ISSUE BRIEF

MÉDECINS SANS FRONTIÈRES ACCESS CAMPAIGN

VACCINATING CHILDREN BEYOND THE 'COLD CHAIN':

EXTENDING THE HEAT STABILITY OF VACCINES

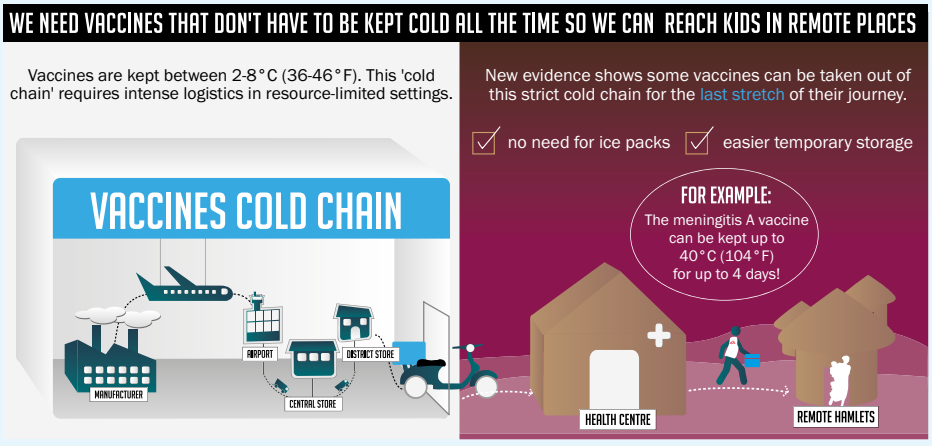
"In many places, you can often arrive at a health centre – a place that should be buzzing with children – to find it is totally empty, no staff or anything. You understand why when you see that the fridge to store the vaccines is broken and no child has been vaccinated in months."

DINA HOVLAND, MSF NURSE AND MIDWIFE

More than 22 million children worldwide did not complete basic childhood vaccinations in 2012 and an estimated 1.5 million children aged under five die every year from vaccine-preventable diseases.[1]

Shipping and storing vaccines in a 'cold chain' in the tropical heat of many resource-limited countries – whereby the vaccine is kept at temperatures between 2°C to 8°C from the point of manufacture until reaching the recipient – is a tremendous challenge and a major cause of poor immunisation coverage rates. Ministries of Health and organisations such as Médecins Sans Frontières (MSF), which carry out vaccination in developing countries, struggle with the immense task of keeping vaccines within the recommended temperatures in contexts where infrastructure is weak and electricity supply and refrigeration unstable.

Growing evidence shows that some vaccines can be safely kept outside the cold chain for certain periods of time. This more flexible use of the cold chain is called the *'controlled temperature chain'* (CTC) or a *'flexible cold chain.'* This approach has considerable potential benefits, including cost savings, preventing vaccine damage caused by accidental freezing, and, most importantly, making it easier to reach children living in remote places who would otherwise remain unvaccinated. However, very few vaccine manufacturers have released information on, or further studied, the stability of their vaccines outside the typical recommendation of keeping vaccines at between 2 to 8°C. This is in part because there is little to no need for a more flexible cold chain in wealthy countries, where refrigeration is unproblematic, and therefore there is little incentive for companies to pursue this matter. It is crucial that manufacturers, regulators and national immunisation programmes work towards evaluating and approving the use of vaccines in a CTC where possible.



ACCESS CAMPAIGN
MEDECINS SANS FRONTIERES

MSF Access Campaign

Médecins Sans Frontières, Rue de Lausanne 78, CP 116, CH-1211 Geneva 21, Switzerland

Tel: + 41 (0) 22 849 84 05 Fax: + 41 (0) 22 849 84 04 Email: access@msf.org

www.msfaccess.org facebook.com/MSFaccess twitter.com/MSF_access


© Pascale Zintzen

"The closer to the patient, the more critical transport can become. In the Democratic Republic of the Congo, for example, large cold boxes are hand-carrier over rough paths which sometimes need to be cleared of vegetation, or include river crossings, in order to reach the vaccination sites."

MALCOLM TOWNSEND, MSF COLD CHAIN LOGISTICIAN.

