Development of 'Olyset® net' as a Tool for Malaria Control

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Olyset® net is composed of a resin-based fiber that incorporates a synthetic pyrethroid called permethrin to form a mosquito net for malaria vector control. The most important characteristic of Olyset® net is a dynamic release behavior for the permethrin in the fiber. Though a washing removes part of the permethrin from the surface of the net, the permethrin migrates from the inside of the fibers to the surface and maintains its efficacy against mosquitoes. In addition, since the fiber itself is tough, the efficacy of an Olyset® net lasts and the net itself can be kept for at least 5 years in Africa.

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Introduction

1. Insect-borne Diseases

Table 1 gives the main diseases that are transmitted by insects. Among these, malaria is a disease where the malaria parasite is transferred from an infected person to a healthy person by *Anopheles* mosquitoes, and the transmitted parasite parasitizes the red blood cells, multiplies and destroys red blood cells one after another. Four types of malaria that parasitize humans, tertian malaria, quartan malaria, falciparum malaria and ovale malaria, are known, and of these falciparum malaria is said to be the fatal malaria. If treatment is not given within 24 hours of the onset of fever when there is an infection, serious symptoms occur, and death may result. These malarias infect 400 million people annually, and the number of deaths amounts to one million with most of the victims being children under five years of age, so it can be called the most serious insect borne disease.

Fig. 1 shows the number of people infected with malaria by region according to WHO, and one can see that the number of people infected in the AFRO region, that is Africa, is much higher than the others. Furthermore, **Fig. 2** shows the number of deaths according to age, and as was mentioned earlier, the number of children under five years old that die is very high. From these statistics, it can be seen that malaria is a serious cause of death in children less than five years of age in Africa. In addition, not only is malaria a serious cause of death in children, but also, for example, there is a drop in labor productivity because of infections even if death does not result; since five dollars is required for one treatment, it puts pressure on

Table 1 Insect Borne diseases [Data from reference 1)]

Diseases	Vector	Annual Death	Annual deaths under 5 years old	Annual cases (x'000)
Malaria	*Anopheles* mosquitoes	1,272,393	1,149,244	408,389
Dengue fever	*Aedes* mosquitoes	18,561	4,109	73
Leishmaniasis	Sand fly	51,134	5,365	12,000*
Sleeping sickness	Tsetse fly	47,774	3,435	400*
Filariasis	*Culex, Aedes* and *Anopheles* mosquitoes	418	45	40,000*
Japanese encepaliasis	*Culex tritaeniorynchus*	13,957	5,055	unknown
Oncocerciasis	Black fly	2	0	unknown
Shagas's disease	Triatomin bug	14,470	6	217

* Citation from different documents of WHO

the finances of families that live on one dollar or less per day and worsens their poverty. In addition, when there is an area where malaria is endemic, it causes sluggishness in the tourist industry and foreign capital investment. According to trial calculations by the World Bank, the losses caused by malaria in Africa amount to 12 billion dollars annually, and not only does it promote poverty in Africa, but also it is a great obstacle to economic development.

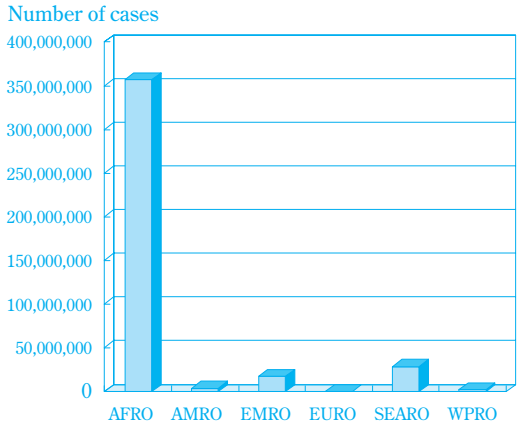

Fig. 1 Malaria cases for each WHO region [Data from reference 1)]

