exposed to excessive heat or freezing



Pandemic prevention preparedness and response

**Quicker, more efficient outbreak response** due to less reliance on cold chain, longer shelf-lives or VVM



Climate change

**Adaptation:** Reach displaced populations, humanitarian refugees and other **hard-to-reach populations** that could increase due to climate-related crisis.

**Mitigation:** Reduces cold-chain requirements.

# On thermostable vaccines, VIPS is currently aiming to understand specific country needs before moving forward

## Heat-stable vaccines



- Refers to **improvement in long-term storage** of vaccines, including shelf-life, e.g., to the following stability targets:
  - a. From ultra cold-chain to  $-20^{\circ}\text{C}$  or  $2-8^{\circ}\text{C}$
  - b. From  $-20^{\circ}\text{C}$  to  $2-8^{\circ}\text{C}$
  - c. From VVM7 or VVM14 to VVM30



## VIPS focus

### Targeted country consultations ongoing

- With cold-chain/ supply chain experts, vaccine program managers and EPI managers at national, regional and local levels
- To understand the **incremental thermostability improvements** needed and **acceptable trade-offs**
- Via **survey** and **in-depth interviews**

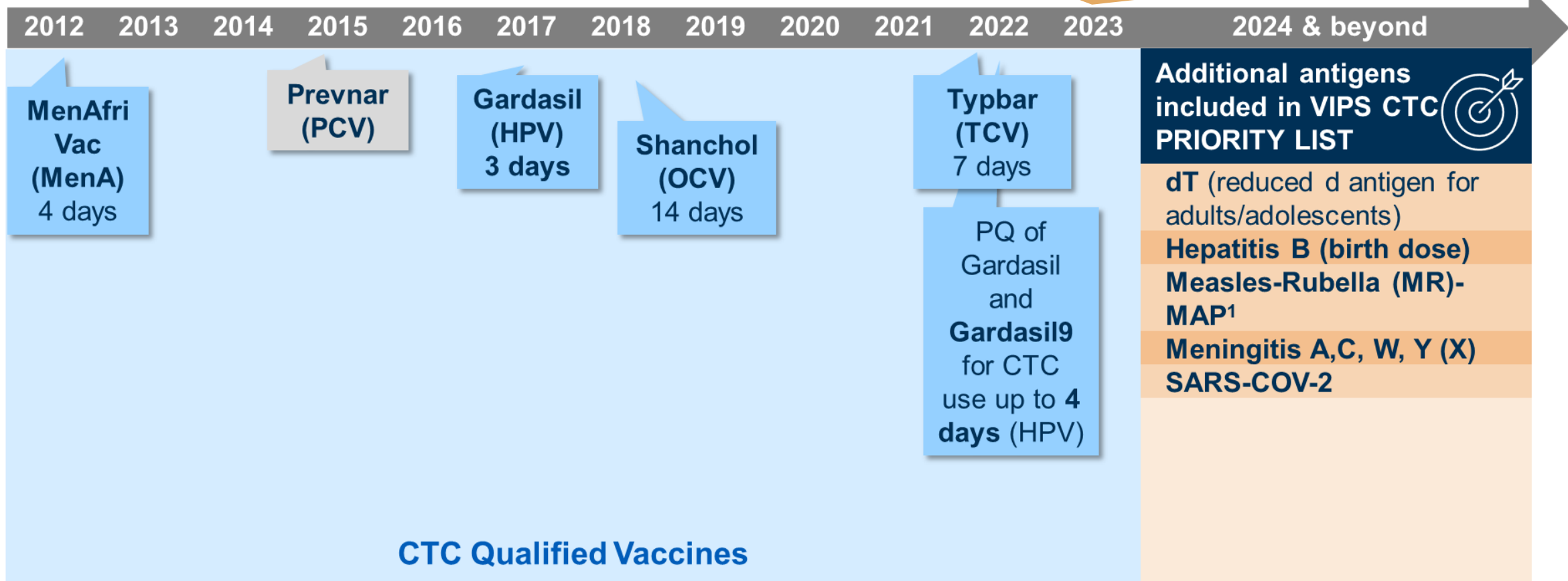
Scan for the survey>>



***We invite you to take this survey (~20-30 mins) as your opinions can inform VIPS as we define next steps on heat-stable vaccines***

# 4 CTC qualified products are on the market & VIPS has identified 5 additional priority antigens for CTC use

SAGE consent to interim off-label guidance on CTC practice for Euvichol (OCV) for up to **10 days**



## CTC Qualified Vaccines

Vaccines can achieve the CTC qualification without reformulation

<sup>1</sup> MR-MAP is included here due to the stage of development and the thermostability data available, but all other vaccines prioritised under the vaccine MAPs prioritisation exercise would be targets for CTC

# To better understand CTC benefits to immunization delivery, we will play a game!





# Orientation to the game

## Mission

Today you will pretend you are all vaccinators working in teams to immunize pre-adolescent girls in the LaEscuela School with **HPV**. The school is a **two-hour** motorbike drive from your health center.