COLD CHAIN MANAGEMENT IN RESOURCE-LIMITED SETTINGS: A CONSIDERABLE CHALLENGE


© Ikram N'gadi / MSF

In resource-limited settings, transporting vaccines in cold chain requires insulated containers filled with frozen icepacks ('passive cold chain'). These ice packs take 24 hours in a freezer to freeze. Once frozen, they need to be 'conditioned' (i.e. reach an appropriate temperature just above 0°C) in order to prevent accidental freezing of vaccines in the container. In the case of vaccination campaigns, where thousands of people in remote areas need to be vaccinated over a short period of time, transporting vaccines creates an immense logistical burden, and can sometimes present an insurmountable obstacle.

Today, nearly all vaccines are recommended to be constantly kept between 2˚C to 8˚C from the manufacturing site until they reach the recipients.

But maintaining a continuous cold chain in resource-limited settings where power supply is non-existent or unreliable is a considerable task. The GAVI Alliance, which supports the rollout of new vaccines in developing countries, estimates that half of the healthcare facilities in the poorest countries have no electricity supply at all, with only 10% having a reliable electricity supply.[2] New tools such as solar refrigerators, and older ones such as kerosene refrigerators, can definitely help. But they are very expensive and maintaining them is also a challenge.

Unintended interruption of the cold chain, or 'ruptures', are not uncommon and often harm vaccine efficacy. These ruptures include exposure to high heat, as well as damaging exposure to temperatures below 0°C. Improving cold supply chains should clearly be prioritised by immunisation programme donors.

COLD CHAIN: COUNTING THE COSTS

- A review published in 2007 concluded that 35% of vaccines in developing countries were exposed to extended periods of accidental freezing in the cold chain.[3]
- UNICEF audits in 2011 in several countries in West and Central Africa reported that more than US$1.5 million worth of vaccines were damaged in five months alone as a result of cold chain ruptures.[4]
- The GAVI Alliance estimates that $650 million is needed by 2020 for new cold chain equipment in the countries supported by the organisation.

WHAT IS MEANT BY VACCINE STABILITY?

The stability of a vaccine is defined as its ability to retain its chemical, physical, microbiological and biological properties within specified limits throughout its shelf-life. If a vaccine's stability is compromised – through exposure, for instance, to temperature variations – the vaccine may lose some or all of its efficacy.

VIEW FROM THE FIELD


© Ikram N'gadi


© Ijean Hereu

"At the base, where we hold our stock, we have 17 fridges full of the vaccines. We also have the 17 freezers to make and store the 5,000 ice packs we need. The ice packs go into a big cold box which is taken out to the vaccination sites. But even there, we then have to transfer the vaccines from the big cold box, into smaller cold boxes, because at each single stage we have to protect the vaccines so that they remain effective. It's a nightmare."