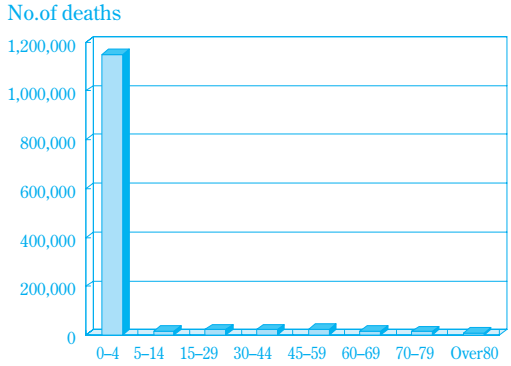

Fig. 2 Deaths caused by malaria infections for each age group [Data from reference 1)]

2. Roll Back Malaria Campaign

The World Health Organization (WHO), along with the United Nations Children's Fund (UNICEF), the World Bank and the United Nations Development Program (UNDP) started the Roll Back Malaria (RBM) Campaign. The goal of this campaign is to reduce the death rate for malaria by 50% by the year 2010. In this campaign, mosquito nets that have been treated with pyrethroidal insecticides, which have fast action on insects, have been employed as a tool for prevention of malarial infections. In other words, with normal mosquito nets, mosquitoes get inside the nets through openings if they are used improperly or damaged and suck blood, but if they are pretreated with pyrethroidal insecticides, the mosquitoes come into contact with the insecticides while looking for an opening to enter and are knocked down and die. A summary of the effects of mosquito nets treated with pyrethroids on malarial infections by Dr. Carnevalle of the Institute of Research for Development of France (IRD-France) from various references is given in **Table 2**.

Table 2 Effect of use of mosquito nets impregnated with pyrethroids on malaria transmission [Data from reference 2)]

Countries	Reduction % of malaria transmission	Authors
Gambia	45%	Snow et al., 1987
Gambia	63%	Snow et al., 1988
Kenya	30%	Sexton et al., 1990
Kenya	40%	Beach et al., 1993
Gambia	45%	Alonso et al., 1993
Guinea-Bissau	29%	Jaenson et al., 1994
Sierra Leone	49%	Marbiah et al., 1995
Tanzania	55%	Premij et al., 1995
Kenya	44%	Nevill et al., 1996

According to this, roughly 50% can be prevented through the use of mosquito nets treated with pyrethroids compared with their not being treated. Based on the results of this research, the RBM Campaign decided to use mosquito nets treated with pyrethroids to prevent infections. However, when mosquito nets treated with insecticides are washed, the insecticides are washed from the surface of the mosquito net, and the efficacy is reduced, so there is the problem of its being necessary to retreat the mosquito nets with insecticides after they are washed. On the other hand, with the goal of reducing poverty in Africa, the Global Fund to Fight HIV/AIDS, Tuberculosis and Malaria was established in 2000 centered on the Group of Seven (G7) to promote support for countermeasures for HIV/AIDS, tuberculosis and malaria, which are serious infectious diseases; the large-scale dissemination of mosquito nets treated with pyrethroidal insecticides was started as a countermeasure for malaria. According to UNICEF, the demand reaches 50 million annually.

History of the Development of Olyset® nets

1. Olyset® net Product Concept

As a technology that fuses insecticides and resins, the authors have developed, marketed and sold resin products with insecticides in them, such as ear tags (1985) for controlling ectoparasites such as blood sucking flies where pyrethroids are kneaded into the identification tags that are attached to the ears of cattle, pet collars (1991) for preventing fleas in dogs and cats, moth-proof sheets (1992) for clothing where a volatile pyrethroid was kneaded into the intermediate layer of a three-layer film, a window screen (1992) for control of insects at factories that prevents agricultural pest insects from flying into factories and a long net (1992) for control of midges that break out in large numbers at lakes and rivers. While we were developing these products, we made progress in accumulating knowledge about the fusion of technologies for various types of resins and insecticide components and systemized the basic data on base resin selection methods, combination of resins suitable for the forming process for sheets and nets and insecticides, the relationship between the resin composition, forming process conditions and insecticidal effects and further the solubility and rate of diffusion of the insecticidal components in the resins.

