Controlled Temperature Chain Working Group

CONTROLLED TEMPERATURE CHAIN: Strategic Roadmap for Priority Vaccines 2017-2020

World Health Organization

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I. ACKNOWLEDGEMENTS

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II. ACRONYMS

CDC	US Centers for Disease Control and Prevention
CPAD	compact prefilled autodisable device
CTC	Controlled Temperature Chain
CTC-WG	Controlled Temperature Chain Working Group
DT	diphtheria tetanus vaccine
ECTC	extended controlled temperature conditions
EPI	Expanded Programme on Immunization
GVAP	Global Vaccine Action Plan
HBsAG	hepatitis B surface antigen
Hep B	hepatitis B
HepB-BD	hepatitis B vaccine birth dose
HPV	human papillomavirus
IPAC	Immunization Practices Advisory Committee
JSI	John Snow Inc.
MNT	maternal neonatal tetanus
MSF	Médecins Sans Frontières
OCC	out of the cold chain
OCV	oral cholera vaccine
Q	Quarter
Td	tetanus diphtheria (low dose) vaccine
Tdap	tetanus–diphtheria–acellular pertussis
TSE	total system effectiveness
TT	tetanus toxoid
TT-CV	tetanus toxoid – containing vaccines
UNICEF	United Nations Children's Fund
WHO	World Health Organization

III. INTRODUCTION

The "Controlled Temperature Chain" (CTC) is an innovative approach to vaccine management that allows vaccines to be kept at temperatures outside of the traditional cold chain of +2°C to +8°C for a limited period of time under monitored and controlled conditions, as appropriate to the stability of the antigen. A CTC typically involves a single excursion of the vaccine into ambient temperatures not exceeding +40°C and for a duration of a specific number of days, just prior to administration.

This strategic roadmap takes stock of progress to date and identifies the path forward (2017 to 2020) for the CTC. It reflects the consensus reached by the Controlled Temperature Chain Working Group (CTC-WG), which reports to the World Health Organization's (WHO's) Immunization Practices Advisory Committee (IPAC). The mission of the CTC-WG is to convene key stakeholders to (i) define a shared vision and strategy for CTC; and (ii) to advocate for this innovative vaccine delivery and supply chain strategy, where appropriate, with vaccine manufacturers as well as with potential implementing countries. The overall objective of the global CTC agenda remains the facilitation of vaccine delivery to achieve immunization coverage and equity targets for CTC-qualified vaccines, as per the Global Vaccine Action Plan (GVAP) for 2011 to 2020.[1,i] The CTC approach, in its licensed standards,[2] is believed to be an effective means of improving access to vaccination, especially in middle- and low-income countries with limited resources and poor infrastructures, by rendering the delivery of vaccines more efficient and with broader reach.

This document defines the necessary activities required to meet the objectives for CTC over the next four years, which consist mainly of:

- Improving stakeholder involvement, advocacy and alignment on CTC work streams;
- Increasing the base of evidence in support of CTC and characterising the value proposition of CTC with respect to improving immunization coverage and equity;
- Developing operational guidance and communication tools in support of CTC practices; and
- Supporting efforts towards the licensure and prequalification of appropriate vaccines for CTC.

This roadmap focuses primarily on four vaccine types selected by the CTC-WG and endorsed by IPAC in February 2017: vaccines against human papillomavirus (HPV), oral cholera vaccine (OCV), tetanus toxoid vaccine (including TT [tetanus toxoid] vaccine, Td [tetanus diphtheria low dose] vaccine, or other TT-CVs [tetanus-toxoid-containing vaccines]) and hepatitis B vaccine birth dose (HepB-BD). These four vaccine types are the leading priorities of the CTC programme of work between 2017 and 2020.

This document provides background information about each of the priority vaccines and the current status of CTC efforts, along with the required steps over the next four years (2017 to 2020) to effectively advance the CTC agenda. The roadmap addresses supply and programmatic issues, aiming for priority vaccines to become licensed for CTC use and facilitating uptake of the CTC vaccine delivery approach. The four-year time frame purposefully aligns with the GVAP. The roadmap also includes efforts to identify

[i] The number of vaccines that have either been relicensed or licensed for use in a CTC is one of the indicators of Strategic Objective 6 of the Global Vaccine Action Plan: Strategic Objective 6: Country, regional and global research and development innovations maximize the benefits of immunization; Indicator SO6.4: Number of vaccines that have either been relicensed or licensed for use in a CTC at temperatures greater than the traditional +2°C to +8°C range.

future vaccine candidates for CTC use and encourages a proactive approach to CTC licensure during product development.

Note that execution of the proposed activities will be contingent on effectively securing the necessary funding support.

IV. BACKGROUND ON CTC: PROGRAMME RATIONALE AND PROGRESS TO DATE

CTC has been on the global immunization agenda for many years.[1] Since 2007, WHO and PATH, with support from the Bill & Melinda Gates Foundation, have explored the possibilities of storing and transporting certain heat-stable vaccines in a CTC. Upstream, supply-level investments and initiatives gained momentum with the licensure of the first CTC-compatible vaccine, MenAfriVac® (meningitis A vaccine), which was followed by intensive downstream, programme-level work with countries to ensure successful implementation of this new approach.

Experience so far shows that CTC use of vaccines relieves health workers of many of the burdens associated with ensuring an adequate cold chain to the point of vaccination, thereby freeing health personnel time and resources, improving efficiencies and potentially enabling increased immunization coverage and equity for CTC-labelled vaccines.[3] Vaccinators in the field welcome this new option for vaccine management as it greatly facilitates their work by saving them from burdensome journeys to renew ice stocks and from carrying heavy vaccine carriers. Finally, staff time that would be required to condition ice packs during campaigns is saved and can be redirected back to maintaining routine immunization services, which often are compromised during campaigns. Today, regulatory and WHO prequalification pathways exist to label vaccines for CTC use.[4,5] Two vaccines currently bear such labels; three additional vaccine products should have CTC labels soon; and work towards CTC criteria for six other vaccines is under way. As of May 2017, close to 4 million individuals worldwide have received MenAfriVac® delivered in a CTC in six countries. WHO produced guidance materials for the planning and implementation of CTC in these countries.

This is a pivotal time for advancing CTC use of vaccines. The CTC experience to date has demonstrated that the approach entails a complex agenda of activities at multiple levels; this agenda has progressed well so far but still requires an extensive amount of work and investment. Manufacturers have confirmed their interest and commitment to qualifying vaccines for CTC use. It remains key that this is matched by an equal level of engagement and action by WHO and partners. HPV vaccine was prequalified in mid-2016 and oral cholera vaccine (OCV) is currently under review for CTC prequalification. Some manufacturers of HepB-BD and TT vaccines are preparing to seek CTC licensure. This will require focused