SOPHIE DUNKLEY, EPIDEMIOLOGIST, MSF MEASLES VACCINATION CAMPAIGN, GUINEA, FEBRUARY 2014

SOME VACCINES ARE MORE HEAT-STABLE THAN OTHERS

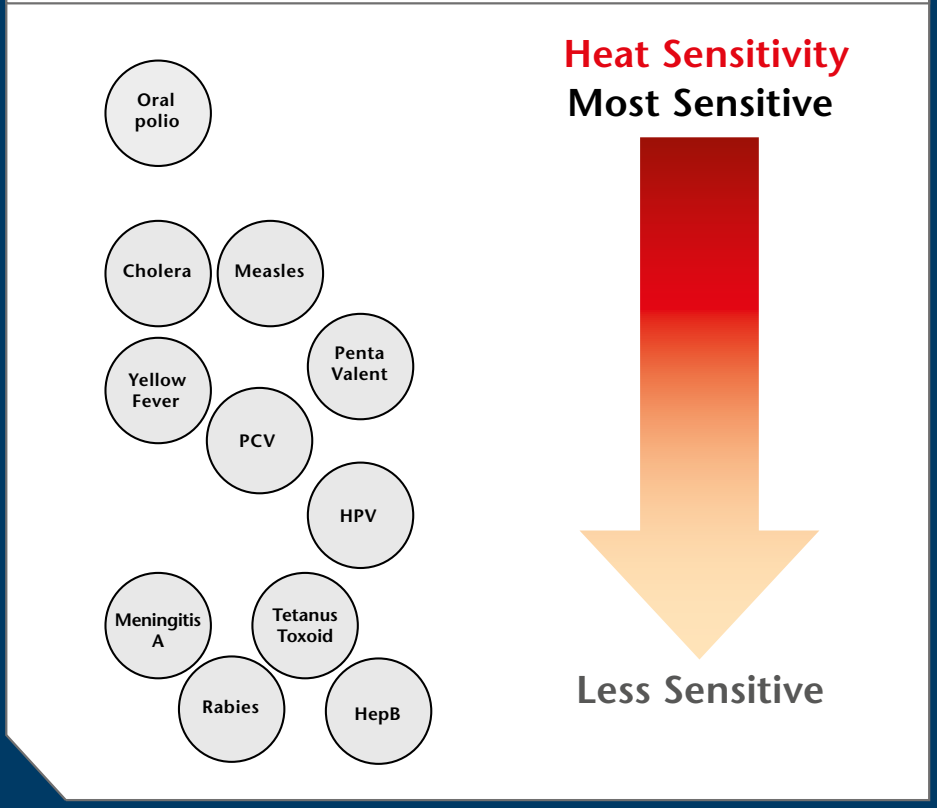
While for more than 30 years, the number one rule for storing and transporting all vaccine products has been to keep them at between 2° to 8°C, some vaccines are actually much less sensitive to heat than others and have the potential to be kept out of a strict cold chain for periods of time without compromising their efficacy.

As some vaccines are exposed to stability tests at different temperatures during their preclinical development, some heat stability data is already available. The Program for Appropriate Technology in Health (PATH) and the World Health Organization (WHO) have recently started to compile this data.[5]

Rabies vaccines, pneumococcal conjugate vaccines (PCV), human papillomavirus vaccines (HPV), hepatitis B vaccines, and tetanus toxoid vaccines are among the least sensitive to high temperatures. On the other end of the spectrum, the oral polio vaccine is one of the most sensitive to heat.

SENSITIVITY TO HEAT OF DIFFERENT TYPES OF VACCINES (SOURCE: PATH/WHO 2013[5])

Note: Individual vaccines of the same type but from different manufacturers can have different stabilities.



A FLEXIBLE COLD CHAIN COULD ALLOW VACCINES TO REACH REMOTE COMMUNITIES MORE EASILY

While there is a clear and immediate need to improve supply and cold chains in developing countries, it is also time to consider using the most heat-stable vaccines outside the cold chain for a certain period of time.

The theory behind a '*controlled temperature chain*' (CTC) or '*flexible cold chain*' is that some vaccines may be transported at ambient temperatures for the last stretch of their journey. In practice, a CTC allows a specific vaccine to be kept at ambient temperatures, up to a specified temperature threshold (e.g. 40°C), for a limited period of time immediately preceding the administration of the vaccine. Up until this 'excursion' from the cold chain, the vaccine should continue to be kept in the traditional 2°C to 8°C cold chain.

A CTC approach would have huge benefits during vaccination campaigns in resource-limited settings. Campaigns require the transport of hundreds or thousands of vaccine vials in insulated containers – cold boxes – filled with frozen ice packs. If vaccination campaigns could be freed up from these demands, it would considerably alleviate the burden on vaccinators who often have to walk long distances, carrying vaccine carriers and cold boxes to reach the most remote communities. Without the need for cold boxes, more vaccines could be carried, and therefore more children vaccinated with the same amount of effort.

How removing the need for ice packs could help:

- Eliminate the need for freezers to prepare the ice packs
- Remove the risk of vaccine damage caused by accidental freezing
- Increase available space (up to two-fold) for vaccine vials inside the vaccine transport containers
- Reduce weight of the containers by half.

MENINGITIS VACCINE IN CTC: MORE CHILDREN REACHED, AT LOWER COST

A recent study[6] has calculated the potential economic benefits of keeping vaccines at ambient temperatures during vaccination campaigns. The case study is based on data collected in Chad for a vaccination campaign in 2011 against meningitis A, using MenAfriVac. At the time, this vaccine was not yet approved for use in a CTC. The costs of the logistics and strict cold chain used for the 2011 campaign amounted to US$0.24 per person vaccinated. Modelling subsequently found that if the vaccine had been kept in a CTC, the logistics costs would have been halved, to only $0.12 per person. When vaccinating millions of people, this represents a massive cost reduction. Most importantly, using a CTC means that more children can be reached.