On the other hand, as was discussed previously, attention became focused on use of mosquito nets treated with pyrethroids as a countermeasure for malaria. However, since efficacies of treated mosquito nets are reduced or lost because insecticides are washed away when they are washed, it was necessary to retreat the mosquito nets with insecticides to recover the efficacy, and therefore, the problems of supplying the insecticides for retreatment, methods for educating users in retreatment methods and disposal of the insecticides remaining after the retreatment arose. In addition, a tenter stretched polyester fabric with an approximately 1.8 mm mesh size is typically used in mosquito nets for insecticidal treatment and for people that have no experience using mosquito nets, particularly in the tropics, sleeping in a mosquito net with a fine mesh is stifling, and it was thought that it would not be well received.

Therefore, as a product concept for the Olyset® net, we decided on an insecticidal mosquito net having good air permeability, no reduction in efficacy and no need for retreatment even if washed, long term effectiveness and the like.

2. Olyset® net Product Design

(1) Basic Design

To realize the Olyset® net concept, we applied the technology of both the window screen for control of insects at factories and the long net for control of midges mentioned above and decided on the basic design of a resin net with insecticides in it. Because of the aspects of safety and efficacy as well as suitable processing we used the synthetic pyrethroid called permethrin, and we wove fibers with permethrin incorporated into them to form the mosquito net shape. In addition, we proceeded with the development of the product using technology where the insecticide gradually bleeds (controlled release) from inside the resin once again after it is washed away from the surface.

(2) Mosquito Behavioral Characteristics on Olyset® net

Fig. 3 is a schematic diagram of the experiments for examining the behavior characteristics of mosquitoes on Olyset® net. Two glass chambers were connected by a cylinder, and a cage containing adult female common house mosquitoes was connected to one side of the cylinder (Chamber B). A mouse was placed on the other glass chamber (Chamber A) to attract the mosquitoes. Olyset® net without the active ingredient was attached to the end of the cylinder connected to the glass chamber holding the mouse. The wall was irradiated by infrared rays, an infrared camera positioned on the opposite side and the behavior of the mosquitoes passing through the net was observed in the dark.

Table 3 gives the results of the observations. All of the mosquitoes passing through the net were stopped

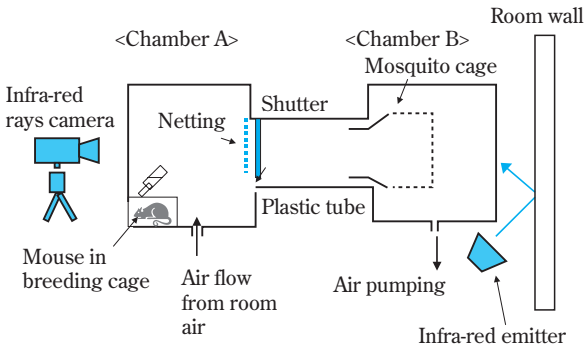

Fig. 3 Observation of mosquitoes passing through a net

Table 3 Observation of mosquito behavior to pass through nets (100 females of *Culex pipiens pallens*, 3 replications)

Netting	No. of mosquitoes passing through net	No. of mosquitoes resting on net when passing through	Resting %
Olyset® net without permethrin	10.7	10.7	100

by the net, and it was clear that it was a chance for them to come into contact with the insecticide in the Olyset® net.