## Team tasks

The teams will begin at the health center, packing the vaccines under either a CTC or a traditional cold chain scenario.

You will move toward the school, administer the vaccines there and return to the health center, happening upon challenges and further instructions along the way. All instructions and everything you need to know is written on your instruction cards and the Scenario cards you will draw along the way.

You will collect “time cards” and depending on the Scenarios you face, you may also collect vaccine waste cards. At the end of the trip you will tally your totals of vaccines administered, vials wasted, and time used. We will then discuss together the experience you had and challenges you encountered along the way.

# Game materials

- Game instructions
- Vaccine carriers
- Vaccines
- Ice packs
- Peak threshold temperature indicator cards (PTTIs)
- TIME cards
- SCENARIO cards
- WASTE cards
- FINISH cards
- Flip chart/White board

## CTC monitoring tools



Peak  
temperature  
threshold  
indicator



Vial marking



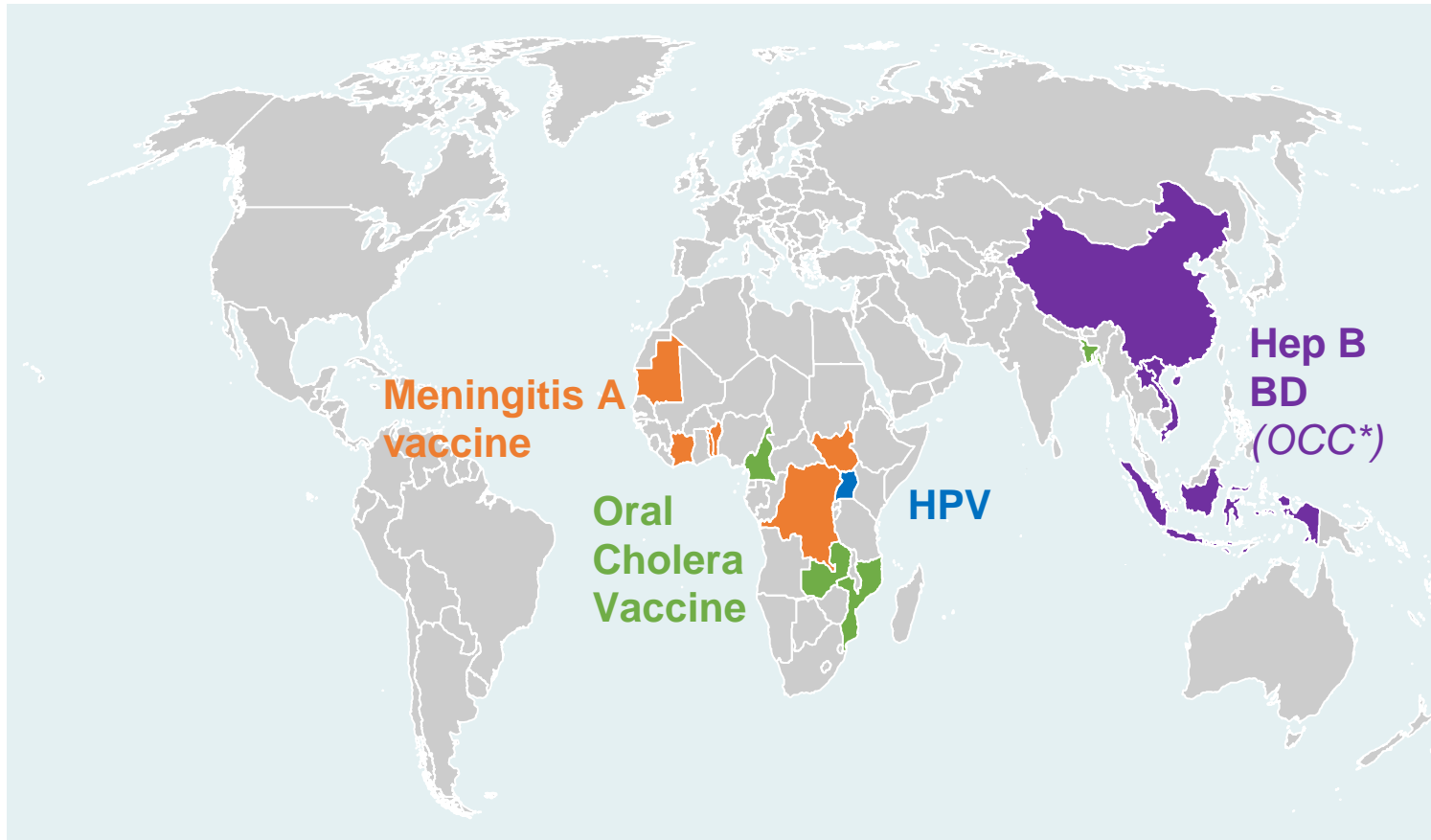
Expiration  
date and  
Vaccine vial  
monitor

