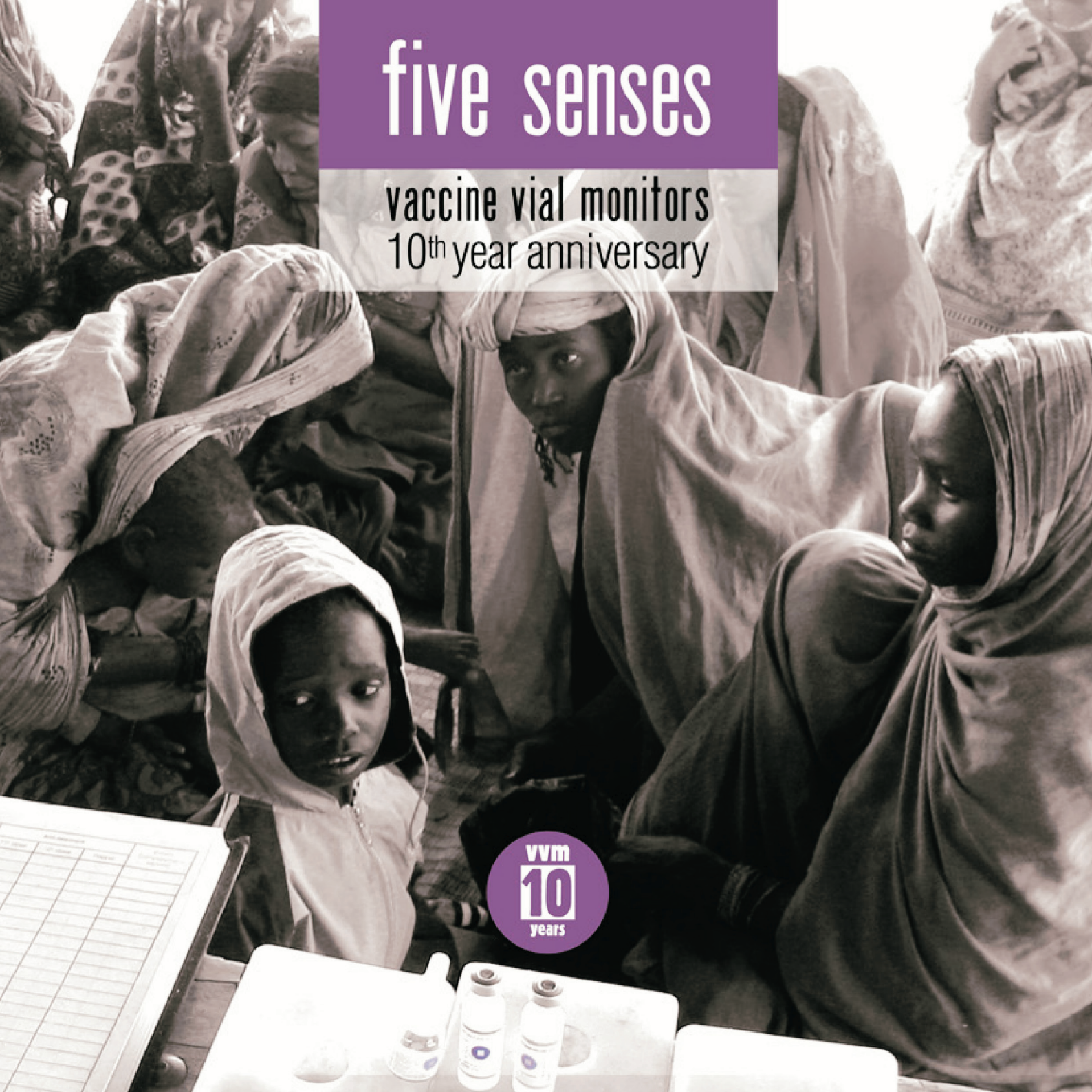
five senses

vaccine vial monitors
10th year anniversary



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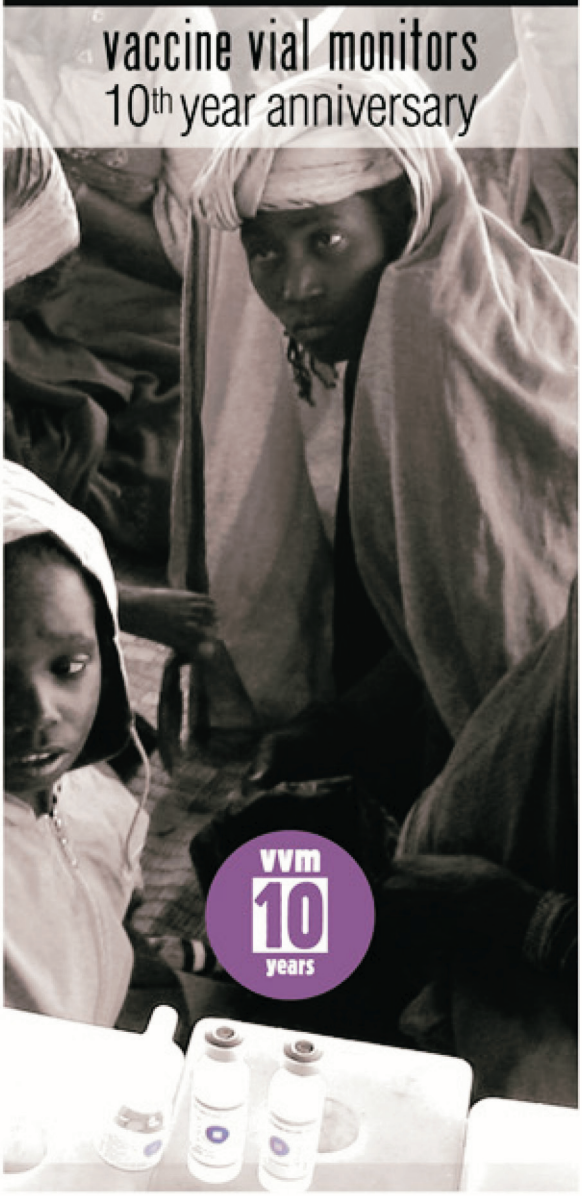


I trust WM.

Vaccinator, Thailand, 1991

photo: ümit kartoğlu, *mungku baru-indonesia*

five senses vaccine vial monitors

Handling vaccines requires great care. All vaccines are sensitive to heat and some to freezing. Careful storage and transport conditions are needed to protect vaccines from harmful temperatures. Imagine the challenge of getting vaccines from a manufacturing facility to the remote settlements in Vietnam, Indonesia or Niger. The vaccines leave the production site in temperature controlled trucks, they are flown as cargo to the country's capital for storage, then transported deeper into the country, stored again, and finally delivered to the location where they will be administered. Storage facilities often have sporadic electricity or no electricity at all. Transport might be between islands or on dirt roads across rivers, and swamps. Health workers carry the vaccine using trucks, motorbikes, boats, canoes, bicycles and in many cases... on foot. With all these steps, the journey might take a year with the most challenging leg at the very end where the vaccinator struggles to reach populations dispersed by difficult geography, famine, or war. The vaccine is at constant risk of damage.

It is impossible to visually identify when the vaccine is damaged by heat. Therefore, in the past, strict conservative measures had to be used by immunization programmes that resulted in often unnecessary disposal of loads of vaccines whenever heat exposure was suspected. In the past, heat damaged vaccines could have also gone unnoticed. Health workers at remote locations had to blindly rely on others who handled the vaccine before it reached them. If errors occurred, heat damaged vaccines may have been given to children leaving them unprotected from disease.

A vaccine vial monitor, or VVM, is a circular indicator, printed directly on the vaccine vial label or affixed to the top of the vial or ampoule. The inner square of the VVM is made of heat-sensitive material that is initially light in colour and becomes darker when exposed to heat over time. By comparing the colour of the square to the reference ring, health workers can determine the extent to which the vaccine has been exposed to heat. The vaccine can be used as long as the colour of the inner square is lighter than that of the reference ring.

This simple, yet elegant, tool indicates whether the vaccine has been exposed to a combination of excessive temperature over time and whether it is likely to have been damaged. It clearly indicates whether a vaccine can be used. This is why health workers today feel very confident. Now they rely on what they see. Now they make informed decisions based on interpretation of VVM indicators.

introduction

photo: ümit kartoğlu, *thach lam-vietnam*

VVM ensures that the administered vaccine has not been damaged by heat. It is estimated that over the next ten years VVM will allow health workers to recognize and replace more than 230 million doses of unusable vaccines. VVM reduces wastage, saving annually around 5 million USD worth of vaccines. VVM facilitates immunization outreach and increases immunization access and coverage. With VVM, over the next ten years health workers will be able to deliver more than 1.5 billion more doses in remote settings including delivering the birth dose of hepatitis B vaccine to millions of newborns in hard-to-reach areas. VVM pinpoints cold chain problems and helps to effectively manage vaccine stocks - store keepers and immunization managers now adopt VVM based vaccine management, making decisions with the help of VVM readings.

VVM shapes the future of cold chain today, a future in which dependency on the cold chain is removed. Today, VVM is seen as a catalyst for much-needed changes in strategies of vaccine distribution via the cold chain. VVM allows immunization programmes to exploit the stability of each vaccine to the greatest possible extent, minimize distribution costs, and increase flexibility in the handling of vaccines in the field, thus helping to make operations more effective.

Although developed as a heat-exposure indicator, VVM also contributes significantly to the reduction of vaccine freezing. VVM makes it possible to detect and avoid excessive heat exposure to vaccines when methods are employed to store and transport vaccines without ice and equipment that is a known source of freeze damage. VVM allows health workers to feel confident that a load of vaccines does not necessarily go bad if the power fails for a night . VVM allows health workers to see the heat stability of vaccines and accept the fact that freezing is a greater danger than mild heat exposure.

Conceived as a dream in 1979, today the availiabity of the VVM is the result of immense efforts and dedication to strengthening public health on the part of many organizations, institutions, companies and individuals. Without VVM, health workers can rely only on the expiry date of a product. But when you are buying a bread in a bakery, besides seeing how fresh the bread is, you can smell it, you can touch and feel it, listen to the crispy sound it makes, and taste it. VVM expands the horizon for all immunization programmes, VVM is a "five senses" offer to health workers, although they only look at it, with VVM health workers discover things other than a printed expiry date, as if they feel, hear, smell and taste... and they know with confidence which vaccine can be used or not... VVM expands the horizon for all immunization programmes, wherever the challenge is. It offers a railroad, a bridge, a tunnel, a motorbike, a canoe, a bicycle, and a pair of shoes to reach the unreachable.

Dr Ümit Kartoğlu *Scientist* WHO/FCH/IVB

Ümit Kartoğlu talked to John Lloyd, Michel Zaffran, Peter Evans, Julie Milstien and Dario Cresci on VVM history. Lloyd, Zaffran, Evans and Milstien worked together in WHO HQ on VVM during its early development stages as well as its implementation. Cresci was on the other side of the table - the industry. In 2001, Kartoglu joined the team, but after the departure of Lloyd and Evans from WHO.

The following interviews bring interesting stories to daylight. When Kartoğlu asked what was next, Lloyd, Zaffran, Evans, Milstien and Cresci all stressed the same point: using VVM to allow immunization programmes to exploit the stability of each vaccine. To use it to the greatest possible extent to minimizing distribution costs, and increasing flexibility in the handling of vaccines in the field, thus helping to make operations more effective. They all agreed that the mission is now reducing the dependency on the cold chain. VVM is seen as the answer to this challenge.

photo: zoe ewart, *divonne les bains, france*

The powerful role of VVM in immunization services is to communicate their ability to reach hard-to-reach children John Lloyd*

The VVM history that I have in the record says that VVM concept conceived by WHO in 1979. Where were you in 1979?

