

## FREQUENTLY ASKED QUESTIONS

# Time temperature indicators for oxytocin

## Monitoring heat exposure of a common drug used to prevent and treat postpartum hemorrhage

### WHY MONITOR THE HEAT EXPOSURE OF OXYTOCIN?

Oxytocin is the World Health Organization's (WHO's) first-line drug for prevention and treatment of postpartum hemorrhage (PPH). WHO recommends that every woman receive a dose of oxytocin within two minutes of giving birth.<sup>1</sup> It is widely recognized that currently available oxytocin preparations lose potency at elevated temperatures. Like other heat-sensitive drugs, undetected heat damage creates the possibility of less-effective oxytocin being administered.<sup>2</sup> Specifically, WHO recommends that oxytocin should be kept protected from light and unless otherwise indicated on the label stored at a temperature between 2°C and 8°C.<sup>3</sup>

### WHAT ARE TIME TEMPERATURE INDICATORS?



Photo: PATH/Umit Kartoglu.

Time Temperature Indicators (TTIs) are visual indicators of cumulative heat exposure. In their simplest form, these small circular labels can be adhered to or printed directly on drug or vaccine packages, labels, and vials. Each TTI's inner square is chemically active and changes color irreversibly from light to dark as the product is exposed to heat over time. By comparing the color of the inner square to the reference color in the outer circle of the indicator, health care workers can determine if the product has been exposed to too much heat before deciding to use or discard the drug.

A widely used type of TTI is the vaccine vial monitor (VVM). The United Nations Children's Fund requires these on all vaccines it procures. As of 2014, more than 5 billion

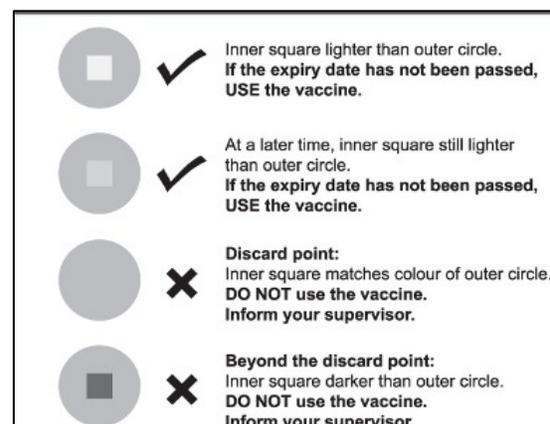
VVMs have been used with vaccines distributed throughout the world. Temptime Corp. of New Jersey is the commercial manufacturer of some of the most widely used TTIs and VVMs.

### WHAT ARE THE BENEFITS OF TTIs?

Following the lead taken by the vaccine community, use of TTIs with oxytocin could improve quality assurance. Without a TTI there is often no way of knowing whether a dose of oxytocin has been exposed to excessive heat during transit or storage. TTIs can also help improve stock management by enabling health care workers to make informed decisions about which doses to use first by checking the color of the TTI. Additionally, TTIs could improve the ability of programs to temporarily transport and store oxytocin outside of the formal cold chain by providing a record of heat exposure.

Providers and pharmacy managers felt that having the TTI was a distinct advantage because providers could easily tell if the unit had been exposed to prolonged high temperatures that would decrease its effectiveness.<sup>4</sup>

### How to read a TTI



Graphic designed by PATH and adapted from WHO.

## DO INDIVIDUAL AMPOULES NEED A TTI?

While it would be ideal to include a TTI on each ampoule of oxytocin, this could lead to a noticeable increase of the per-dose cost, given the low selling price (often below US\$.15 per ampoule)<sup>5</sup> of most oxytocin. An alternative is to incorporate one TTI per pack of oxytocin ampoules to spread the TTI cost across multiple doses. This could help to improve the assurance of oxytocin quality even if individual ampoules were separated from the TTI pack for a short time before use.

## DO TTIs NEED TO BE ADDED AT POINT OF PRODUCTION?

Typically TTIs are added to a drug or vaccine at the point of production during labeling and packaging. This requires significant cooperation from drug producers—a process that can be challenging for widely produced generics such as oxytocin. Alternatively, countries could add a TTI to each box of oxytocin ampoules at the central, in-country warehouse before distribution throughout a country.

## WHAT ARE TTI CARDS?

In addition to the individual label format, TTIs are also available in a card format which can be inserted into a box or pack of individual doses.



Photo: PATH/Patrick McKern.

## DOES ADDING A TTI INCREASE THE COST OF OXYTOCIN?

Adding a TTI will add to the cost of oxytocin, just as it adds to the cost of other vaccines or drugs. However, the benefits in terms of assured quality could outweigh the added cost.

Even with the addition of a TTI, oxytocin remains a low-cost solution for the treatment and prevention of PPH.

## DO TTIs MEASURE OXYTOCIN POTENCY LOSS?

TTIs measure heat exposure, and heat exposure is correlated with loss of potency for oxytocin. However, TTIs do not directly measure the potency of oxytocin or any other drug or vaccine.

## DOES USING A TTI MEAN THAT GOOD OXYTOCIN WILL HAVE TO BE DISCARDED?

TTIs serve a similar function as drug expiration dates. If the TTI indicates excessive heat exposure, the full potency of the drug—such as oxytocin—can no longer be ensured. The same is true of expiration dates. Drugs do not suddenly degrade when they reach their expiration dates; however, the probability increases that the drug no longer meets specifications. Using a TTI allows health workers to make better-informed decisions on whether to use a drug.

## MORE INFORMATION

For additional information about VVMs, please see PATH's web page, "World's smartest sticker" at [http://www.path.org/projects/vaccine\\_vial\\_monitor.php](http://www.path.org/projects/vaccine_vial_monitor.php).

## REFERENCES

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