© Ikram N'qadi

CAMPAIGN VACCINES ARE FIRST IN LINE FOR THE CTC APPROACH:

Vaccines that would currently benefit most from a CTC approach are mainly those which are often used in specific mass vaccination activities, typically called vaccination "campaigns."

Vaccines such as yellow fever and measles are already widely in use in mass preventive or reactive campaigns. The oral cholera vaccine is also likely to be increasingly used this way in the future to prevent or react to outbreaks. As part of the global effort to eliminate maternal and neonatal tetanus, multiple campaigns to immunise tens of millions of women of child-bearing age with the tetanus toxoid vaccine are planned to take place before 2015. Following a collaborative study by MSF and partners[i] showing that the Serum Institute of India's tetanus toxoid vaccine is still stable and immunogenic after being exposed to high ambient temperatures (up to 40°C) over 30 days (SEE BOX on page 6), this vaccine will hopefully soon be re-licensed with new temperature recommendations to facilitate such campaigns.

Some of the newest vaccines are also being used with special delivery strategies. HPV (human papillomavirus vaccine) and to a lesser extent PCV (pneumococcal conjugate vaccine), fall into this category. Outreach activities with the HPV vaccine are planned in many developing countries to vaccinate teenage girls in secondary schools, where cold chain systems may not be adequate. PCV mass vaccination campaigns are increasingly being considered, following MSF's experience using PCV in a refugee camp in South Sudan in 2013.

At the moment, global CTC efforts are focused on alleviating the logistical burden associated with the mobile vaccination activities outlined above. They are not prioritising the vaccines that are nearly exclusively used in fixed healthcare settings for routine immunisation, such as the pentavalent vaccine (combined diphtheria-tetanus-pertussis-hepatitisB-Hib vaccine) or the rotavirus vaccine. However, in the future, very heat-stable products that could be kept at ambient temperatures for longer than one month could help to remove the need for permanent refrigerators in more remote health centres. This may not be possible for most current vaccines used in routine immunisation, but is an achievable target for the next generation of vaccines in the pipeline.

i MSF's partners: Epicentre, the Ministry of Health of Chad, OPTIMIZE (WHO / PATH) and the Institut Scientifique de Santé Publique de Bruxelles

> *"We spend hundreds of thousands of euros each year just on the equipment alone – the fridges, the freezers, the monitoring tools that we need in order to make sure that these vaccines stay effective."*
>
> **MALCOLM TOWNSEND, MSF COLD CHAIN LOGISTICS**

ROUTINE IMMUNISATION VERSUS VACCINATION CAMPAIGNS

Routine immunisation refers to immunisation activities in fixed health posts that should be available at any time as part of a country's Expanded Programme on Immunisation (EPI). The World Health Organization recommends that all children around the world receive 11 vaccines as part of the standard EPI package.

Vaccination campaigns are usually deployed either in reaction to a specific outbreak of a disease in order to contain its spread, or as a preventive measure to head off any potential outbreak in high-risk settings. In addition, in districts where coverage of routine immunisation services in fixed health posts is low, "catch up" campaigns with some specific vaccines are typically set up to reduce the number of children left unvaccinated. Usually only one or two vaccines are included during campaigns. This kind of vaccination activity may take place over a wide geographical area, over a comparatively short amount of time – several days to a week – requiring a considerable logistical burden to transport and store the vaccines outside the health centre.

AIM HIGH: FIVE VACCINES TARGETED FOR CTC USE BY 2020?

The Global Vaccine Action Plan (GVAP), endorsed by major global health stakeholders as the overarching framework for global vaccination activities over the decade 2010 – 2020, recognises the need to use more vaccines in a flexible cold chain and includes a CTC indicator as a part of the targets set in the plan.

Unfortunately, the GVAP does not include a specific target on how many vaccines should be re-licensed for CTC use by 2020. MSF would like this objective to be quantified and calls for five different vaccines to be licensed or re-licensed for use in a CTC during the Decade of Vaccines. This is an ambitious but realistic target.