In 1976 I made a proposal to WHO for a vaccine 'cold-chain' based on the cold chain in the food industry. It was a proposal which rationalized why we needed a cold-chain. In that document, I stated that the main problem with vaccine distribution was that there was no way to see whether the vaccine had been damaged by heat. I was sure that there would be chemicals which could show visibly whether the vaccine was being damaged by cold-chain breaks or not. So when WHO contracted me as a consultant in May 1976, I went to see a company that built ships in Malmo, Sweden, who were diversifying to a number of other market areas because ship-building was declining at that time. They had started a big chemical company and one of the people they employed was Dr Mandayam Tiru who was a professor of bio-chemical engineering. He invented an enzyme indicator of time and temperature for the food industry and I went to see him early in May 1976. He explained to me that this enzyme indicator could follow the Arrhenius characteristic of the vaccine decline in potency due to time and temperature. This is the nearest, he said, that we can get to a visible change to show the effect of exposure to heat. He showed me his indicator, a small pouch of plastic full of a liquid which when exposed to time and temperature passed, changed colour.

Which colour?

I think it started as a mauve colour and changed progressively to a yellow colour. It reacted both to high temperatures for short periods and low temperatures for long periods, and we started a series of tests. The technology eventually evolved to become the current food market time-temperature indicator CheckPoint®.

Attached to each vial of vaccine?

No, at that time the indicator was too bulky to be attached to a single vial of the vaccine so we started to test it on the internal packaging of vaccines. Of course it couldn't represent the potency of the vaccine because it was too far away physically from the vials.

Which vaccine were you trying it for?

*John Lloyd *Former Technical Officer at WHO, currently Senior Technical Adviser to PATH, France*

Vaccine Vial Monitor (VVM) History and Milestones

1979
VVM concept conceived by WHO. Success with Cold Chain Monitors at higher levels of the cold chain prompted interest in a vial indicator to extend monitoring to the periphery.

Product development on a VVM for measles vaccine began at PATH using a PTS (p-toluenesulfonate) chemical licensed with permission from Allied Corporation.

1980
Connaught Laboratories conducted testing of early VVM prototypes (based on PTS technology).

We were trying for measles and worked for about five years towards this goal until, in the early 80s, there were other options. A polymer-based indicator from Allied Chemicals was superior in many ways and became the focus of work at PATH. The concept of trying to represent the sensitivity of vaccine to time and temperature is as old as the cold-chain itself, but the realization of that idea has taken a very long time.

Was 'TechNet' conceived as a small network, mainly for vaccine vial monitor-related discussion?

Mogens Munck, in the late '70s working for UNICEF India, proposed the formation of Technet as a forum to bring a field perspective to many activities in the domain of training and technologies, including vial monitors that were seen as emanating from Geneva. UNICEF and WHO organized the first meeting of Technet in Cyprus and the subject of VVMs was one of the main topics of discussion.

Technet was a meeting of logistics consultants, UNICEF, WHO, Save the Children Fund and other people working in the field discussing the new training materials and cold chain technologies that were in development and setting priorities for further work in this area.The development and first field testing of VVMs was driven and organized by PATH because at that time the concept still being pursued by WHO was a secondary packaging indicator to help monitor cold-chain and to build the cold-chain. The more radical concept of PATH at that time, led by Vivien Tsu, was to transform the paradigm of the vaccine supply chain, using the VVM to reduce dependency on refrigeration and the cold chain. I was worried at the time that VVMs on vials of vaccine would be demonstrate to health workers how much more stable the vaccine was than they believed and that this would lead to people being disrespectful of vaccine handling.

I helped to make two films for WHO on the vaccine cold-chain. The first film was about vaccine production and its message was that vaccines are precious items - delicate biological substances. They must be treated with care and kept cool. So it seemed very revolutionary and unwise to suggest that vaccines may be taken out of the cold-chain at that time. I confess that as leader of the cold-chain activity in WHO, I preferred the idea of maintaining the cold-chain.

When did it happen and how did it happen that we all started to speak the same language? How did that happen?

As you suggested earlier - TechNet made it happen. Once we began to involve a wider group of stakeholders, people asked at TechNet meetings "Where are the VVMs? We need them for the management of the vaccine in the field." Technet participants said "It's the ultimate device to have on the vaccine vial: you can't put indicators on the box of the vaccine and pretend that they have anything to do with the potency of the vaccine. You have to get the indicator on the vial". So, I think that TechNet made it happen in many ways.

How about the future? How do you see it?

The original vision of PATH was to have a vaccine supply chain which contained refrigeration but which was not dependent on refrigeration, which removed vaccines from refrigeration where possible and which used vaccines to the limit of their stability.

That is still the vision of the future vaccine supply chain. PATH is now working on a long-term

'brainstorm' analysis of what we call the 'stability-driven' vaccine supply chain, based on the principle that the stability of the vaccines should be used to their limits in the supply chain to assure the best access to immunization services.

Can we call it VVM-based vaccine management?

Yes. We see a cold-chain with a highly protective top-end where we keep the vaccines refrigerated in high quality primary stores at central and province levels. Then, towards the periphery of the distribution system we see a cold-chain which will not require much, if any refrigeration and some more stable vaccines taken out of the entire the cold chain.

If we can have a cold-chain which does not use ice, I think this would be an important objective. Ice is a potential danger to vaccines but it also provides a very good cold-life, assuring a long 'reach' for the cold-chain if we need a long reach. Vaccines are becoming more stable and we have ways without ice to protect vaccines against extreme heat. Do we need to reach out with 2 to 8°C? I believe we don't.

So, I think a critical objective is to include vaccine manufacturers in these discussions and work as closely with them as possible.

You are right John... One recent development was the Panama cold chain workshop. What happened in Panama?

We had eight Latin- American countries around the table who knew very little about VVMs. We explained the function and rationale of VVMs and we presented the experience of other countries. The greatest interest among participants was the concept that the VVMs would help reach the un-reached and improve immunization coverage in areas of difficult physical access.

VVM is the answer in reaching the un-reached... increasing coverage...

Yes, I believe that the first step towards acceptance of the powerful role of VVMs in immunization services is to communicate their ability to reach hard-to-reach children. Of course, our motive in the longer term is to transform the cold-chain, to have management of vaccines based on VVM indication and to remove vaccines partially or completely from refrigeration. That is the long term goal and it may take many years to get realize this goal. But the starting point is to communicate the rationale for the VVMs assuring potent vaccine for children who are as yet, un-reached by immunization services and therefore un-protected against disease.

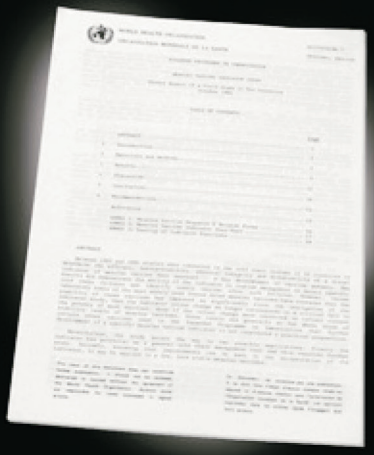
Thank you John...

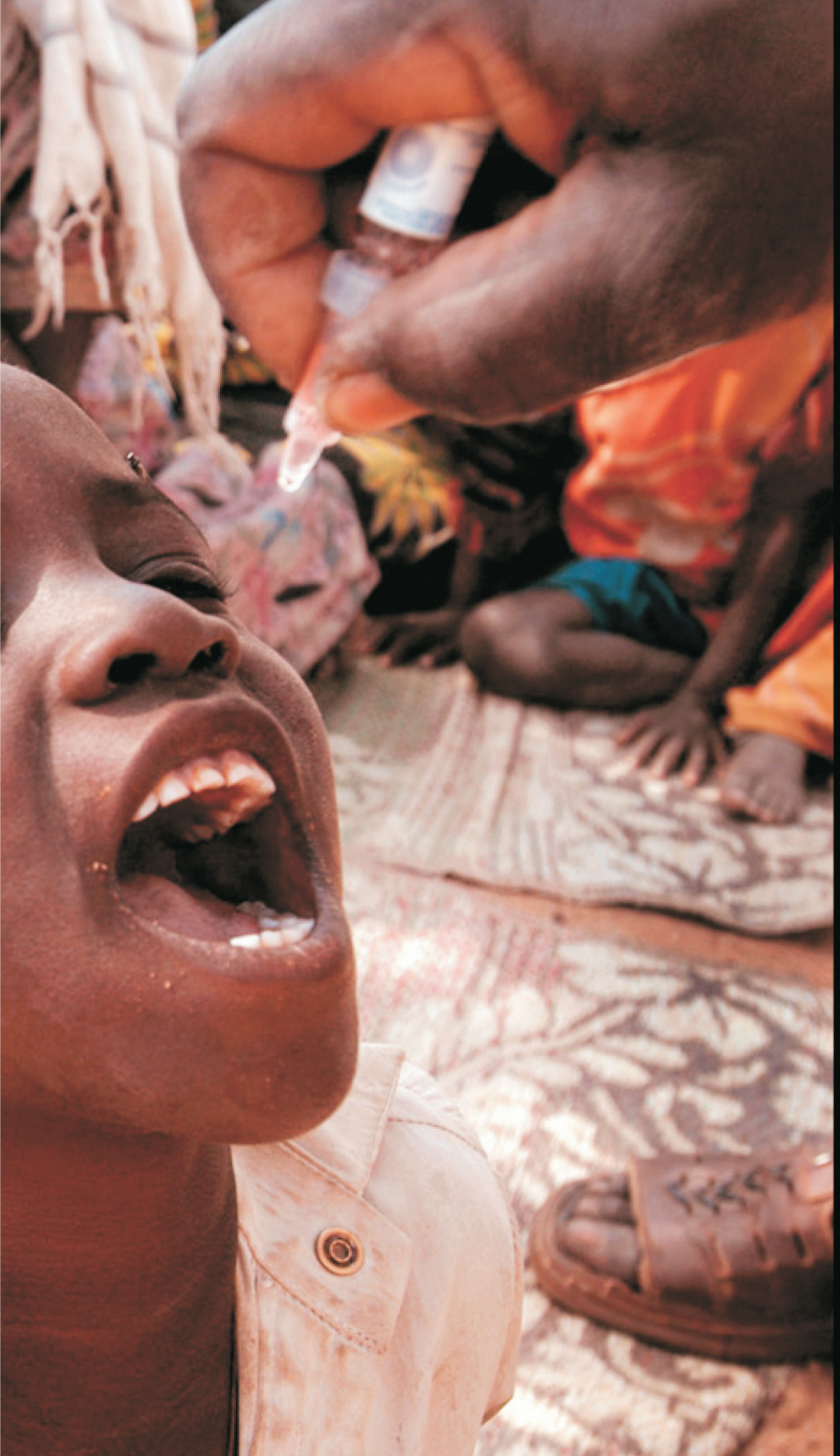
photo: john lloyd, *divonne les bains / france*

1981
VVM design field trials conducted by PATH in Mexico and Philippines.

1982-1985
Measles VVM prototypes (based on PTS technology) produced and refined by PATH.

Validation field trials conducted by WHO, PATH, and MOHs in Argentina, Brazil, Egypt, Kenya, Nepal, Pakistan, Peru, Philippines, Yemen and Zimbabwe.





1986 - 1987
The PTS manufacturing process was improved and PATH developed a format for use on vaccine cartons.

1986 -1989
Introductory field trials of the measles VVM and carton indicator (PTS technology) were conducted by WHO, MOHs, and PATH in Indonesia, Kenya, Sierra Leone,Thailand, and Zambia. (1987-1991)

1988
PATH (under USAID funding) identified a new core technology for VVMs (using diacetylene polymers), owned by Lifelines Technology, Inc., that overcame Constraints of the PTS technology included:
a) reaction rate too slow for use with oral polio vaccine,
b) dermal toxicity issues, and
c) printing difficulties.

1989
PATH began work with LifeLines to adapt and produce VVMs using their core technology.

photo: jean-marc giboux, *eastern chad*

photo: ümit kartoğlu, *port elizabeth / south africa*

Make better use of the real stability of the vaccine - use the VVMs Michel Zaffran*

How did you get involved with VVM Michel?