(3) Contact Effect of Olyset® net on Mosquitoes

We investigated the effects of short exposure to the net on the blood feeding behavior of mosquitoes. The method for testing the biological effects is shown in **Fig. 4**. A piece of Olyset® net affixed to plywood panel was placed in a mosquito cage, and a plastic dish with a 1 cm diameter hole in it was placed upside down on the Olyset® net. Five adult female of yellow fever mosquitoes (*Aedes aegypti*) were confined to contact the net inside the dish for three minutes. Afterwards, the dish was removed, and the mosquitoes were allowed to fly freely inside the cage. After one minute, a hand was inserted into the cage, and the number of mosquitoes landing on the hand to feed was counted for one minute (When mosquitoes landed on the hand, the hand was vibrated for avoidance of actual biting). The knock down of mosquitoes in the cage was observed for 60 minutes.

The results of the observations of the times landing on the hand and the results of the observations of knockdown are shown in **Fig. 5**. When the net was untreated, they landed 40 times in one minute, but with the Olyset® net, it was only five times. In the results of the knockdown observations in Fig. 5, knockdown phenomenon started approximately 10 minutes after contact, but there were a few individuals that were knocked down in 1 – 2 minutes. They seemed normal at a glance, but it was clear that the mosquitoes that were in contact with the Olyset® net for a short period of time could not recognize the host (source of blood). Therefore, it can be assumed that individuals that pass through a net with a 0.4 × 0.4 cm mesh always come into contact with the Olyset® net, so they cannot feed on blood for example.

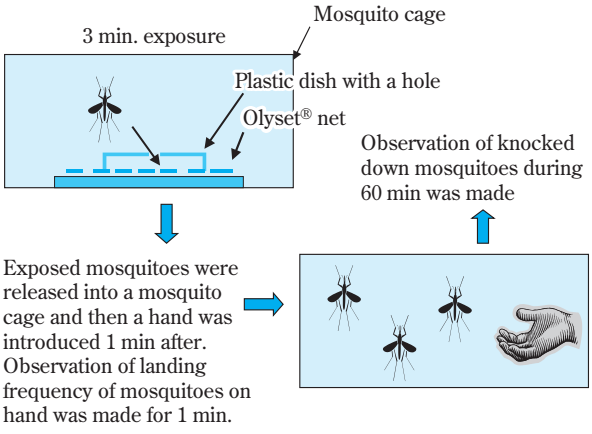

Fig. 4 Influence of short exposure to Olyset® net on biting behavior of females of *Aedes aegypti*

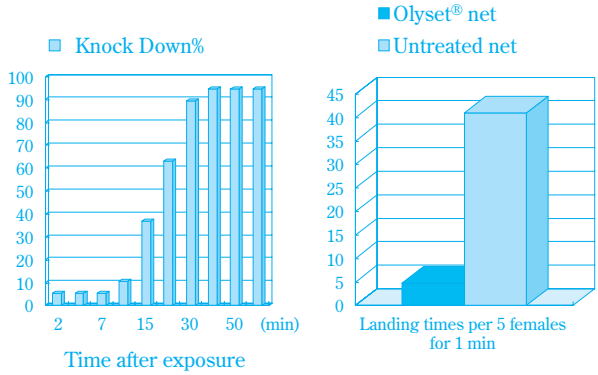

Fig. 5 Landing frequency of females of *Aedes aegypti* after 3 min exposure to Olyset® net

(4) Bleeding of the Insecticide from the Olyset® net Fiber

To confirm the bleeding of the insecticide to the surface of fiber, we washed the Olyset® net with acetone for one minute to remove the insecticide from the surface of the fiber. We then kept the washed Olyset® net at 60°C for one hour or five hours. After that time, the efficacy of the net on common house mosquitoes was investigated using the same test method as in Fig. 4. In other words the mosquitoes were confined in contact with the Olyset® net for three minutes, cotton soaked with a sugar solution was given to them, and the mortality rate after 24 hours was recorded.

Fig. 6 shows the results. After washing of the Olyset® net, the insecticide on the surface of the net fiber was washed away, and the efficacy for mosquitoes was insufficient. However, after being kept for one hour or more at 60°C, a mortality rate of 100%, the same as that for an Olyset® net that had not been

washed with acetone, was obtained, confirming the recovery of the high effectiveness, and it was confirmed that the migration speed of the active ingredient in the fiber is fast at high temperatures.