# Discussion on the game

- What challenges did you face, in the traditional cold chain and in the CTC chain?
- For those who played using CTC, what would you like to share with the group about your experience?
- Based on this experience, what are the different implications vaccine delivery for outreach settings in the real-world?

# Several activities are ongoing to accelerate CTC adoption in countries (1/2)

15 countries have reported experience using vaccines in a CTC\*



\*Hep-B birth dose was used out of cold-chain in CTC-like conditions

## Development of guidelines or strategic documents

- **2016** - SAGE approval of **HepB-DN** OCC use (off-label)
- **2017** - Publication of the Roadmap on the priority strategy for CTC
- **2022-23** – VIPS action plan & Addendum to the CTC Roadmap
- **2023** – SAGE interim approval of OCV delivery with off-label CTC practice

# One vaccine of importance to CTC moving forward is oral cholera vaccine (OCV) for rapid outbreak response

## Deep-dive on OCV-CTC

- **SAGE recently acknowledged the public health benefits of using the Euvichol-Plus vaccine under CTC conditions** (*not more than 10 days at ambient temperatures not exceeding 40°C*) on an interim basis until Euvichol-S or another new OCV product receives PQ for CTC.
- OCV has been used in CTC-like conditions in **Malawi, Bangladesh, Mozambique and Zambia**.
  - **Positive feedback from healthcare workers** on CTC use to generate demand, experience on safe and compliant use, efficiency gains and improved vaccination coverage.
  - In **Mozambique** the use of OCV in CTC confirmed the **ease of adoption** even in emergency settings and a favourable impact on **timeliness** of vaccination



**Partners and country programs planning an upcoming cholera vaccination campaign and interested in more information on use of OCV in CTC should reach out to WHO & VIPS.**

# VIPS has developed a strategic roadmap to identify key opportunities to accelerate CTC development & adoption

## LONG-TERM VISION

To accelerate qualification of CTC qualified vaccines and enable their use in countries as a tool to help overcome barriers and improve equity in immunization.



**TO\* 1: Impact of CTC is demonstrated** via generation of evidence to enable future decision-making



**TO 2: Value proposition of CTC** is clearly defined and communicated



**TO 3: Industry is incentivised** to develop priority CTC vaccines through an enabling environment



**TO4: Country demand for CTC** is generated and **adequate support** is provided to introduce and use sustainably, beyond pilot introductions

VIPS has commissioned **2 studies** to generate evidence on the impact of CTC – especially on improving **coverage, equity and campaign efficiency**. Planning underway for **HPV and TCV** in selected countries in 2024-25. Evidence on impact is also anticipated for **OCV**.<sup>1</sup>

\* TO: Target Outcome; <sup>1</sup>Evidence on impact is also anticipated for OCV, generated through GTFCC's research agenda.

# Thank You!

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We have a **poster** on CTC experiences in countries – please check it out. You can also join our **discussion within the TechNet Conference Group** (Discussion CTC October 2023)



**Hepatitis B Birth dose (Shanvac®-B) in LAO-PDR (2013)**

**SITUATION:** To overcome low HepB-BD coverage in areas with known cold chain constraints and high rate of home births

**INTERVENTION:** 6-month pilot study to determine impact and feasibility of OCC/CTC policy (28 days at ambient temperatures < 40°C)

**MAIN OUTCOMES:**

- ✓ 27% increase in coverage in intervention districts with no increase in adverse events
- ✓ Good acceptance by healthcare workers
- Preference expressed by MoH for on-label use, no subsequent scale-up of OCC policy.



**HPV (Gardasil) in UGANDA (2017)**

**SITUATION:** Difficult to reach communities: refugee camps and remote villages with more cold chain constraints.

**INTERVENTION:** 2-week pilot during HPV campaign in 2 intervention districts (up to 3 days in ambient temperatures < 40°C.)