Well, I'd been working in the cold-chain section in WHO, in EPI. I had to get involved in a range of issues. It was John Lloyd's primary responsibility but because I was doing a lot of the work relating to testing, to cold-chain in general and so on,. My first interactions were with PATH - discussions on why was WHO so opposed to VVM and how to develop specifications …

I was in charge of performance specifications and standards, overseeing their development. So we developed specifications to ensure that something existed for industry to react to for VVM - initially for polio. Polio vaccine. Because we had a VVM for measles, not for polio, and we wanted something for polio.

And this around which year? Was it late eighties?

Yes. It was late eighties or very early nineties. There was a recurrent message at each one of the TechNet consultation, people would ask "Where are the VVMS?" or "VVMs, where are they?".

Copenhagen consultation?

No, no. Manila. We actually had the first VVMs - it was maybe 95, 96 - we had the first VVMs on vials and we started the meeting saying you've been asking where are the VVMs - here they are.

My recollection is that there was a turning point when - after having the technology manufactured by Lifelines, we actually got the first producer to put VVMs on a vaccine - that was Pasteur Mérieux - I had talks with a number of people in Pasteur Mérieux that I knew well. Told them "You're going to supply vaccines to Vietnam for NIDs. Will you put VVMs ? So we can start having some measure of whether it works or not." And –they did it, almost as a favour to us -. And then, because they had started, they agreed to supply to other areas.

That was really a turning point, and the next thing is a call from Chiron saying we understand that WHO wants VVMs on all the polio vaccine - can you clarify that this is the case because we're about to purchase the labelling machine. And, Chiron had the specific …

… a different type of vial …

… a different type of vial, yes.

For them it was a problem to use the label. They had to put a dot. So they had Lifelines develop a dot.

And only to attach this VVM onto OPV, they had to change the cap of the vial.

That's right. The size of the …

… the cap of the vial or plastic tube.

* Michel Zaffran, *Former Team Leader of Access to Technologies at WHO, currently Deputy Executive Secretary and Chief Technical and Policy Officer at GAVI*

They had to redesign the cap …

That's right. Make it bigger.

… make it bigger for VVM to attach properly.

That's right. We also - one of the criticism that we faced primarily by industry and by UNICEF with the VVM was the fact that there was only one supplier and this monopoly was creating of difficult situation in terms of price, competition, reliability, and so on. And we worked quite hard to, you know, look at possible manufacturers. In fact, 3M developed an interesting technology which they eventually did not bring to market because it was too expensive.

But there was another manufacturer…

When we showed that in fact, we have other manufacturers and technologies and none of them was able to bring it to market or to compete with Lifelines, then industry got much more comfortable working with Lifelines. Lifelines has also improved tremendously. Quality control, processes and so on. And they've become more credible to industry because, in terms of quality control and quality assurance, they initially were not at the level the pharmaceutical industry expected.

Wasn't it TechNet Copenhagen 1998 the most critical one in terms of VVM because it brought up the recommendation that it should go to all vaccines …

All vaccines, yes. We had the VVM for the OPV for two or three years before it started to be implemented. It was primarily used in NIDs. And then, at that point, the TechNet made a very strong recommendation - we need VVMs on all vaccines. And then we developed all the specifications for all the other vaccines - quite closely with Julie Milstien's group at that time - and started sharing that with industry, and Lifelines basically had the technology to make them against any type of specifications, yes.

Since today we have VVMs almost on all vaccines procured by UNICEF, is the mission over?

The mission is not over. I think this is the first step. The VVM is not an end in itself. The vision of the cold-chain of the future that was presented to the CVI meeting in Senegal describes this relatively well. The future is really about eventually getting rid of the cold-chain, making more use of the real heat-stability of the vaccines, by using the VVM, and allowing vaccines to be taken out of the cold-chain, institute vaccine management rules which will enable countries to reduce the financial burden that the cold-chain equipment represents - primarily for the periphery. At the periphery it's much more difficult to assure cold-chain because there's no electricity. It's either gas, kerosene or solar. And you're much more remote. You could actually make better use of the real stability of the vaccine - using the VVMs …

Hepatitis B is an example …

This is already happening in some countries but not enough.

When you look at the new, for example, rotavirus vaccine, the requirement of cold-chain is enormous because of the packaging design that you have to multiply five times of your cold-chain capacity to facilitate the introduction …

Yes. Well, I think we should not be satisfied with

photo: jean-marc giboux, *yemen*

1990 - 1991
Design field trials were conducted by PATH with HEATmarker™ VVMs in Bangladesh, Bolivia, Cameroon, Indonesia, Kenya, Sierra Leone, Thailand, and U.S. (1990-1992)

1990
VVMs were discussed at a Technology Introduction Panel meeting at UNICEF New York.

WHO and PATH representatives met with Connaught Laboratories, Conpharma Vaccines, Evans Biologicals, Interexport, Pasteur Merieux, Sclavo, SmithKline Beecham, and Swiss Serum to discuss the feasibility of integrating VVM labeling into their products.

photo: ümit kartoğlu, *port elizabeth / south africa*

photo: ralph henderson, *versoix / switzerland*

the presentations that we have today. These presentations need to be changed, to be reduced in volume. But, whether or not we reduce the volume of the presentation - with the new vaccines, we will still probably go for limited number of doses per vial, may be mono-dose, because they're very expensive. So, we can't afford the wastage. So even if we have good efficient packaging - we will have a need for much larger storage volume. Here we need to be able to show whether n the countries need to purchase more refrigerators or can actually, with an efficient distribution of the vaccine, with air-conditioned room or good environments which is protecting the vaccines from the heat but not literally putting it in a cold environment.

Here we'll be facing lots of difficulties. One of them is the dogma that we've been working for in the past 30 years: "Vaccines must be kept cold!" So, having said that for 30 years, it's difficult to now tell countries you don't need to keep them cold. You have also regulatory aspects, which I'm sure you're very familiar with. .

Could it ever be possible that the, for example, one of the heat-stable vaccines that come to the market as a new product, could be licensed with a higher temperature storage recommendations/options? Could it ever happen, do you think?

That's probably the way we should influence things. If the vaccines are licensed, for storage at 25°C then of course you no longer have that problem. What you have as a problem is just changing the mentalities but you don't have the regulatory hurdle. What sort of data would the industry be required to provide? Probably data they already collect. But would the regulatory authorities be happy with those data? I think it's probably not that complicated to determine what sort of data they have to provide because, for instance, drugs are licensed for storage at ambient temperatures. So, these are biological products so they will deteriorate faster. Here emerging suppliers might be the better suppliers to work with in terms of having this first licence.

I agree Michel. It's important to have one example.

Right… because if one manufacturer does it the others say, well, we need to do something. That's right. . First, understanding exactly what would be required and then working with the manufacturer. I believe that from the manufacturer's perspective, they probably will have the data. I mean, it may take longer, of course, for them to accumulate the data.

So, you were saying is the mission accomplished? Certainly, a part of the mission which is critical …

No, what I asked - I believe that it's not accomplished!

I'm sure. But that's a really major, major achievement. We have VVM on all the products. What's amazing to me, though, is that we thought that vaccine would

follow a trend which the food industry would take. And we haven't seen such progress in the food industry. Lifelines, at some point, was trying to promote their products - and I think they have a few clients - in France, in some countries - which use a dot which changes colour with exposure to temperature, for the food-chain,. And I thought that the consumer environment would be so strong that the consumers would be requiring a proof that the cold-chain has not been broken.

Well, things are pretty different in biological fields than in food …

Oh, yes.

… Because in the field of vaccines, it is me as a health worker who decides which vaccine to use first referring to the VVM. So I take the one that is more exposed to heat to use it first. But when it comes to the food industry it is different- let's say, when I go to the market and find only two milk cartons, I will pick the one that has a fresher indicator even if the other one is still OK but exposed to some degree some temperatures. I would not pick the other one. Everybody's going to pick the same - this is like looking to the expiry date. If you have a fresher expiry date, you would pick that one. I always try to reach deep in the shelves where storekeepers place more fresh products to the back. It is extremely challenging for the food industry to put such indicators. Much more difficult than vaccines, I guess. Because the decision maker is the client, not the seller.

Interestingly, VVMs were developed from the idea of an indicator that was designed for the food industry.

That's right.

Initially of course. And I am not sure whether at early stages Lifelines ever imagined that this technology for the food industry would ever do something good for the vaccines. May be they did not think of it until PATH approached them - identified them as a potential supplier. It was also a very critical switch.

A very critical switch, yes. I mean, the Lifelines factory or plant in the early days - I visited them - it was very small and they had only one machine. But, you know, it's become very professional over time.

Regarding VVM availability, what made the current situation possible?

I think there were two critical factors. First, that we were able to start with polio but we could have gotten stuck with polio forever. And so the change to the next generation was made possible, I think, because Serum Institute of India moved and because they had such a range of products and they were producing so many doses of vaccines. I think also the fact that GAVI put in money to purchase vaccines and said we want the VVM on the vaccines - put a bit of pressure. So I think there was a combination of factors that influenced the acceleration –for VVMs to become available on all vaccines.

There were a number of people that believed in VVM, or wanted it, that really made it possible, and that had a big influence on the evolution. And GAVI coming with money and saying, yes, we'll purchase VVMs, not really looking into at all the pros and cons and making the investment decision I think, was a good opportunity to start.

Thank you Michel.

1990

HEATmarker™ prototypes were sent to Connaught, Conpharma, Evans Biologicals, Interexport, Pasteur Merieux, Sclavo, SmithKline Biologicals, Swiss Serum for evaluation.

1991

Albert Browne, Ltd. (UK) emerged with a competitive VVM technology for evaluation and began discussions with WHO and PATH.

Meeting held at UNICEF New York during which WHO requested UNICEF to include VVMs for OPV in the 1992-1994 EPI vaccine tender.

"Live" HEATmarker™ VVMs were sent to WHO, Connaught, Evans Biologicals, Human Institute, Institute of Immunology, Interexport, MAIMEX, Pasteur Merieux, Sclavo, SmithKline Biologicals, Swiss Serum and PAHO for evaluation.

1992
Independent laboratory evaluation of LifeLines HEATmarker™ VVMs for OPV completed by Strasburger and Siegel laboratory.

Zimbabwe study completed by PATH and MOH on the impact of VVMs on measles vaccine discard rates due to heat exposure. (1992)

UNICEF included a clause in the 1992-1994 vaccine tender notifying manufacturers that they would request labeling with VVMs prior to 1994.

1993
Albert Browne developed prototype VVMs for evaluation, but indicators had a slow initial color change and did not meet specifications.

The VVM helps achieve confidence at really remote places Peter Evans*

Peter, I see your name mentioned in VVM history. If we start with the idea conceived by WHO...

Actually, the idea was definitely conceived by John Lloyd, and this was before my time. Everything I'm going to say makes John Lloyd a hero because he absolutely was. He was the driving force for everything - VVMs right from the start to the end. He is an absolutely amazing person. I was in UNICEF at the time and I knew nothing about vaccine vial monitors. I only knew about them six or seven years later. John Lloyd joined WHO and, I believe, even before he came into the office, he went to look for a solution. It was one of the very first visits that he did.

At that time there were some problems. The indicators were designed for the food industry and the food industry wasn't so sure whether they wanted to go ahead with this or not. So, the project at that time was still nebulous as to whether there would be large-scale production of time temperature indicators. It didn't go ahead at that time. The food industry decided that the negative side of indicators for food was too great. People would be looking and saying "this food is slightly".

Of course, informed clients always want the most fresh produce [I explain to Peter what we discussed with Michel Zaffran - the client perspective].

Yes, they want the most fresh one. An expiry date is fine because you can say, "Ok, that expires next week". You prefer it to expire within one month,

photo: ümit kartoğlu, *geneva / switzerland*

but you don't know when it was produced. It may have been there for two years but at least you know the expiry date.

The development of the vial monitor was designed for food, not for vaccines, but without the food business it would not have been developed.

People who are buying food look at the expiry date. If they were looking at the manufacturing date, which is what the vaccine vial monitor allows them to do, it would actually give negative information and it would make distribution difficult, so they abandoned it.

When did you join WHO and what was your involvement with this VVM-related work?

