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Review

# The origins of the vaccine cold chain and a glimpse of the future ☆

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ABSTRACT

International efforts to eradicate smallpox in the 1960s and 1970s provided the foundation for efforts to expand immunization programmes, including work to develop immunization supply chains. The need to create a reliable system to keep vaccines cold during the lengthy journey from the manufacturer to the point of use, even in remote areas, was a crucial concern during the early days of the Expanded Programme on Immunization. The vaccine cold chain was deliberately separated from other medical distribution systems to assure timely access to and control of vaccines and injection materials. The story of the early development of the vaccine cold chain shows how a number of challenges were overcome with technological and human resource solutions. For example, the lack of methods to monitor exposure of vaccines to heat during transport and storage led to many innovations, including temperature-sensitive vaccine vial monitors and better methods to record and communicate temperatures in vaccine stores. The need for appropriate equipment to store and transport vaccines in tropical developing countries led to innovations in refrigeration equipment as well as the introduction and widespread adoption of novel high performance vaccine cold-boxes and carriers. New technologies also helped to make injection safer. Underlying this work on technologies and equipment was a major effort to develop the human resources required to manage and implement the immunization supply chain. This included creating foundational policies and a management infrastructure; providing training for managers, health workers, technicians, and others. The vaccine cold chain has contributed to one of the world's public health success stories and provides three priority lessons for future: the vaccine supply chain needs to be integrated with other public health supplies, re-designed for efficiency and effectiveness and work is needed in the longer term to eliminate the need for refrigeration in the supply chain.



**Contents**



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## 1. Introduction: Immunization in the 1960s and 1970s

Only a few vaccines were available in the early 1960s, and few children around the world received them. Smallpox was among the infectious diseases that were rampant, and the World Health Assembly received numerous reports of the catastrophic consequences of smallpox among its Member States. But vaccine technology existed for smallpox, offering the potential for protection.

In 1966, the World Health Organization (WHO) launched a global campaign to eradicate smallpox. This successful campaign demonstrated both the power and portability of vaccines. Within less than two decades, smallpox had been eradicated—a public health achievement that still stands as one of the greatest in history. Encouraged by the success of the smallpox campaign, health officials advocated for an expanded range of vaccines to be given routinely to infants under one year and women of child-bearing age.

In 1974, WHO established the Expanded Programme on Immunization (EPI), and Dr. Rafe Henderson became its first director shortly after. EPI was initially piloted in Ghana to assess the feasibility of establishing a single, global immunization schedule incorporating six antigens: tuberculosis, polio, diphtheria, pertussis, tetanus, and measles. The schedule was optimized to provide maximum protection for a minimum number of contacts through—what was then—a nascent primary health care system.

One of the key challenges of the early EPI work was to find a way to safely deliver vaccines, which are temperature-sensitive biological products, from the point of manufacture to the point of administration. Smallpox eradication established stepped vaccine distribution systems based on existing health services infrastructures but separate from the routine distribution of medicines. Recognizing the managerial weaknesses of medicine distribution at that time, WHO helped build the capacity of countries by developing the technologies, systems, and guidance towards a vaccine 'cold chain' to distribute vaccines routinely.

## 2. Challenges and solutions during development of the cold chain

In 1976, Professor David Morley of the Institute for Child Health, London, proposed that WHO establish a team within EPI to address three critical issues constraining WHO's ambition to establish routine immunization services globally:

- An absence of systems to monitor the temperature of thermosensitive vaccines.
- An absence of appropriate equipment to store and transport vaccines.
- An insufficient number of adequately trained staff to handle vaccines.

WHO consultants prepared a strategy paper and a plan of action to tackle these issues by creating and disseminating appropriate technology and training materials for distribution and administration of vaccines [1]. The strategy envisaged separate 'vaccine stores' based on the typical pre-existing distribution hierarchy to ensure rapid implementation. Starting from the central or national store and ending at fixed, peripheral health facilities where immunization services would be provided. This cold chain extended to periodic 'outreach sessions' held in communities that were far from the health facilities.

The vaccine distribution strategy also included injection and other supplies that are essential for the service. However, the strategy was targeted at immunization alone. Integration with medicines and other hospital supplies was rejected because the necessary control over stock management, transport priorities, maintenance and monitoring of storage temperatures could not be achieved at that time.

### *2.1. Absence of systems to monitor the temperature of thermosensitive vaccines*

#### *2.1.1. Challenges*

All but one of the original EPI vaccines were sensitive to heat. Some were sensitive to freezing, although the extent of sensitivity was not fully known and freezing damage attracted little attention at the time. Because there was no way to assess the effects of heat exposure once the vaccines had been distributed, strict requirements ruled the process of vaccine handling and storage temperatures.

The standard procedure for temperature monitoring in 1976 was to read and record the temperature in each vaccine refrigerator twice daily and display the temperature profile on a chart each month. Large national stores had continuous temperature recorders that used a rotating disk of paper on which an ink stylus left a record of the temperature. Although compliance with standard procedures was good in some cases and action was taken when temperatures deviated beyond pre-set limits, compliance in other cases was poor and temperature reports were unreliable. The lack of systematic temperature monitoring also made it difficult to determine when cooling equipment required maintenance.

#### *2.1.2. Solutions*

From the beginning, WHO envisioned the need for an 'end-to-end' temperature monitoring system for vaccines in the cold chain. Beginning in the early 1980s, companies in the United States and Switzerland, including Berlinger & Co. AG, developed a cold chain monitor (CCM) based on blue wax absorption on a visual 'track'. The CCM followed shipments of vaccine from manufacturer to countries and was used to monitor stores at all levels.

PATH (an international non-profit organization) and WHO began working in the late 1970s to find a way to track the heat exposure of individual vials of vaccine. Building on previous work to develop an enzyme indicator to warn of failures in the food cold chain in the United States, PATH and the Temptime Corporation developed and then commercialized a vaccine vial monitor (VVM) based on polymerization technology. VVMs are small stickers that adhere to vaccine vials and change colour irreversibly as the vaccine is exposed to heat, enabling health workers to easily determine whether the vaccine has been heat damaged [2]. WHO now requires that all vaccines purchased through the United Nations Children's Fund (UNICEF) use VVMs.

The VVM solved a major problem presented by the absence of temperature monitoring, yet additional challenges remained. When and where did the temperature deviation occur? Was it the result of faulty equipment or poor practices? How would a