TAKING TETANUS TOXOID VACCINE OUT OF THE COLD CHAIN

In 2013, MSF and Epicentre, its research arm, together with partners,[ii] carried out a two-phase study to determine the stability and continued efficacy of the tetanus toxoid vaccine produced by the Serum Institute of India, when kept in a controlled temperature chain at ambient temperatures of up to 40°C for up to 30 days.

In the initial phase, laboratory tests confirmed that the vaccine retained its chemical and biological properties, under these conditions.

The second phase was a clinical study undertaken in the Moissala district in Chad to see how effective the vaccine remained in practice, under similar conditions. The participants – all women of childbearing age – were assigned to two groups and received two doses of the tetanus toxoid vaccine: in the control group of the study, vaccines were kept in a strict cold chain; in the other group, vaccines were kept out of the cold chain for up to 30 days at up to 40°C. The study showed that participants in both groups reached adequate levels of protection against tetanus.

These results strongly suggest that the Serum Institute of India's tetanus toxoid vaccine, when used in a CTC, maintains its efficacy. As campaigns targeting women of child bearing age with tetanus toxoid vaccine are part of the global strategy to eliminate maternal and neonatal tetanus, these results could help to reach the millions of poorly immunised women who live in remote areas where access to routine tetanus immunisation is very limited.

epicentre
ÉPIDÉMIOLOGIE • EPIDEMIOLOGY

ii The Ministry of Health of Chad, OPTIMIZE (WHO/PATH) and the Institut scientifique de Santé publique de Bruxelles.

BREAKING THE REGULATORY VICIOUS CIRCLE: ALLOWING THE USE OF EXISTING VACCINES IN CTC

In order for a vaccine to be authorised for use, it must first be approved by the medicine regulatory agency of the country of manufacture and then by the regulatory bodies of every single country where it will be used. Any change in the vaccine's packaging, formulation, administration or any other variation, including new storage conditions, also needs to be approved by the same regulatory agencies.

This process is more colloquially known as *'re-licensing'* or *'re-labelling'* and can be time-consuming. Companies are reluctant to seek re-licensing of their vaccines for use in extended temperature conditions. Although considerable data is already available on the heat stability of most vaccines, which could form the basis of a good case for re-licensing, only one single vaccine, MenAfriVac, has completed the process successfully and been approved for use in a CTC to date.

WHO, whose guidance is carefully followed and trusted by many developing countries and humanitarian organisations, should ideally play a pivotal role in promoting appropriate re-licensing to enable more vaccines to be used in a CTC in resource-limited settings. However, as the WHO prequalification programme is not technically a regulatory agency, it cannot itself approve or recommend new storage conditions beyond those set out by the medicine regulatory agency of the country where the vaccine is manufactured.

In an attempt to overcome this obstacle, WHO has started consultations with some regulatory agencies in order to clarify what type of *in vitro* or clinical bridging studies are required to demonstrate that a specific vaccine can be safely used at ambient temperatures. Additionally, the aim is to standardise the definition of CTC, so that the temperature thresholds under which vaccines used in a CTC must be kept, do not change from one vaccine to another.[7] WHO intends to release guidance to inform the labelling and re-labelling of vaccines for use in CTC before the end of 2014.

As for now, the obstacles remain in place; for instance WHO cannot recommend even minor changes in cold chain requirements for Pfizer's pneumococcal vaccine, because the Food and Drug Administration (FDA) in the US, where the vaccine is produced, does not yet allow any sort of flexibility outside the 2° to 8°C temperature range for this product.

Likewise, the medicine regulatory agency of the country of manufacture may choose to adjust temperature requirements in a way that is relevant only to the country's own climate, infrastructure and setting. This is the case of the authorisation granted by the US FDA to Merck for its HPV vaccine. The vaccine is approved for use up to 72 hours at temperatures at or below 25°C. This is only really useful for clinics in the US equipped with air-conditioning, but not for resource-limited tropical settings where ambient temperatures often reach 40°C.

In addition, re-licensing a vaccine for CTC may incur additional costs to vaccine manufacturers, as more heat stability studies may be needed. Unless procurement agencies and donors provide incentives for vaccines that are licensed for use in a CTC, most companies will continue to be reluctant to pursue this time-consuming and costly regulatory process.