I joined WHO around 1984, 1985 and I was brought in primarily to look at contracts for auto-destructive syringes, and that project went quite well. Then I

*Peter Evans, *Former Chief of Vaccine, Supply and Quality at WHO, currently retired.*

took on the vaccine vial monitors project. The concept had been well defined and it just needed people to deal with the industry side of things and to look at the contracts.

I can tell you my funny story from vaccine vial monitors. I championed, not the Lifelines, but the Albert Brown. Early on we had three different competitors for vaccine purposes and the Albert Brown went from a pale yellow to a dark blue. The advantage of the Albert Brown was that it was cheap, it was very easy from the manufacturers' perspective, and the reading was absolutely clear. It went from yellow to dark blue almost instantaneously. You had the vaccine vial going for several months and then suddenly it would change, therefore the health worker would have no questions about it.

The VVM from Lifelines is sophisticated. You can do imaging control, you can tell how far along it's going, whether you need to rush, and so on. But the brown one was cheap and simple.

But if the brown one was changing color instantly, it was a threshold indicator then.

We were in a TechNet meeting in the early 1990s and we had the room full of people and I'm holding up examples of indicators, pushing the boundaries by asking "Is this circle black?" And they all yelled out "Whiiiiiiiiiiiite!" And I said, "Can you see this one?" and they go "Noooooooooo!" This group made it very clear that they did not want the brown ones. We became a champion of the Lifelines.

I know that you are a bit outside of this area now, but how do you see the future for VVM work in general - cold-chain in relation with VVM? The reason I'm asking is that VVM started with OPV in 1996 and if we look at the UNICEF market, almost all vaccines have VVMs attached, except for just a couple of presentations from [manufacturers]. I could say almost 100% of the UNICEF-procured vaccines are with VVMs now. So what is next? Does this lead us somewhere? Is the mission over or should we open a new page for VVMs?

VVMs were chosen for polio because polio was the most sensitive vaccine and eradication had started. When the VVMs were first conceived, eradication was not being considered. When the VVMs were being seriously considered, eradication as a goal had not been considered, but it was obvious that it would be declared at some point. The stability of the vaccines was of great concern. I was heading up Vaccine, Supply & Quality at that time and we were doing a lot of work. Julie was leading the field on making polio vaccine more heat-stable. It was considered to be extremely important work. But half-way through that work we were dealing with vaccine vial monitors which were saying if we can take advantage of the stability of the polio vaccine, we don't need a more stable vaccine. We can take it a month beyond the cold chain with various cooling factors and, in that respect, it was extraordinarily important.

We stopped making heat-stable vaccines because all the goals of heat-stable vaccines could be met with the vaccine vial monitors. So we achieved a major objective that we didn't have to change vaccines just at the time we were considering eradication, which was an extremely important decision. It was highly controversial. J.W. Lee actually made the decision because the various parties of WHO could not decide it. He made a very sudden announcement that we would stop development of heat-stable vaccines. It was the right decision. We could have confidence that polio eradication would occur and that it wouldn't happen without VVMs. So that was an extraordinary

LifeLines developed the capability to print VVMs on vial labels for liquid vaccines to overcome vaccine manufacturer resistance to purchase of labeling equipment for a separate VVM label.

(Sample Instruction Booklet)

How to Use HEATmarkers™
A Guide for Health Workers

How Do I Use HEATmarker?

Whenever you receive a vial of oral polio vaccine, check the expiry date and see if there is a HEATmarker on the label of the vial. If the expiry date has not passed, compare the colour of the inner square with the colour of the outer circle.

If the **inner square** is **lighter** than the outer circle, **use** the vial.

USE!

If the **inner square** is the **same colour** or **darker** than the outer circle, **do not use** the vial.

DO NOT USE!

Use vials with the **lightest** inner square **last**. They have received the least amount of heat exposure.

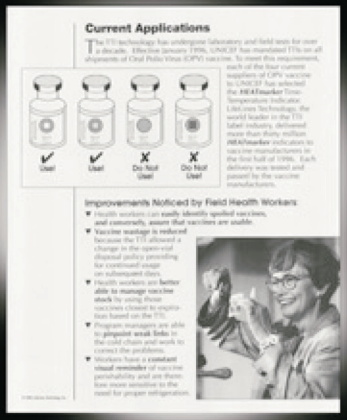
IF YOU ARE NOT SURE OF THE COLOUR, DO NOT USE THE VIAL!

For further information, please contact: HealthTech Project Director
PATH, 4 Nickerson Street, Seattle, WA 98109-1699
Tel: (206) 285-3500 Fax: (206) 285-6219

1994
3M (US) and Bowater (UK) emerged as potential VVM suppliers.

The UNICEF tender for 1994-1995 requested quotations for VVMs on measles and OPV, but only a few manufacturers provided such quotes.

1994
The Technical Network for Logistics in Health (Technet) consultation recommended that VVMs be included on all vaccines, beginning with OPV.


Current Applications

The VVM technology has undergone laboratory and field tests for over a decade. Effective January 1996, UNICEF has mandated VVMs on all shipments of Oral Polio Virus (OPV) vaccine. To meet this requirement, each of the four current suppliers of OPV vaccine to UNICEF has selected the **HEATmarker** Time-Temperature Indicator Label (see Technology), the world leader in the VVM label industry, delivered more than thirty million **HEATmarker** indicators to vaccine manufacturers in the first half of 1996. Each delivery was tested and passed by the vaccine manufacturers.

Use! Use! Do Not Use! Do Not Use!

Improvements Noticed by Field Health Workers

- Health workers can **easily identify spoiled vaccines, and conversely, assure that vaccines are usable.**
- **Vaccine wastage is reduced** because the VVM allowed a change in the open-vial disposal policy providing for continued usage on subsequent days.
- Health workers are **better able to manage vaccine stock** by using those vaccines closest to expiration based on the VVM.
- Program managers are able to **pinpoint weak links** in the cold chain and work to correct the problems.
- Workers have a **constant visual reminder** of vaccine perishability and are therefore more sensitive to the need for proper refrigeration.

WHO, UNICEF, and OPV manufacturers met and determined that all OPV would include VVMs beginning in January 1996, with pilot introduction beginning in April 1995.

1995
Pilot introduction of VVMs in Tanzania and Vietnam by WHO and MOHs.

WHO released official specifications for VVMs for OPV.

important thing.

The other thing which John was most concerned about was the age of the cold-chain. You could no longer trust the periphery and that was only going to get worse over the next five years. It was hard to get the money for the investment in cold-chain. We are in a different age now. At that time, getting a million dollars was extremely difficult. Now, to get one hundred million dollars is not so difficult. At that time, it looked as if cold-chain was going to just wear out so the VVM was going to be the answer to that and the moderately stable vaccines would benefit. We would have cold-chains up to large cities and then beyond that we would have a variety of solutions. It wouldn't have to be one standard cold-chain.

Peter, do you remember the recent TechNet posting, the story of returning vaccines back to cold chain after weeks of being out of cold chain, the earthquake in Jogjakarta Indonesia? They referred to VVM readings when taking decisions.

Yes, this example from Jogjakarta, Indonesia, is a clear example where the cold-chain was a management system. Although there was equipment in there, it was actually a management system. To keep it simple, we had standardization of everything and that was great. The cold-chain concept could not have been put in place around the world without a standard process and standard training materials for everybody. This advantage was that you had to basically treat tetanus vaccines the same way as polio vaccine and they are vastly different. Tetanus probably does not need to be in the cold-chain, and if it does, it only needs to be cooled at an international level, perhaps. But it was the idea of saying that you treat vaccines like this because if there's a failure for two hours and you throw the vaccine away - vaccine wastage was not considered to be important. You save the child, not the vaccine. And that turned out to be unnecessarily expensive, and the VVMs, which is relatively modest, saved all that.

So, I would say that the knowledge that the vaccine is still potent is extraordinarily important. There is a feedback mechanism to the health centre that they're doing the job right. That's one thing. To the health worker who is going to give the vaccination, it's a positive reassurance. They've got that extra test so they know they're not wasting their time, which is a good thing. And it probably will result in not needing a cold-chain. I think cold-chain could disappear. I think expensive

photo: ümit kartoğlu, *geneva / switzerland*

cold-chain could disappear and I think that would be great.

I will give you an example, Peter. Within this VVM 10th Year Anniversary activities, we've also been targeting some industry meetings. There was one in Philadelphia and one in Berlin. I was invited to speak in these two meetings on vaccine vial monitors. Part of my presentation was that I distributed vaccine vials to around 10 participants in the hall. We had around 100 to 120 people in the hall. These vaccines did not have any VVM. Some of them had good expiry dates and some were expired. I said that they're coming out of the cold box and I told them "It's time for your daughter's, or your son's, vaccination". I continued, asking "Would you vaccinate your child with this vaccine?" The ones holding the expired vaccines said definitively no, but others did not answer. They kept rolling and looking at the vial in their hands. Then I distributed the similar vials this time, with the VVM on them, and I said "These vials are not coming from the cold chain. For some time there was no electricity, so they were exposed to some degree of heat" and I repeated the same questions. What happened at the end? Of course, following the presentation, I did not have any chance to grab a tea or coffee as I was circled by participants with many questions eager to learn more about VVMs.

Absolutely. VVM is a very good feedback mechanism.

I have one other example and it's a pity I did not have my camera with me to make a picture of it. I took my son to the Paediatric Emergency Clinic in the University of Geneva Hospital. He had a cut on his chin and the doctor said they needed to give him a TT shot. The nurse opened the drawer of a desk - not the refrigerator - and there were mono-dose TT vials. When she took one, I could not restrain myself and blurted out "Oh, I wish I had my camera to make a picture of this". She thought that I didn't like it because it was not refrigerated, and in a defensive mode she started to explain. I said "No, I like what you are doing" and I explained the work I do in WHO. This was even done with vaccine without any VVM on.

That's probably right.

I really wish I had my camera with me. I don't know whether they would have let me take a picture but it was shocking for me to see in Geneva, a University Hospital, an Emergency Department, and they keep their TT vaccine in desk drawers and not in the refrigerator, and without VVM.

It's actually good that we have kids. I was called, without notice, to make a presentation in Syria and I had nothing prepared because I wasn't expecting to be called to make this presentation. So, I gave the example of when my daughter needed tetanus vaccine and the situation that happened was very similar. So, we take a lot of things for granted in our industrial surroundings, but the VVM helps achieve the same sort of confidence at really remote places.

Thank you Peter.

Very enjoyable.

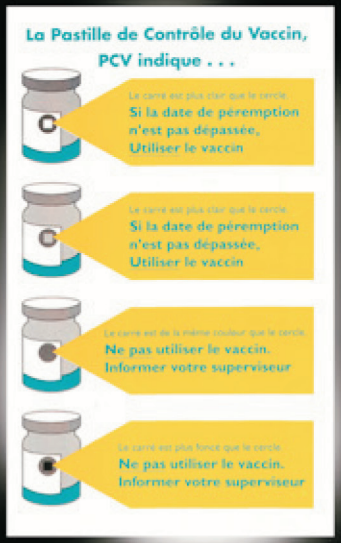
1996

3M released a public statement that they would supply VVMs on OPV supplied via UNICEF.

All OPV procured by UNICEF included VVMs from this year onward from SmithKline Beecham, Biocine, Pasteur Merieux Connaught, Chiron Behring, and PT BioFarma.

PAHO refused to purchase OPV with VVMs.

SAGE released a statement in support of VVM introduction that is published in the Weekly Epidemiological Record 30 August 1996.



VVMs are helping our mobile and outreach teams stay a little longer in the field.

Peripheral Health Unit staff member, Sierra Leone, 1990

photo: jean-marc giboux, *van / turkey*

How far you can push the envelope, how much can you use VVMs to take vaccines out of the cold-chain? Julie Milstien*

When I was hired by the WHO in 2001, I became the focal point for VVMs. But the story with VVM goes way back to 1979. Where were you in 1979?

