



# Monitoring ambient and cold chain temperatures during delivery of human papillomavirus vaccine in Vietnam and Uganda

## Summary report

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## Introduction

A five-year human papillomavirus (HPV) vaccine demonstration project is under way in Vietnam, Uganda, India, and Peru to generate evidence for government decision-making about successful vaccine delivery strategies to provide HPV vaccine to young adolescent girls. HPV vaccine prevents persistent infection with HPV, the primary cause of cervical cancer, and precancerous cervical, vaginal, and vulvar lesions, which nearly always precede cancer itself. HPV vaccine is a strong candidate for storage and transport in a controlled temperature chain at temperatures higher than the standard 2° to 8°C cold chain storage given its characteristics of high-heat stability and freeze sensitivity.

There have been a number of studies both in the field<sup>1-5</sup> and laboratory<sup>6-8</sup> evaluating the effectiveness of vaccines that are kept out of the cold chain for a defined period of time. Published data on the stability of the Cervarix™ (GlaxoSmithKline Biologicals, Rixensart, Belgium) HPV vaccine show that the product is stable for up to three years when stored at 2° to 8°C with simulated cold chain breaks of either one week at 37°C or two or four weeks at 25°C.<sup>9</sup> A research paper on GARDASIL® (Merck & Co., Inc, Whitehouse Station, NJ, USA) HPV vaccine showed this product to be extremely stable—for periods of 130 months or longer at 25°C. At higher temperatures of 37° to 42°C the vaccine maintained more than 50% of its potency for several months.<sup>10</sup> Furthermore, the storage and handling information for GARDASIL® includes the statement that it can be stored out of refrigeration (at temperatures at or below 25°C/71°F) for a total time of not more than 72 hours.<sup>11</sup>

## Objective

The primary objective of these particular temperature monitoring studies was to gather ambient temperature data during different HPV vaccine delivery strategies and in multiple geographic settings and seasons. These data will be compared to the known heat-stability profile of the HPV vaccines to further the international dialogue on the potential appropriateness of storing and transporting HPV vaccine at controlled ambient temperatures during the final stages of distribution to ease logistics and protect the vaccine from freeze damage. A secondary objective was to collect data about temperatures inside the cold chain (ICC) during storage and transport of HPV vaccines. All vaccines used in the HPV vaccine project studies were approved and licensed by the country governments prior to the study.

## Methods

Temperature surveys were conducted in January, February, May, and June 2009 in Vietnam and in July and October 2009 in Uganda. Twelve health centers in each of two districts in Uganda and the same number of health centers in two provinces in Vietnam were chosen for the study. Participating districts were chosen in order to provide a variety of conditions with respect to rural versus urban setting, mountainous or low-lying

geography, location of immunization (school versus health center), and distance that vaccine was carried during immunization outings. Seasonal differences also occurred across the different sessions in each country.

Small temperature recording devices were attached to the interior and exterior of vaccine carriers during immunization activities and kept in refrigerators with vaccines during storage times. All vaccines were stored ICC at all times. The temperature recorders were kept with the vaccines until the vaccines were returned to the district level. Health workers documented the date, time, and location of each place that the vaccine was stored and administered.

## Notes on climate and weather

In Vietnam, weather patterns vary considerably from north to south and from coastal or delta areas to mountainous regions. In the south the weather is warm with little seasonal variation. For example, in Can Tho monthly average temperature ranges from 25°C in January to 28°C in May.<sup>12</sup> However, in the north, temperatures are hot in the summer and cool in the winter—in Thanh Hoa City average monthly temperature ranges from 17°C in January to 29°C in July.<sup>12</sup> In the northern mountainous regions the temperatures again vary from season to season but do not reach quite as high as in the low-elevation areas.

In Uganda, there are two wet seasons, the wettest from March to May and a lighter rainy season in October and November. Dry seasons are December to February and June to August. Annual rainfall ranges between 500 mm to 2500 mm, and the relative humidity is 70% to 100%. Temperatures are fairly consistent year round with monthly average high temperatures from 25° to 30°C and monthly average low temperatures from 13° to 15°C.

## Results

Detailed results are available in longer reports prepared for each of the country studies. A few key findings are summarized below:

- During the study periods in Vietnam and Uganda, the ambient temperatures recorded by the temperature recorders never exceeded 36°C except in one instance where a single district in Uganda recorded a brief temperature spike to 40.9°C.
- The mean ambient temperatures by study site as measured during the immunization sessions in Vietnam ranged from 10.4° to 26.9°C in January and February and from 22° to 31.8°C in May and June.
- In Uganda, the average ambient temperatures during immunization outings ranged from 22.2° to 30°C.
- In both countries we learned that there is a risk of exposing vaccines to temperatures below the recommended limit during storage and transport.

It is important to note that the data collected in this study only reflect the temperatures that the loggers were exposed to; therefore, we cannot conclude absolutely that vaccines were exposed to the same temperatures as the ICC recorders. Variations in temperature in different areas of the refrigerator or carrier and variations in user compliance with study protocols could lead to differences between temperatures of the logger and the vaccine.

## Conclusions

Based on the data collected in these studies, the following conclusions are drawn:

- If 37°C were to become established as a limit for HPV vaccine exposure, as supported by some manufacturers' published stability data, then this study shows the possibility of managing vaccine sessions in these geographic areas under ambient temperature conditions that are within that limit.
- The data collected from vaccine carriers and refrigerators during this study demonstrate that the cold chain is sometimes colder than recommended. This is consistent with previous findings from multiple studies around the world.<sup>13</sup> It is important to practice good temperature management to prevent exposure of freeze-sensitive vaccines to freezing temperatures. Vaccine storage and transport in a controlled temperature chain higher than the traditional 2° to 8°C could be one strategy to manage the risk of vaccine freezing.
- Currently, studies are ongoing to evaluate the stability of several hepatitis B vaccine products at 37°C. If results are positive, this study indicates that ambient temperatures in Vietnam and Uganda might also be compatible for hepatitis B vaccine storage and transport over similarly short time periods.
- More testing could be done by manufacturers or research institutes to better understand the behavior of vaccines that are kept at higher temperatures or that experience fluctuating temperatures. Similar studies such as this one could be conducted in other countries with varying climates and weather to gain further knowledge on locations and situations where storage and transport of vaccines at controlled ambient temperatures might be feasible and useful.

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