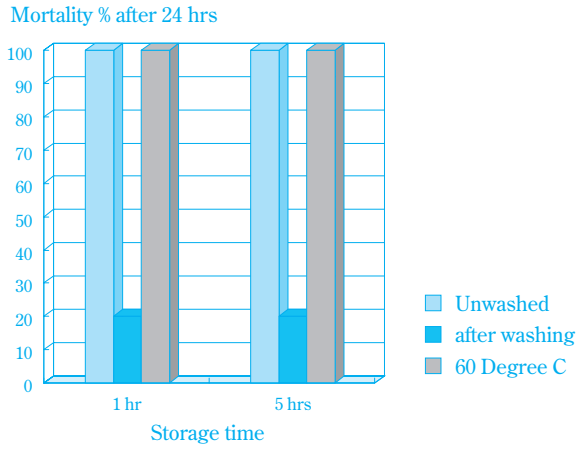

Fig. 6 Bleeding of permethrin in Olyset® net

On the other hand, in actual usage, typical family washing detergent will be used for washing, so the active ingredient that is already on the net surface will not be washed away as with acetone washing, and further, since the main location for use is in the tropics in Africa, it can be assumed that rapid recovery of the effect after washing can be confirmed.

3. A Field Trial on Malaria Control in Cambodia

A field trial on malaria control was carried out in a forested area 650 km from Phnom Penh by the National Malaria Center form June through December 1994. The malaria vectors in this area are *Anopheles dirus* and *Anopheles minimus*, and it is an area with 60% falciparum malaria, 30% tertian malaria and mixed infections of 10%. There were 860 residents of the village where the Olyset® net was distributed and there were 1,000 residents in the village where untreated conventional mosquito nets were distributed. In an entomological survey conducted for two consecutive nights each month, mosquitoes were collected and their Parous rate was determined. For an epidemiological survey, the changes in the positive rate for malaria were examined by blood tests in 50 pre-selected children under 5 years old and 50 children 5 years old or older once per month. Out of the large amount of data, the transitions in the Parous rate for *Anopheles dirus* are shown in **Fig. 7**.

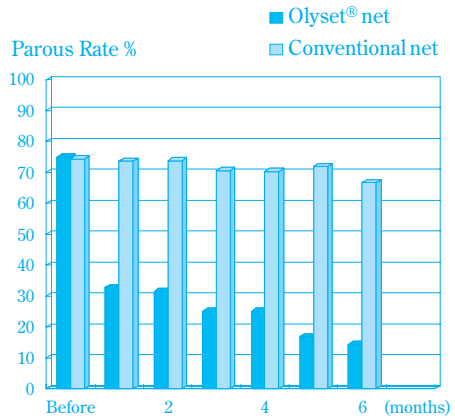

Fig. 7 Change in parous rate of *Anopheles dirus* collected inside houses
[Data from reference 3)]

The Parous rate means the ratio of mosquitoes in the mosquito population that have experienced oviposition. In other words, a high Parous rate means a high proportion of older mosquitoes in the mosquito population. After the malaria parasites have been taken into the body of the mosquito through feeding on an infected person, they develop to the sporozoite stage during two weeks inside the body of the mosquito and reach the salivary glands of the mosquito; then the parasite can be transmitted to a healthy person by injecting the sporozoites at the time of blood feeding. Therefore, having a large number of older mosquitoes means that the risk of a malarial infection is high.

From Fig. 7, it can be confirmed that the Parous rate for the villages where the Olyset® net was distributed quickly dropped in comparison with the changes in the Parous rate in the villages where untreated mosquito nets were distributed. It was suggested that there was an active destruction of mosquitoes by the Olyset® net, and an increase in the proportion of young mosquitoes present was exhibited. Expanding on this further, it shows that the number of mosquitoes that get to the sporozoite stage is lower, and the risk of infection is lower.