In 1979 I was working for the Food and Drug Administration (US) and wasn't involved with WHO at all. My first involvement was in 1983 when I was working for PAHO and I went down to Peru and there I saw the prototype VVMs that were on measles vaccine.

Did you take part in that study?

No, no I didn't. I was working on vaccine storage issues because we were looking at potency testing and I wanted to have it on video to document the conditions vaccines were being exposed to, and I went to Iquitos, Peru, and we saw them, I guess it was the regional store there, doing the field test on the prototype indicators.

When I came in - I think Michel (Zaffran) and Peter (Evans) came about the same time - and Peter was mostly working at that time on the auto-disposable syringes - that was what he came to WHO from UNICEF for - and John - there was work already on

photo: samba sow, *tombouktu / mali*

*Julie Milstien, *Former Team Leader of Access to Technologies at WHO, currently Adjunct Associate Professor, University of Maryland, School of Medicine, Baltimor, USA*

In one clinic the drug storeroom key was broken and it took staff six days to obtain a copy. Upon opening the room, they discovered that the gas cylinder was empty, a situation which would normally necessitate discarding all vaccines in stock. In this case, all the vaccines were discarded except those with VVMs showing no heat exposure damage, which were kept and used.

Health worker, Zimbabwe, 1992

1996
Rexam (formerly Bowater) withdrew from further VVM development due to inability to make a viable product.

CCL Label (US) emerged as a potential VVM supplier.

India imported OPV with VVMs for NIDs and after the experience issued an official request to WHO for assistance in supplying VVMs on locally produced OPV.

Meeting held at WHO Geneva with UNICEF, OPV suppliers, LifeLines, 3M, WHO, and PATH to discuss VVM introduction on OPV.

1997
UNICEF sent a questionnaire to 50 countries to determine whether they had any difficulties with VVM introduction.

VVM impact studies completed by WHO during NIDs in Kenya, Nepal, Tanzania, and Turkey.

the VVMs, but I wasn't really directly involved in them until early 1990s. It was the time we started to discuss with UNICEF. By that time there were three manufacturers...

VVM manufacturers you mean?

Yes, VVM manufacturers. But they dropped out fairly early. 3M was the last one to drop out.

What were the issues on VVMs when you got involved?

When I was involved we had really two challenges. One was to convince UNICEF that this was going to be a good thing. And the second one was to make sure that the specifications were reasonable. Polio was the first start to go forward with UNICEF.

Around that time we were working with the Children's Vaccine Initiative which started, I think, in 1991, and the idea of the Children's Vaccine Initiative, if you remember, was to get a thermo stable liquid vaccine that was given orally that would be against all the diseases of childhood. And so, my part of it was to work on a thermostable polio vaccine. And so we were working very, very hard on trying to get a thermostable polio vaccine and we actually got a thermostable polio vaccine or a polio vaccine that was stabilized with deuterium oxide. At that point, I guess, UNICEF had just agreed that we could go forward with VVMs on polio vaccine and so, at that point, EPI decided, well, we really didn't need a more thermostable polio vaccine because we had VVMs, and if we could use VVMs we really wouldn't need more stable vaccines. And so the project died and it was very painful and we lost credibility with the manufacturers that were working on it.

But, anyway, that's the way it went. Our challenge then was to try to develop the VVMs so that we would know what would be the temperature ranges and that whole work on specifications was way beyond my capabilities - at the time John was bringing that forward - but one of the things that we decided to do was then to do a couple of experiments to show that the stability of the vaccines actually matched what was happening with the VVMs.

This is the famous correlation study?

Yes, the correlation study. That study was actually done by David Wood when he was in the NIBSC. But that was fairly late in the development. I mean, the early part was really trying to come to same page with UNICEF

Julie, how do you see the future now?

photo: ümit kartoğlu, *yvoire / france*

photo: lassana keita, *mopti / mali*

I think - and this is what we talked about at TechNet - that there is a lot of work that could go forward now, and on really how far you can push the envelope, how much can you use VVMs to take vaccines out of the cold-chain. I mean that was - from my point of view - the real advantage of the VVMs, to really take advantage of the stability of products. And my challenge to the TechNet - of course, the TechNet felt that they couldn't actually make policy decisions - but my challenge to the TechNet was why not, you know, push WHO to actually make some sort of recommendations on specific vaccines that countries can now use the VVMs to take vaccines out of the cold-chain completely? Hepatitis B, for example. Tetanus toxide, for example - the ones that are most stable, and really start using them that way.

Because what's going to happen - the presentation that I gave to the TechNet that John asked me to do was to look at, first of all, the current products and divide them up and they fell into two groups. The one group was products that were relatively unstable but could be frozen so it wouldn't be damaged by freezing. And the other group was products that were relatively stable - in fact, very stable - that were susceptible to freezing and so, that's the group that you would want to take out of the cold-chain. Although, there's been history with the VVMs of taking even the less stable vaccines out of the cold-chain, like polio. But the new vaccines that are coming along don't fall into that clear-cut group and the other challenge for some of the new vaccines, for example - I think, it's GSK's rotavirus vaccine - won't even fit into one of the little vaccine carriers because it's so big. And so, there's going to be different challenges that are coming along which is why now is the time to actually start to use the VVMs the best way they can be used.

When a new product comes up, actually who decides at what temperature it should be kept? If it is a very stable vaccine - say more than a year at 20-25°C, is there a way that the vaccine could be licensed with storage recommendations out of cold chain?

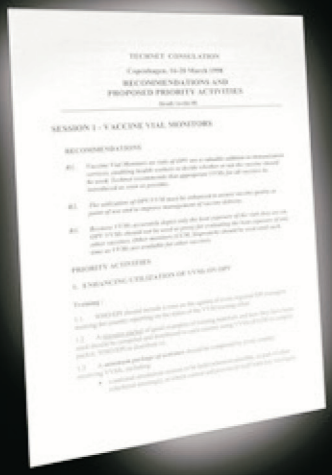
Manufacturers are required to present data in their licensing application to support the stability and the dating period that they propose for it. Obviously, if they can, they want to have a product that's as stable as possible and can be stored as easily as possible so they would like to have a product that could be stored virtually indefinitely at 2-8°C but they don't always have that data because it takes a long time to get definitive data. You cannot get it concurrently for licensing purposes, although you can then update it using concurrent data. For most products, products for which WHO already put together the guidelines - that's the ECBS - already put together guidelines - there is a recommended dating period of stability and so they will try to match that. But it's basically the manufacturer. The burden is on the manufacturer to determine what would be the stability of the dating period for the product.

1998

3M discontinued work on VVMs due to inability to produce product at a competitive price.

CCL Label submitted VVM prototypes to a WHO independent laboratory for evaluation, but they did not meet specifications.

The Technical Network for Logistics in Health (Technet) formally recommended that VVMs be introduced for all vaccines as soon as possible.



Consumer Association Research and Testing Centre (UK) began validation of HEATmarker™ VVM2 samples under a WHO contract.

photo: ümit kartoğlu, *boboye / niger*

But do you see whether it is ever possible that a manufacturer would come up with a product recommending that the product can be kept out of cold chain?

Well, they certainly do it for drugs! So, if they had the data to support it they might do it. I would doubt it because it would be very difficult for them to get the data to support it over a long enough period of time.

But because out of the cold-chain means it could be anything, it could be any temperature so they would only be able to provide data at specific temperatures. They might be able to provide data at 25°C and at 37°C and at 2-8°C and freezing temperature, but they wouldn't be able to provide the whole range of temperature extremes that the vaccine might be subjected to.

Thank you Julie.

How can you feel safe if you do not see the VVM? Dario Cresci*

Dario, I remember you telling me the famous lipstick- top label story during the 2002 VVM technical consultation meeting in Geneva. We will come to that, but first I want to ask you how you came across VVM for the first time?

I came across VVM when I joined Chiron in 1996. I joined the vaccine world and polio was one of our major products. I found this strange label that had to be taken care of. The more I learned about the concept, the more I found it to be a very good concept - very easy to understand, simple and straightforward.

We looked at different and additional ways of extending our products portfolio so they could have a VVM on it. Since I'm a believer of the concept, it is easy for us to work with VVM, and we really enjoy what we do.

Let's come to the Geneva meeting...

That was a typical example of serendipity. WHO wanted to extend the usage of VVM, and one of the requirements for freeze-dry vaccines was that VVM should have been applied on top of the vial. The reasons behind this were legitimate, but we were caught unprepared. I have a very, very committed staff who are creative and innovative. So I launched the challenge to my people and said, why not being the ones who make it happen?

Here is the story: I was looking at my wife and she

photo: ümit kartoğlu, *rosia / italy*

was putting on lipstick. When she placed the cap of the lipstick onto the dressing table, the label on the cap, most probably giving the code number and color information of the lipstick, caught my eyes. My eyes fixed on the label. I was actually seeing a vaccine vial with a VVM on the cap. That was the vision. From this, we developed a whole concept of modifying the vial in order to accept the VVM, and then I personally found the company who was applying the label on the lipstick. But to my surprise, when I talked to them, they said, yes it's possible and no problem, we can apply 50 labels a minute, and I said, 50 labels?! This is a free-strain. "My machines are working at 400 labels per minute". So we had to do something because the top management would never accept that I slow down the production speed.

*Dario Cresci, *Secondary Manufacturing Site Head Novartis Vaccines & Diagnostics Soviolle Italy*

In-depth VVM impact study completed in Bhutan by WHO.

A meeting on the introduction of VVMs on all EPI vaccines was held at WHO Geneva and attended by WHO, UNICEF, PATH, USAID, LifeLines, and 3M.

PATH, CCL Labeling Equipment, LifeLines and a pharmaceutical company conducted a collaborative cap labeling demonstration project to demonstrate feasibility to vaccine suppliers, WHO, and UNICEF. WHO sent a letter to all WHO pre-qualified vaccine producers requesting feedback on VVM specifications.

1999

CCL Label confirmed interest (in letter to UNICEF) in further VVM development.

Sensitech (US) expresses interest to WHO regarding VVM development.

WHO and UNICEF issued a joint policy statement advocating the use of VVMs on all vaccines.


Quality of the cold chain

WHO-UNICEF policy statement on the use of vaccine vial monitors in immunization services

At a pre-tender meeting in Copenhagen, UNICEF announced that VVMs would be included on all vaccines in the 2000 tender.

WHO updated VVM specifications to make them relevant for all vaccine types.

2000
Consumer Association Research and Testing Centre (UK) finalized the conformity test of HEATmarker™ VVM2 samples.


photo: ümit karloğlu, *rosia / italy*

We worked together, bringing our different expertise together - our expertise in high-speed labelling, or higher than what the lipstick company has, and their expertise in the technical capability of applying a round label on top of a very small top of the lipstick. At the end of the day, we came out with a top labelling machine (design) that could work at the same speed as our labelling machine, which meant no reduction in lead times, no idle time on the lines, and, especially, having the VVM on top of a range of products that were not being met before.

Thank you Dario, I like this story so much. How do you see the future with VVMs now? Where do we go from here?

I'm a manufacturer and not a health worker. I find the whole concept of VVM to be a really interesting, simple and nice concept. I do not understand why a vaccine should not have a VVM, especially in countries where storing and transportation of vaccines could be a problem. How can you tell otherwise if a vaccine was properly stored before it reaches you? How can you feel safe if you do not see the VVM?

Which countries need VVM then? Interestingly, when you look at literature on cold-chain problems, you will see many studies published coming from the industrialized world - from the US, from France, from the UK, from Australia and from Canada. Cold-chain problems do not only belong to the developing world. It is a global problem. In that sense, I would go one step further and say that "VVM for all vaccines", no matter where they are used - be it in Ghana, in Gabon, in Vietnam or in the US. It doesn't make any difference.

Yes.

What is important is, as you said, if you're the health worker at the end of the line that receives a vial ...

... how can you be sure? Yes.

... because VVM is the only tool that is available

at all times on the vaccine from the moment of its production.

Exactly.

Even it is stored and transported correctly. Yes, there are other temperature monitoring devices but you don't have the history VVM provides. Without VVM, health workers can only assume "things" were all right before vaccines reached their facility, like blindly believing in something you do not see before your very own eyes.