**MAIN OUTCOMES:**

- ✓ Where training was strong, CTC implementation was **successful and well accepted**
- ✓ CTC was useful to overcome burdens associated with **cold chain** and **reduce risk of exposure to freezing**
- ✓ Findings led to **CTC increase from 3 days to 4 days** for more flexibility and reduced wastage.



**OCV (Shanchol) in MOZAMBIQUE (2019)**

**SITUATION:** Lack of functional cold chain infrastructure following damage and flooding caused by Cyclone Idai. Need for rapid response to emergency outbreak.

**INTERVENTION:** Use of OCV at 14 days at temperatures up to 40°C

**MAIN OUTCOMES:**

- ✓ **Successful uptake of CTC** after brief training, though some confusion reported on proper handling of PTTIs.
- **Continued demand of CTC unmet** due to discontinuation of Shanchol

# We want to hear from you!

Please scan the QR code to provide responses



- 1. Do you have any questions for us?**
- 2. What is the biggest learning about CTC you will take away today?**
- 3. Based on the discussion, which key vaccine(s) do you want to deliver in CTC?**



# Annex

# One vaccine of importance to CTC moving forward is Hep B birth dose to target out of facility births

## Deep-dive on Hep B Birth Dose

- Gavi has recently **'unpaused' VIS 2018 vaccines** including Hep B birth dose with 6.0 ambition to target **out of facility births**.
- Use of CTC can help reach such remote home-births, with **strong evidence of impact** seen with past experiences **out of cold chain**.

1

### Use in Laos (2016)

Non-random comparison trial showed **27% increase in coverage**

2

### Solomon Islands trial (2017)

Timely BD **coverage** increased from **30-68%** in facilities and from **4-24%** in home births

3

### Cost effectiveness study across 72 countries (2018)

Mathematical modelling showed CTC outreach strategy is likely to be **cost-saving**.

We are currently exploring if Hep B BD vaccines could be qualified for CTC. **Partners and country programs interested in more information about the use of Hep B birth dose in a CTC should reach out to WHO & VIPS.**

# Country Case study no.1

- **WHERE:** LAO-PDR
- **WHEN:** Sep-Nov 2013
- **VACCINE:** Hepatitis B Birth dose – Shanvac®-B
- **HOW:** 28 days at ambient temperatures < 40°C
- **WHY:**
  - a. 6-month pilot study to determine impact and feasibility of OCC/CTC policy
  - b. to overcome low HepB-BD coverage
  - c. Known cold chain constraints
  - d. High rate of home births
- **MAIN OUTCOMES:**
  - ✓ 27% increase in coverage in intervention districts with no increase in adverse events
  - ✓ Good acceptance by healthcare workers
  - ✓ Preference expressed by MoH for on-label use, no subsequent scale-up of OCC policy.



# Country Case study no.2

- **WHERE:** UGANDA
- **WHEN:** November 2017
- **VACCINE:** Human Papillomavirus vaccine (HPV) – Gardasil
- **HOW:** 3 days at temperatures up to 40°C
- **WHY:**
  - a. 2 week pilot study during HPV vaccination campaign in 2 intervention districts (with 2 control districts) to assess impact
  - b. Difficult to reach communities, including refugee camps and remote villages where cold chain constraints are more pronounced.
  - c. Interest to improve coverage and promote equity in vaccination
- **MAIN OUTCOMES:**
  - ✓ Where training was strong, CTC implementation was successful and well accepted
  - ✓ Confirmed need for longer excursions to enable greater flexibility and reduce closed-vial wastage
  - ✓ CTC recognized was useful to overcome burdens associated with cold chain and reduce risk of exposure to freezing



# Country Case study no.3

- **WHERE:** MOZAMBIQUE
- **WHEN:** July 2019
- **VACCINE:** Oral Cholera Vaccine (OCV) – Shanchol
- **HOW:** 14 days at temperatures up to 40°C
- **WHY:**
  - a. Lack of functional cold chain infrastructure following damage and flooding caused by Cyclone Idai
  - b. Need for rapid response to emergency outbreak
  - c. Interest to improve coverage and promote equity in vaccination
- **MAIN OUTCOMES:**
  - ✓ Successful uptake of CTC after brief training, though some confusion reported on proper handling of PTTIs.
  - ✓ New implementation approach moving away from vial marking to bright stickers on secondary packaging showing new CTC expiry date.
  - ✓ Continued demand for CTC unmet due to supply of Euvichol (not yet approved for CTC) rather than Shanchol.