© Nabila Kram

While clearly a complex procedure, these potential regulatory blockages are also used as an excuse for inaction by some vaccine producers. This is happening right now with the inactivated polio vaccine (IPV), the worldwide roll-out of which is about to start as part of the global polio eradication plan. Sanofi-Pasteur's IPV, one of the principal products, likely has a good thermostability profile, with potential to be kept in CTC, but very scarce data has been disclosed. Sanofi-Pasteur claims it is not worth striving to get its IPV vaccine approved for use with a different temperature range, because, it says, the regulatory process would take years.

Regional regulatory networks in developing countries are currently in the process of being set up. Streamlining regulatory pathways to assess and approve wider variations in vaccine storage conditions should be a priority for these new regulatory bodies, in collaboration with related national medicine regulatory agencies, so as to ensure that more vaccines are adapted to the conditions of use in resource-limited settings.


© Guillaume Ratel

MENAFRIVAC: AN EXAMPLE OF REGULATORY ACTION TO FOLLOW

In 2012, the Indian drug regulatory authority approved the delivery in a controlled temperature chain of the meningitis A conjugate vaccine (MenAfriVac), produced by the Serum Institute of India. WHO swiftly followed suit in the same year, and has approved the use of MenAfriVac out of the cold chain for up to four days at up to 40°C, provided that proper temperature monitoring tools are used.[8] As a result, Benin has already started campaigns, using the vaccine in a CTC.

PULLING POWER: HOW VACCINE PURCHASERS CAN STIMULATE THE MARKET FOR HEAT-STABLE PRODUCTS

Under the current research and development (R&D) model, where investments in product development are driven by the potential to charge high prices, industry is neither incentivised nor mandated to develop vaccines tailored to the realities of resource-limited settings.

As a result, developing country climate and infrastructure conditions aren't considered when bringing a vaccine through the development pipeline. But the high purchasing power of UNICEF, the GAVI Alliance (in 2011, GAVI bought vaccines for 73 countries representing 57% of the world's newborns), PAHO, and others such as the Gates Foundation, could redress this market failure, by favouring vaccines from manufacturers who deliver better-tailored products.

For example, there are currently four producers of measles vaccines prequalified by WHO. But none of them is yet validated for use in a CTC. Producers who make the effort to pursue the regulatory pathway in order to get their vaccines approved for use in a CTC, could be rewarded by the donors that support measles vaccination campaigns. This could take the form of prizes, financial premiums, or the grant of a larger share of the market.

Preferential procurement by large purchasers, prizes, or push and pull funding to enable targeted clinical development, could also positively impact the characteristics of new

vaccines currently in the product development pipeline. Several PCV or rotavirus vaccines, as well as new vaccines for pathogens currently unaddressed by any vaccine (e.g. malaria, dengue), are in clinical development.

There is still time for the companies involved to fine-tune the profile of their final products, include extended thermostability testing during development, and prioritise stabilisation against high temperatures so that the vaccines are better suited for use in settings where cold chain is a tremendous challenge.

In combination with preferential procurement by donor agencies, governments or other push or pull funding initiatives, the target product profiles set by WHO – which determine the characteristics sought from future vaccines and are used to guide the R&D strategies of many companies and institutes – need to incorporate clear and ambitious attributes in terms of heat stability.

SHARING NEW TECHNOLOGIES, SPREADING THE KNOWLEDGE

New technologies have already been developed to better protect both vaccines and adjuvants from damaging exposure to heat and cold (adjuvants are added to vaccines to help stimulate the recipient's immune system response).

These technologies should now be shared more widely among scientists and companies. The method developed by PATH for instance, to protect some liquid vaccines from freezing, has been put in the public domain without any intellectual property restrictions, so that companies can appropriate it for their own products. Similar collaborative provisions should be incorporated into the recent deal between the Bill & Melinda Gates Foundation and GlaxoSmithKline (GSK) to increase the stability of the AS01 adjuvant that is used in different vaccine candidates, including GSK's malaria vaccine candidate.

WHAT NEEDS TO HAPPEN

A more flexible management of the cold chain for the last stretch of a vaccine's journey can help us reach more people with life-saving vaccines in resource-limited settings. After more than three decades of strict cold chain rules, it is time to take advantage of the existing potential of some current vaccine products to be kept in a controlled temperature chain, as well as to develop more thermostable new vaccines in the future. For this to happen, coordinated efforts by pharmaceutical companies, regulatory authorities, Ministries of Health, WHO, UNICEF, the GAVI Alliance and other global health stakeholders are required.