Exactly.

VVM brings an end to this "assumption". Now, all health workers working with VVMs have this confidence. They see what has happened to the vaccine before.

It is confidence at a glance.

... before it came into their hands.

I agree. That is why I think it's really ingenious because you take a glance and you say yes/no - full stop!

In terms of reading whether or not it can be used, it's very straightforward. But when it comes to VVM-based vaccine management, when you have different shades, and let's say you have a fixed immunization activity point or you have an outreach, which one to take first? This requires some additional training.

Exactly. Well, I've always been a believer because when I'm doing something, being a manufacturer - the last link of the chain is in the manufacturing - I see myself as a user of what I'm doing. I dislike things that are not easy to use or easy to understand because it creates problems and that's what I like.

Thank you Dario.

photo: veronica guzzi, *seychelles*

Precision Measurements and Instruments Corporation (US) began conformity tests of 3 other HEATmarker™ VVM types (VVM7, VVM14, and VVM30) under a WHO contract.

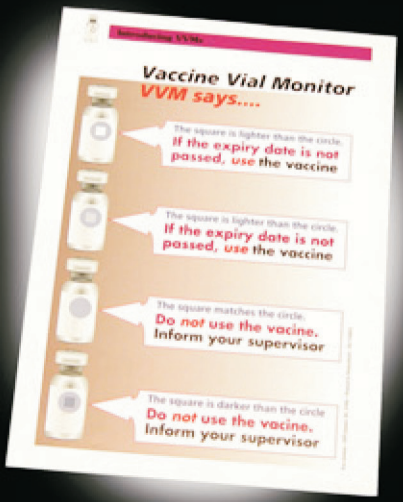
UNICEF included VVMs among the "minimum requirements for vaccines to be procured by UNICEF" in the invitation to bid for 2001-2003.

VVMs were also included among the minimum requirements for vaccines in the RFP for GAVI for under-used vaccines, related products and contributions.

WHO publishes the "Making use of vaccine vial monitors. Flexible vaccine management for polio supplementary immunization activities" manual.

2001
Precision Measurements and Instruments Corporation (U.S.) completed conformity tests of HEATmarker VVM2, VVM14, and VVM30.

Only three UNICEF vaccine suppliers Japan BCG, Pasteur Dakar, and Chiron fully complied with the VVM attachment for vaccines other than OPV.



UNICEF solicited documentation from vaccine suppliers on all issues limiting their ability to provide VVMs on vaccines and WHO provided UNICEF with a document addressing each technical concern raised.

JICA ordered measles vaccine with VVMs from Chiron and donated it to Vietnam.

2002

Impact study being conducted in Vietnam by MOH and WHO with VVMs on measles vaccine.

WHO published the "Getting started with vaccine vial monitors" manual.

WHO revised the current VVM specifications (E6/IN5) and test procedures (E6/PROC5).

photo: jean-marc giboux, *al gabeen / yemen*

One more UNICEF supplier LG Chemical Inv. Ltd. fully complied with the VVM attachment for vaccines other than OPV.

WHO sent a letter to all WHO pre-qualified vaccine producers requesting feedback on revised VVM specifications and test procedures.

Technical review of VVM implementation at WHO Geneva, 27 March 2002.

2003
WHO holds a regional meeting with vaccine manufacturers in New Delhi to accelerate expansion of VVMs beyond OPV.

PATH assist Indonesia MOH to conduct a cold chain study to remove icepacks to prevent freezing and reinforce usefulness of VVM in freeze prevention.

UNICEF SD issues a new tender for 2004-2006 and includes VVMs among the minimum standards for all vaccine purchases.

As we visited the centers, we found more and more vials with dark red (expired) indicators (early VVMs), even though the daily temperature charts recorded temperatures between 2°C and 10°C. Our first reaction was, "the indicator doesn't work". In the last health center we visited, with 25 dark red indicators, the thermometer read -2°C. Another thermometer was left in the fridge overnight and the next morning the readings were compared. The original thermometer read 4°C, but our thermometer read 18°C! The mystery was solved - the health centers had been using unreliable thermometers to regulate refrigeration where vaccine is stored - thus, dark red indicators. If it were not for the indicator, it might never have been discovered that vaccines were cooking in the Amazon! *Consultant, Peru, 1984*

photo: ümit kartoğlu, *kaou / niger*

Vaccine vial monitors - is the waiting almost over?[1]

A simple device could protect children from receiving heat-damaged vaccine and save millions of dollars' worth of wasted vials. Phyllida Brown investigates

Every year, millions of doses of vaccines are thrown away for fear that they might have been heat-damaged, whether or not they actually are. Heat damage is not visible, so health workers have been trained to discard anything that they suspect could have been exposed, for example after two trips out to the field. More serious still, where failures in the cold chain go unnoticed, children are probably receiving heat-damaged vaccines that offer no protection.

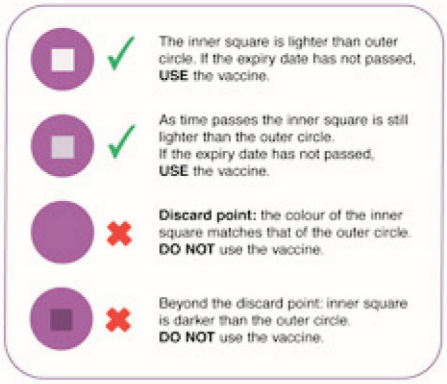


Figure 1. How to read a vaccine vial monitor, source WHO.

But these problems are largely avoidable. Since 1996, a tool called a vaccine vial monitor (VVM) has been available. A VVM is a label that contains a heatsensitive material. It is placed on a vaccine vial, where it registers heat exposure over time, for example if an ice pack melts, or if a fridge suffers a short power cut. As time passes, the colour darkens. The warmer the temperature, the faster the colour changes. The label shows clearly when the cumulative heat exposure has reached the point where the vaccine should be discarded (see Figure 1). As long as the vaccine has not reached the discard point, and has not reached its expiry date, it can be used even if it has been out of a fridge several times (see "How does it work?", Box 1).

"Used properly, this can be a miracle tool to reduce wastage and prevent the use of heat-damaged stock," says Ümit Kartoglu of WHO's department of Vaccines and Biologicals. In Bhutan, a study showed that wastage fell by 49% on polio vaccine where VVMs were used (1). Comparable results have emerged from studies in Nepal, Turkey, Ghana, Kenya, Sudan, Tanzania and Vietnam. The benefits are greatest during national immunization days, when large volumes of vaccine are transported into the community, but VVMs can also cut wastage in routine programmes, especially in remote rural areas where teams must travel far from base to reach children. The technology is inexpensive, with each VVM adding.

So why don't all vaccines carry a VVM? Only and polio vaccine, the most heat-sensitive of the vaccines used by the Expanded Programme on Immunization, has carried VVMs since 1996. Even though UNICEF and WHO have requested manufacturers to supply VVMs with all vaccines

1. How does it work?

The VVM is a coloured circle with a pale square in its centre. It can be printed on a label or attached to the cap of a vaccine vial, or the neck of an ampoule. The square gradually darkens until it matches the surrounding circle. At the point where the inner square matches the surrounding circle, the vaccine has reached its discard point.

The colour change is due to a chemical reaction known as polymerization. With heat and time, the initial agent, a monomer, is converted irreversibly to a polymer. The chemical reaction speeds up when the temperature is raised. As different types of vaccines have different levels of heat sensitivity, VVMs come in four types whose rates of colour change at specific temperatures have been designed to reflect these different heat sensitivities. The type of VVM that is attached to a particular vaccine is the type appropriate for that vaccine's heat stability. For example, VVM2 is designed for oral polio vaccine, the least heat-stable of the vaccines used in the Expanded Programme on Immunization, which reaches its discard point after two days at 37ºC. At the other end of the spectrum, VVM30 is suitable for certain types of hepatitis B vaccine, which are relatively heat-stable and survive undamaged up to 30 days at 37ºC.

A VVM does not measure the potency of a vaccine, but simply its heat exposure. Heat exposure is one of the main factors that can affect vaccine potency. VVMs do not provide information about whether a vaccine has been frozen, another potential source of damage, especially for hepatitis B.

[1] *Reprinted from GAVI Immunization Focus, Global Alliance for Vaccines and Immunization, July 2003*

WHO Global Training Network on Vaccine Management (GTN-VM) develops training materials for VVM.

In its first meeting of the year, GAVI Board recommends immediate intensive action by appropriate GAVI Partners to accelerate the implementation of VVMs, consistent with ensuring vaccine security.

Immunization Focus, published by GAVI isues an article on VVM implementation questioning why don't all vaccines carry a VVM.

photo: ümit kartoğlu, *bandung / indonesia*

since 1999, and included VVMs in the minimum requirements for UNICEF tenders since 2000, VVMs are still only available from a minority of the 23 manufacturers that supply vaccines to the UN agencies. They appear on some, but not all, vials of BCG, yellow fever, measles, hepatitis B and tetanus-toxoid vaccines. Some multivalent vaccines also carry VVMs, including measles-rubella, measles-mumps-rubella and DTP-Hib liquid vaccine (3).

At its meeting in Dakar in November 2002, the GAVI Board resolved that all vaccines purchased by the Vaccine Fund will include VVMs after 2003. When the Board meets this month, its vaccine industry members will provide an update to the other members on action taken by industry to meet this requirement.

WHO, UNICEF and the other members of the Alliance are working with the industry and hopeful that consensus is gradually being achieved. At present, manufacturers hold differing positions on VVMs. Some, such as Chiron in Italy, Japan BCG, Green Cross Vaccine Corporation, LGLS and the Institut Pasteur in Dakar, Senegal, have introduced them for products sold to UNICEF. Other manufacturers have clear plans to introduce them. For example, says Walter Vandersmissen at GlaxoSmithKline in Belgium, the company's tetravalent vaccine DTP+HepB is expected to carry VVMs later this year, while its pentavalent DTP+HepB+Hib should follow early in 2004. The Serum Institute of India has been validating VVMs on its products but, says Suresh Sakharam Jadhav at SII, this process is now almost complete and staged introduction of VVMs will begin in January 2004.

Aventis Pasteur added VVMs to its oral polio vaccine in 1996 and says it recognizes the tool's benefits for highly heat-sensitive vaccine. But it says it has "reservations" about using VVMs systematically on all vaccines for developing countries, and it has not yet put them on any of its other relevant products. Nonetheless, Aventis Pasteur says it has evaluated the feasibility of expanding the use of VVMs to three of its products: DTP-Hib, yellow fever and measles vaccines. "Aventis Pasteur has targeted the end of 2003 to complete the feasibility evaluation, at which time it hopes to have the ability to respond

to the special needs of GAVI," says the company.

Some manufacturers have expressed doubts about the technical accuracy of VVMs and their validation. But VVMs are validated rigorously, both in the laboratories of both the VVM manufacturer, LifeLines in New Jersey, USA, and the laboratories of vaccine manufacturers that currently use them. Each batch is tested by exposure to heat in water baths and using a colour reflectance densitometer, to ensure that the VVM changes colour correctly in response to heat exposure. Vaccine manufacturers also conduct tests before accepting each shipment from the VVM manufacturer. WHO has also commissioned various independent laboratory tests, for example at the UK National Institute for Biological Standards and Control, to compare these results with those of the manufacturers. "We have shared the results of these studies with all industry members, and none of them raised any questions," says Kartoglu.

Still, some in the industry fear that manufacturers could be held liable for products bearing "healthy" VVMs that were later blamed for adverse events. However, says Kartoglu, concerns about liability are nothing new. All vaccine manufacturers risk being held liable for adverse events attributed to their products, and VVMs do not change this. If anything, a VVM should reduce the risk that a manufacturer will be held liable for adverse events, because heatdamaged products are less likely to be used. The risk that a VVM will fail in the field is only theoretical, says Kartoglu: it is a validated device that is checked, lot by lot, by the producer. Manufacturers that use VVMs already perform regular audits on the producer. And, just like any other material used in a vaccine production line, the vaccine manufacturer checks every lot as part of its acceptance process. In six years of use, with more than 800 million vials of vaccine bearing VVMs, there has been no documented case of a child receiving heat-damaged vaccine due to a faulty VVM.

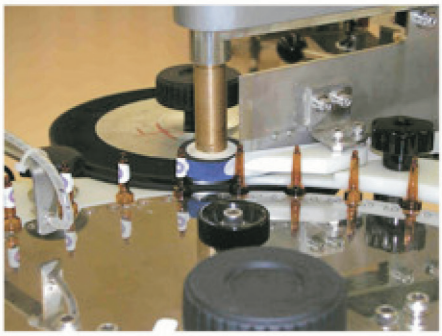


photo: Japan BCG

For some vaccine manufacturers, the strongest objections are not technical but logistic or economic. Aventis Pasteur told Immunization Focus that its reservations about universal use of VVMs for developing countries include the size of the investment relative to the expected returns, and concerns that there is currently only one manufacturer of VVMs. Aventis Pasteur also has concerns about how to manage its own inventory, given that VVMs are required only on vaccines supplied through UNICEF, and not currently on vaccines supplied through the Pan American Health Organization (PAHO).

Firm contracts for vaccines

Vandersmissen at GSK says the company may lose flexibility in the use of its filling-line capacity if it has to add VVMs to some vaccines. He says

2004

WHO presents study findings on the use of cold water packs to prevent freeze damage and accelerate VVM implementation in TechNet21 Antalya global consultation.

TechNet21 Antalya

WHO changes the VVM nomenclature from ABCD to VVM 2, 7, 14 and 30.

Six more vaccine manufacturers introduce VVMs on all their vaccine products.

WHO GTN/VM develops VVM card game and vaccine management board game to be used as interactive training tools.

photo: ümit kartoğlu, *indaman / niger*

that manufacturers would be encouraged to devote space and capacity to VVM-bearing products if they had firm contracts from public-sector vaccine buyers to purchase a given quantity of vaccine. At present, only a "gentleman's agreement" is in place until the vaccines are bought, and this uncertainty makes manufacturers wary of risking wasted capacity.

Some manufacturers are reluctant to introduce a new technology that they believe will need to clear yet further regulatory hurdles. WHO says it is the responsibility of the individual manufacturer to contact their national regulatory authority about any approval it may need for VVMs. However, WHO has already taken steps to find out the position in some countries, and will continue informally to work with national regulatory authorities on this issue. France and Belgium have told WHO that VVMs do not require regulatory approval from their national authorities. In the US, for vaccines licensed for distribution in the US, manufacturers would need a supplement to their licence application, and vaccines not licensed for US distribution have to meet export regulations. However, these are not seen by WHO as difficult to achieve.

UNICEF, as a key public-sector buyer of vaccines, is responsible for sending clear messages about VVMs to its suppliers. "We are working with all manufacturers to ensure the implementation of

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GLOBAL HEALTH

HOW TO SAVE A LIFE

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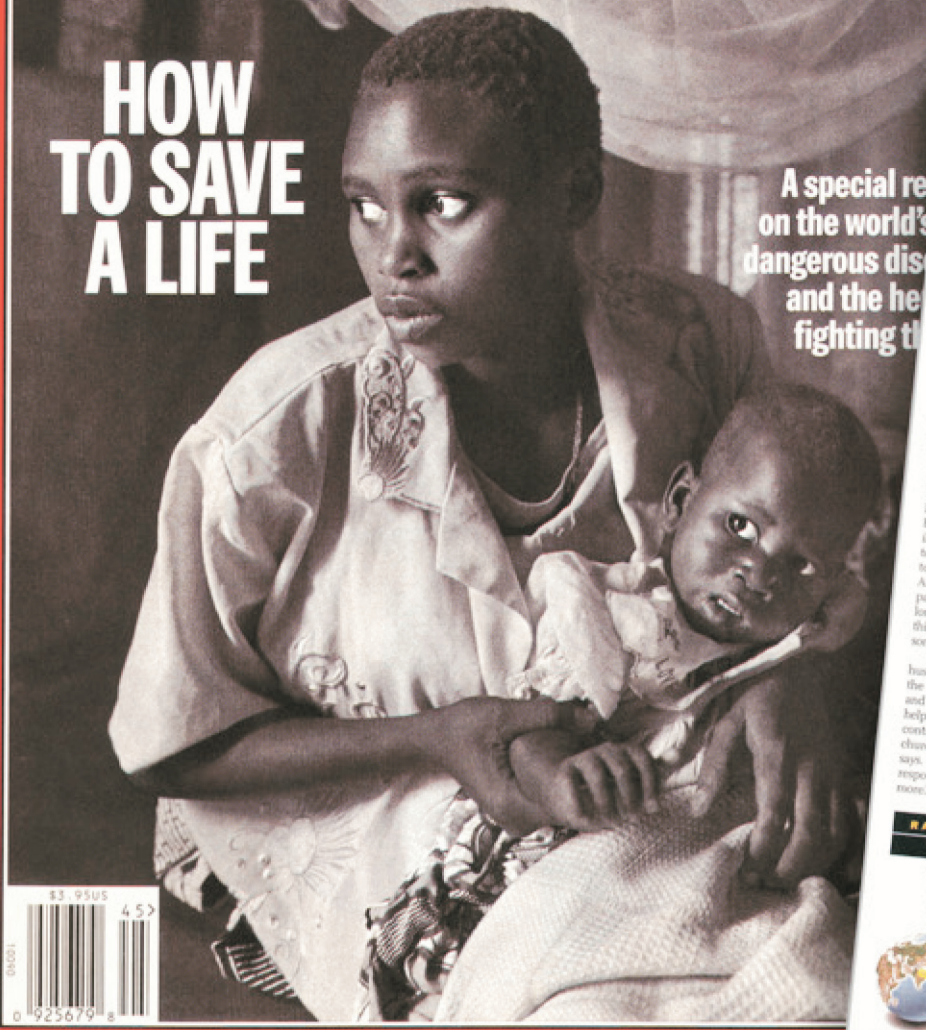

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says Okaalet, who has lost three brothers to AIDS, is to provide accurate information and realize that "the messenger is as important as the message."

By way of example, Okaalet recalls a ministers' workshop that MAP organized in Zambia. The leader was a dynamic young woman named Bridget who was HIV positive but didn't reveal her status at first. Toward the end of the program, after she had reviewed how HIV is spread, she told the participants that she was infected. "They were shocked," Okaalet says. "She didn't look like somebody with HIV." They were even more stunned to learn that she contracted HIV from her husband, who was a minister, and that he became infected after having sex with a woman he knew had AIDS because he had been counseling her about her illness. Bridget's husband was too scared and embarrassed to tell his wife what he had done. After listening to her story, the pastors realized they could no longer think of AIDS as something that happens only to someone else.

Both Bridget and her husband have since died. But the efforts to educate ministers and their congregations and help them face the epidemic continue. "For a long time the church was very quiet," Okaalet says. "We are beginning to respond, but we have to do more." —By Christine Gorman

RAM SHRESTHA
NEPAL

Vitamin Sherpa

Saving the lives of sickly children doesn't take much: a little money, some medicine, the right food. In Nepal, they've discovered one more factor: the power of the grandmother.

HIGH TECH FOR THE LOW-TECH WORLD

Battling disease is easy if you're on a power grid with access to effective tre
But what if clean water and electricity are unavailable luxuries? These produc
designed for use in just those low-resource settings. —By Alice Park

▲ PLUMPY'NUT
The peanut-based nutritional paste, inspired by Nutella, comes ready to eat and doesn't require clean water for mixing

▲ ONE SHOT
One-dose, single-use packaging of this hepatitis B vaccine means no measuring and no dangerous needle reuse

▲ SAFETY NET
The latest textile techniques
in long-lasting nets, which repe
causing mosquitoes even after

It was Ram Shrestha, chemist and health expert, who figured out how to unleash it.

The poverty in Nepal and the toll it exacts on its smallest citizens are staggering. Twenty years ago, the infant-mortality rate was 133 for every 1,000 births, most of the babies claimed by pneumonia and diarrhea. By the 1980s, it was clear that a lack of vitamin A in the Nepalese diet was a factor in the high rates of infant mortality and in a form of blindness. All it would take to reduce both would be a low-cost vitamin-A capsule taken as infrequently as twice a year.

Great news, but how to get the word—and the vitamins—out? The government set up a program to do the job, but in a rugged country like Nepal, with a scattered population inately suspicious of strangers, it wasn't going to be easy.

Shrestha had some ideas. A onetime Peace Corps employee who earned his master's degree in international health at Tufts University in Massachusetts, he returned to Nepal in 1991, at about the time the vitamin program was getting under way, at his assistance.

The first thing he was that no matter wh sponsored the progra villagers were not goi receptive unless they ownership of it. So he traveling through remo areas, explaining the be

2005
Two more vaccine manufacturers introduce VVMs on all their products

2006
WHO, UNICEF, PATH and Temptime start planning of 10th year VVM anniversary meeting.

WHO issues new Performance, Quality, Safety (PQS) product specifications and verification protocol for VVM.

VVMs at the earliest opportunity," says Shanelle Hall at UNICEF Supply Division. She points out that because there are so few suppliers of certain vaccines, UNICEF does not always have a choice; to ensure enough doses are bought, UNICEF must sometimes buy vaccines without VVMs at present. "But by having VVMs as part of the technical specification for vaccines, and through continuous communication with manufacturers, we are building up the number of vaccines we receive with VVMs." Hall points out that it would help if all buyers also required VVMs. Steps are being taken towards indroducing VVMs in the PAHO region. Programme managers from PAHO countries will meet in Peru later this year to discuss the options.

Mercy Ahun, formerly the manager of Ghana's national immunization programme, and now with the GAVI Secretariat, is clear. "VVMs are currently one of the best contributions that vaccine manufacturers can make to the lives of children".

References

(1) Vaccine Vial Monitor Impact Study Results. Kingdom of Bhutan. July 1997 through November 1998. Program for Appropriate Technology in Health, Seattle, 1999.

(2) Quality of the cold chain. WHO-UNICEF policy statement on the use of vaccine vial monitors in immunization services. WHO/V&B/99.18

(3) United Nations Prequalified Vaccines (June 2003). www.who.int/vaccines-access/quality/un_prequalified/prequalvaccinesproducers.html

Further reading

Getting started with vaccine vial monitors. WHO, 2002. WHO/V&B/02.35

photo: ümit kartoğlu, *bandung / indonesia*

photo: ümit kartoğlu, *boboye / niger*

UNICEF, PATH and USAID hold a cold chain workshop in Americas focusing on vaccine freezing issue. Meeting brings heightened awareness of vaccine heat stability and an interest in adopting VVMs to reduce vaccine wastage and to enable out-of-cold-chain strategies for vaccine storage and distribution.

2007

VVMs are available on all prequalified vaccine products with the exception of 15 out of 72.

VVM celebrates its 10 successful year of implementation. Since its introduction in 1996, close to 2 billion doses of VVMs are used on WHO prequalified vaccine products.

vvm 10 years

photo: WHO/EPI, *southern sudan*

VVM helps me to understand whether there is a cold chain problem.

Health worker, Vietnam, 2003

I like being able to see how much heat exposure a vial has received.

Vaccinator, Thailand, 1991

photo: philippe blanc, *ethiopia*

"Look my friend, your VVM is as good as mine".

A supervisor of a number of vaccination teams is waiting for vaccine carriers and icepacks to start immunizing against polio in the region for which he is responsible. He received the vaccines, but to his astonishment, he hears over the radio that the vaccine carriers were delivered on the wrong spot, and that he is expected to manage by whatever means he can think of.

The local population tells him about what they call, "the local fridges": gourds with water and charcoal, that allow to keep the contents cool. The supervisor decides to ask the population for a number of gourds. First there is some resistance, because the people are afraid the gourds will break, but when the supervisor asks whether they prefer polio or broken gourds, the argument is settled. The supervisor puts a "kick Polio out of Africa" t-shirt on top of the water and charcoal and places the vaccines, wrapped in "kick Polio out of Africa" caps, on top of these. He then sets off for the cattle camp, where he starts immunizing after arrival.