- **The vaccination community** must push for current vaccine products to be used at their full thermostability potential, while continuing to invest in improving cold chain capacity. Vaccines used during vaccination campaigns – and not in routine immunisation activities – are the priority targets in the immediate term.
- **Ministries of Health** in affected countries and agencies providing technical assistance to immunisation programmes should support the implementation of vaccination activities in a controlled temperature chain (CTC) at national level. This needs to happen now for campaigns with MenAfriVac, and it may be soon possible to do so with the tetanus toxoid vaccine produced by the Serum Institute of India.
- **WHO** should finalise its guidelines on regulatory requirements for re-licensing of vaccines in a CTC adapted to the conditions and needs of developing countries; regulatory agencies in countries of manufacture should expedite the review of the stability data submitted by producers accordingly.
- **Ministries of Health** of affected countries should be voicing the need for more thermostable vaccines to key players like GAVI.
- **GAVI and UNICEF's** procurement policies should be designed to set preferences for vaccines adapted to resource-limited settings, including heat-stable vaccines, to create incentives so that companies are encouraged to develop them.
- **Manufacturers** should include ambitious heat-stability targets in their next-generation vaccines. In the shorter term, they should actively seek regulatory approval of their vaccines with optimised temperature requirements. This involves sharing all their thermostability data with regulatory authorities, and conducting additional studies as needed.

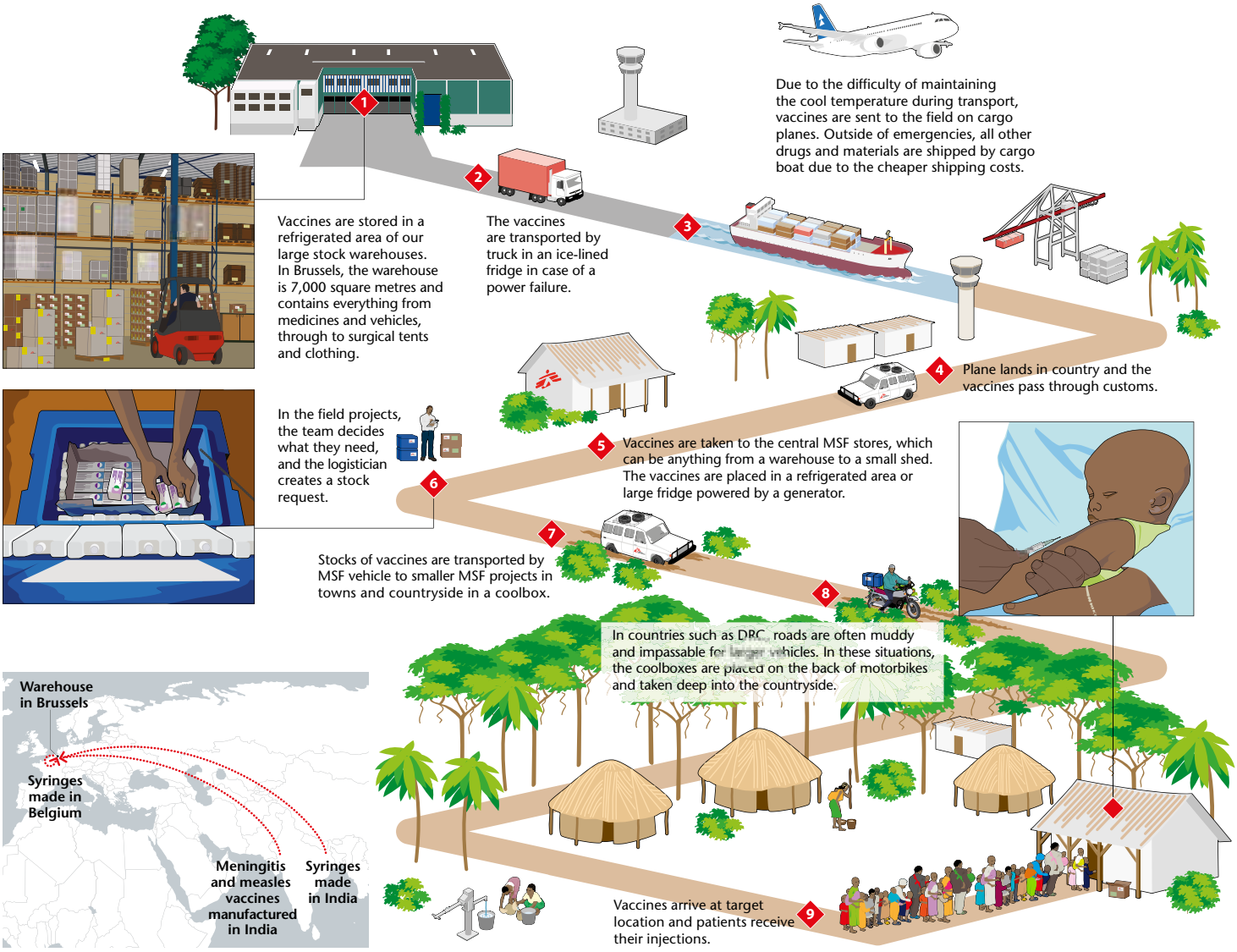
In particular:

- All producers of vaccines most frequently used in vaccination campaigns today and in the future (i.e. measles, yellow fever, cholera) should conduct more heat-stability studies and share the results publicly to determine whether they can be used in a controlled temperature chain (CTC). These producers include **Sanofi-Pasteur, Shantha, Serum Institute of India, Bio-Manguinhos and Biofarma.**
- **Pfizer's** PCV 13 is already known to be stable for several days at high temperatures. Based on these data, the company should actively pursue re-licensing the vaccine for use in a CTC adapted to hot climates.
- **Merck's** HPV vaccine is approved for storage at up to 25°C for up to three days in the US. A complementary recommendation of up to 40°C is needed for resource-limited tropical settings.
- **GSK** should start conducting studies to determine the safety of its preservative-free HPV and PCV multi-dose vaccines if open vials are left at temperatures up to 40°C.
- **Sanofi-Pasteur** and other suppliers of IPV should disclose the true heat-stability of their vaccines and start conducting additional needed studies.


© Yann Libessart/MSF

MSF AND VACCINATION

Each year, MSF teams vaccinate millions of people, primarily as an outbreak response to diseases such as measles, meningitis, diphtheria, pertussis and yellow fever. In 2012, MSF vaccinated 496,000 people against meningitis in response to outbreaks of the disease, and in the same year 690,700 people were vaccinated against measles also in response to outbreaks. MSF also supports routine immunisation in the places where where we provide healthcare to mothers and children. In 2012, routine vaccination was administered to 432,000 children.



1 2008 estimates, The WHO Global Health Observatory: http://www.who.int/gho/immunization/en/ accessed 26 December 2013

2 The GAVI Alliance, Report to the Programme and Policy Committee: GAVI's supply chain strategy framework, 9–10 October 2013

3 Matthias DM et al, Freezing temperatures in the vaccine cold chain: a systematic literature review. Vaccine. 2007;25:3980–6

4 Personal communication

5 PATH-WHO, Temperature sensitivity of vaccines, February 2013, http://www.technet-21.org/resources/documents/vaccine-presentation-packaging-and-wastage/1719-temperature-sensitivity-of-vaccines/file, accessed 26 December 2013

6 Lydon P. et al, Economic benefits of keeping vaccines at ambient temperature during mass vaccination: the case of meningitis A vaccine in Chad, Bull World Health Organ 2014;92:86–92

7 WHO, Meeting Report: WHO/ Health Canada Drafting Group Meeting on Scientific and Regulatory Considerations on the Stability Evaluation of Vaccines under Controlled Temperature Chain – Ottawa, Canada, 4–6 December 2012

8 WHO, Revolutionary meningitis vaccine breaks another barrier; first to gain approval to travel outside cold chain, November 2012, http://www.who.int/immunization/newsroom/menafrivac_20121114/en/, accessed 26 December 2013

ACCESS CAMPAIGN
MEDECINS SANS FRONTIERES

MSF Access Campaign
Médecins Sans Frontières, Rue de Lausanne 78, CP 116, CH-1211 Geneva 21, Switzerland
Tel: + 41 (0) 22 849 84 05 Fax: + 41 (0) 22 849 84 04 Email: access@msf.org
www.msfaccess.org facebook.com/MSFaccess twitter.com/MSF_access