However, another team, with vaccine carriers and ice, had also decided to immunize in the same camp. The supervisor of this team accuses the gourds team of using non-potent vaccines, because of improper storage, and advises people to bring their children to his teams. The supervisor of the gourds team can of course not accept this insult to his professional pride and clearly expresses his opinion in front of the VC supervisor. This nearly develops into a fight, when the village elders decide to interfere. They ask the VC supervisor why he thinks his vaccine carriers are any better than their gourds. On his guard, and realizing how delicate the question is, the VC supervisor challenges the gourd supervisor by accusing him of using non-potent vaccine.

The latter takes two vials of OPV, one out of the gourd and one out of the vaccine carrier and says proudly:

"Look my friend, your VVM is as good as mine".

Hans Everts
Technical Officer, WHO

Abstracted from a Report by Hans Everts of WHO/GPV, 1998.

photo: ümit kartoğlu, *salalah / oman*

Use of vaccine vial monitors to manage vaccines after the recent earthquake in Jogjakarta, Indonesia[1]

Indonesia has applied vaccine vial monitors (VVMs) to all its EPI vaccines except for the BCG vaccines (due to economic reasons). It is used forMeasles, OPV, DTP and DTP-HB, HB, TT and DT vaccines. This application is very helpful to supplement the "Earliest Expiry First Out" (EEFO) system and it improves the confidence of the health workers at all service levels regarding the "quality" of the vaccine to be delivered.

During the May 2006 earthquake centered in Yogyakarta (on the island of Java in Indonesia), much of the infrastructure was damaged including the cold store facilities at the district and health centers. Electricity supply was out for some days and generators were not functioning or used. By observing the VVM condition on the vaccines, health workers were able to decide which vaccines were still viable for use and which needed to be discarded. In the disaster areas, VVMs on the OPV vials were already reaching the usage limit, giving visual indications to health workers that vaccines needed to be discarded and re-supplied. The other vaccines with VVMs still showing good condition were not discarded and could still be used to reduce wastage. As for the BCG, the MOH decided to discard all BCG vaccines because there was no indicator to show the heat exposure effect in a non-functioning cold chain condition. In total, vaccine in 5 districts and more than 50 health centers (an estimate of up to 50,000 doses) was saved from being wasted due to the presence of VVM on the vials. The practicability of VVM as an indicator that can be read visually without any accessory devices is a great advantage. This is one example how the use of VVM is able to reduce vaccine wastage and improve health workers' confidence in vaccine quality before administration.

Anton Widjaya and Vanda Moniaga
PATH/Indonesia Immunization Team

(1) From TechNet POST 00960E : VVM USE / INDONESIA, 5 August 2006, http://www.technet21.org

photo: ümit kartoğlu, *jogjakarta / indonesia*

photo: Umit kartoğlu, Jogjakarta / Indonesia

photo: jean-marc giboux, *peshawer/ pakistan*

I personally think that VVM is the best invention made in the recent history of medicine, which has larger implications of doing common good to all without any discrimination. Whoever discovered it, should receive Nobel for Peace (since it is so universal in nature) and WHO has to share the any greater award for convincing whole lot of nations to follow this standard.

Dr Giridhara R Babu, UCLA, Los Angeles, USA, 2007

WHO recognition certificates for contribution to global public health

In order to mark the 10-year anniversary of VVM implementation and to acknowledge the efforts put into this tool, WHO has distributed recognition certificates to the countries, organizations, agencies, industries and individuals listed below, for their contribution to global public health through their critical involvement in VVM development, implementation and expansion.

COUNTRIES

Argentina - conducted validation study with early VVM prototypes in early 1980s.

Bangladesh - participated in HEATmarker™ VVM design study between 1990-1992.

Bhutan - conducted most in-depth study of VVMs ever; assessing multi-dose vial policy and impact of use of VVMs on multiple vaccines in 1998.

Bolivia - participated in HEATmarker™ VVM design study between 1990-1992.

Brazil - conducted validation study with early VVM prototypes in early 1980s.

Cameroon - participated in HEATmarker™ VVM design study between 1990-1992.

Egypt - conducted validation study with early VVM prototypes in early 1980s.

India - imported OPV with VVMs for NIDS and after the experience issued an official request to WHO for assistance in supplying VVMs on locally produced OPV. With funding from DFID, India successfully implemented labelling of all locally produced OPV with VVMs. In 2007, India adopted a policy demanding VVMs on all locally procured vaccines.

Indonesia - conducted introductory trial with early prototype VVMs for measles vaccine in late 1980s. Participated in HEATmarker™ VVM design study between 1990-1992. Indonesia also demands VVMs on locally procured vaccines.

Kenya - conducted validation study with early VVM prototypes in early 1980s. Conducted introductory trial with early prototype VVMs for measles vaccine in late 1980s. Participated in HEATmarker™ VVM design study between 1990-1992. Conducted impact study of VVMs on OPV in 1997.

Mexico - participated in VVM design study in 1981

Nepal - conducted validation study with early VVM prototypes in early 1980s. Conducted impact study of VVMs on OPV in 1997.

Pakistan - conducted validation study with early VVM prototypes in early 1980s.

Peru - conducted validation study with early VVM prototypes in early 1980s.

Philippines - participated in VVM design study in 1981. Conducted validation study with early VVM prototypes in early 1980s.

Sierra Leone - conducted introductory trial with early prototype VVMs for measles vaccine in late 1980s. Participated in HEATmarker™ VVM design study between 1990-1992.

photo: ümit kartoğlu, *boboye /niger*

South Africa - conducted VVM knowledge, attitudes and practices (KAP) study in 2000.

Tanzania - conducted pilot introduction study of VVMs on OPV in 1995. Conducted impact study of VVMs on OPV in 1997.

Thailand - conducted introductory trial with early prototype VVMs for measles vaccine in late 1980s. Participated in HEATmarker™ VVM design study between 1990-1992.

Turkey - conducted impact study of VVMs on OPV in 1997.

Vietnam - conducted pilot introduction study of VVMs on OPV in 1995. Impact study on use of VVMs on measles vaccine in 2002.

Yemen - conducted validation study with early VVM prototypes in early 1980s.

Zambia - conducted introductory trial with early prototype VVMs for measles vaccine in late 1980s.

Zimbabwe - conducted validation study with early VVM prototypes in early 1980s. Conducted a study on the impact of VVMs on measles vaccine discard rates due to heat exposure in 1992.

PUBLIC SECTOR AGENCIES

Basic Support for Institutionalizing Child Survival Project - Provided a sub-contract to PATH to draft a written summary of early field experiences with VVMs.

Canadian Public Health Association - Supported an introductory field trial of PTS-based VVMs in Sierra Leone and an impact study of HEATmarker™ VVMs in Zimbabwe.

Canadian International Development Agency - Supported an introductory field trial of PTS-based VVMs in Zambia.

Centers for Disease Control and Prevention - Provided co-funding to the USAID HealthTech program (managed by PATH) to advance availability of VVMs for measles vaccine. Activities included demonstration of cost-effective solutions for labelling vial caps and ampoules, and development of VVM training materials.

Department for International Development - Funded and managed activities that resulted in successful integration of VVM labelling onto OPV vials produced in India for government purchase and VVM training material development for national use.

Edna McConnell Clark Foundation - Provided initial product development feasibility funding to PATH for VVMs using the PTS chemical licensed to PATH by Allied Corporation. Supported design studies of PTS-based VVMs and VCMs in Mexico and the Philippines.

International Development Research Centre of Canada - Co-funded above activities with the Edna McConnell Clark Foundation.

Japan International Cooperation Agency - In 1998, adopted a policy to include VVMs in all vaccine donations.

Japan International Cooperation System - Adopted a policy to include VVMs in all vaccine donations. . The first Grant-Aid project handled by JICS included vaccine supply was titled "The project for eradication of poliomyelitis in the United Republic of Tanzania", since then JICS includes VVMs on all tender documents for vaccine purchase.

London School of Hygiene and Tropical Medicine (UK) - Collaborated with PATH and WHO in search for initial VVM technologies which resulted in selection of PTS format.

OXFAM - Supported design studies of PTS-based VVMs and VCMs in Mexico and the Philippines.

Pan American Health Organization - Involved in early dialogue with WHO and PATH regarding

VVMs beginning in 1985. Provided support for a validation field trial of PTS-based VVMs in Brazil. Provided oversight to PTS and HEATmarker™ VVM field trials in PAHO countries.

Program for Appropriate Technology in Health - Facilitated VVM development and advancement with support from a variety of donors, the largest of which is the USAID Technologies for Health (HealthTech) program. Developed and produced early PTS-based VVM and VCM prototypes. Collaborated with a variety of private sector companies, including Allied Corporation, LifeLines Technology, 3M, and CCL Label, to advance potential VVM technologies. Collaborated on early design, validation, and introductory field studies of VVMs/VCMs. Met with vaccine suppliers to discuss VVM implementation issues. Provided two equipment loans to LifeLines Technology via the PATH Fund for Technology Transfer. Purchased VVM prototypes from LifeLines for use in field studies. Demonstrated feasibility of cap and ampoule labelling in collaboration with Serum Institute of India, CCL Label, and LifeLines. Assisted WHO with development of VVM training materials.

United Nations Children's Fund - Supply Division involved in early discussions on VVM introduction via the "Technology Introduction Panel" in 1990. Held two meetings (New York-1991, Copenhagen-1994) to discuss inclusion of VVMs in upcoming vaccine tenders. Developed 1999 policy statement with WHO advocating use of VVMs on all vaccines. Responsible for inclusion of VVMs in tender specifications and negotiations with vaccine suppliers.

United States Agency for International Development - Primary supporter of funding to PATH for VVM development, field evaluation, and introduction via the Technologies for Health (HealthTech) program.

photo: jean-marc giboux, *konso / ethiopia*

photo: jean-marc giboux, *zendeh jan / afghanistan*

Without VVMs I could never be sure what happened to the vaccine before it came to the health center. *Health worker, Kenya, 1983*

When temperatures rocketed to 10°C, we had to throw away all the vaccines except those with VVMs. Supervisor, Zimbabwe, 1982

Today, the best contribution vaccine manufacturers can make would be to provide VVMs on all vaccines to make a difference in the life of a child. *Mercy Ahun, Immunization programme manager, Ghana, 2002*

"VVMs do have the advantage in that they are easier for health officials to see when and which vaccine is losing its potency and needs to be used first".

Health worker, Thailand, 1989

I find that VVM makes vaccine management a lot easier, from the planning stage up to service delivery for all strategies (fix, outreach, mobile and mass campaigns). With all these benefits, I can say that VVM has contributed to the reduction of vaccine wastage, and shows that with optimum utilization it avoids adverse secondary effects until now.

Josoa RALAIVAO, Specialist Access to Health Services Delivery, Madagascar, 2007

You know what others cannot see if they do not have VVM.

Health worker, India, 1994

photo: ümit kartoğlu, *boboye / niger*

five senses

vaccine vial monitors
10th year anniversary

" Conceived as a dream in 1979, today the availiabity of the VVM is the result of immense efforts and dedication to strengthening public health on the part of many organizations, institutions, companies and individuals. Without VVM, health workers can rely only on the expiry date of a product. But when you are buying a bread in a bakery, besides seeing how fresh the bread is, you can smell it, you can touch and feel it, listen to the crispy sound it makes, and taste it. VVM expands the horizon for all immunization programmes, VVM is a "five senses" offer to health workers, although they only look at it, with VVM health workers discover things other than a printed expiry date, as if they feel, hear, smell and taste... and they know with confidence which vaccine can be used or not... VVM expands the horizon for all immunization programmes, wherever the challenge is. It offers a railroad, a bridge, a tunnel, a motorbike, a canoe, a bicycle, and a pair of shoes to reach the unreachable."

vvm 10 years

photo: ümit kartoğlu, indaman / niger