On the other hand, **Fig. 8** shows the results of blood inspection in children. In the villages where Olyset® net was distributed, the positive ratio for malaria became 0 after three months. The positive ratio for the villages where the untreated mosquito nets were distributed did not go to 0. From these field trials, it was clear that it was possible to effectively prevent malaria transmission through use of Olyset® net.

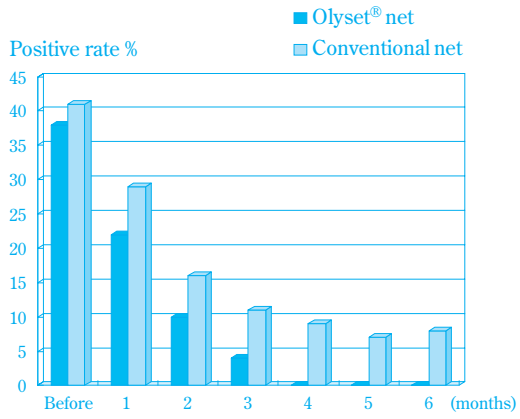

Fig. 8 Change in positive rate of children [Data from reference 3)]

Fig. 9 Package of Olyset® net

4. WHO Pesticide Evaluation Scheme

WHO has a framework for carrying out evaluations of the effectiveness of insecticides called the WHO Pesticide Evaluation Scheme (WHOPES), and it is a system that starts with laboratory evaluation of products for controlling insect vectors transmitting diseases, goes through large-scale field trials and makes recommendations for the use of these products when the utility is verified and they are determined to be useful.

Olyset® net was the world's first long-lasting mosquito net judged to be effective in preventing malaria by WHOPES.

Olyset® net Products and Production

1. Overview of Olyset® net Product

When creating Olyset® net as a mosquito net, product design was carried out based on the results of behavioral analysis of mosquitoes and basic investigations into resins as discussed previously, and the product was brought to fruition.

Olyset® net is a long lasting mosquito net woven in a net form of resin fibers containing permethrin, which is the active ingredient, and it is devised so as to have permethrin bleeding over a long period of time. **Fig. 9** shows a global package of Olyset® net with instruction for use in English and French.

Olyset® net has two basic colors, white and pale blue, and five net sizes based on the width, Single size (70 cm), Double size (100 cm), Family size (130 cm), Large-family size (160 cm) and Extra-family size (180 cm). The length of all of the sizes is 180 cm, and the height is 150 cm. The appearance of Olyset® net is shown in **Fig. 10**.

Fig. 10 Apperance of Olyset® net

2. Safety of Olyset® net

Table 4 gives the safety of Olyset® net. In addition to the safety of permethrin, which is the active ingredient, the product is superior in terms of safety for the user since a small amount of permethrin bleeds to the surface of the fiber gradually and users are exposed to only a small amount of permethrin.

Table 4 Safety data of Olyset® net

Items	Conditions	Results
Acute oral	Rat (male, female)	Higher than 10,000mg/kg
Acute dermal	Rat (male, female)	Higher than 10,000mg/kg
Eye irritation	Rabbit	Negative
Skin irritation	Rabbit	Negative
Skin sensitization	Guinea pig	Negative

3. Olyset® net Manufacturing Process

When establishing the manufacturing process for Olyset® net, we considered product quality and pro-

duction efficiency, and optimized the manufacturing conditions.

The basic process is made up of two processes, the process of incorporating permethrin into the resin and manufacturing resin pellets containing permethrin (compounding process), and the process of producing the mosquito net product (product production process) by processing the pellets into fibers by melt spinning, knitting into a net shape using a knitting machine, cutting and sewing. **Fig. 11** shows production processes for Olyset® net.

In the compounding process for Olyset® net, special processing techniques are used to disperse the permethrin uniformly in the resin, fiber forming technology used to obtain homogeneous fibers in the product production process and process management and quality control technology used to produce a high quality mosquito net product.

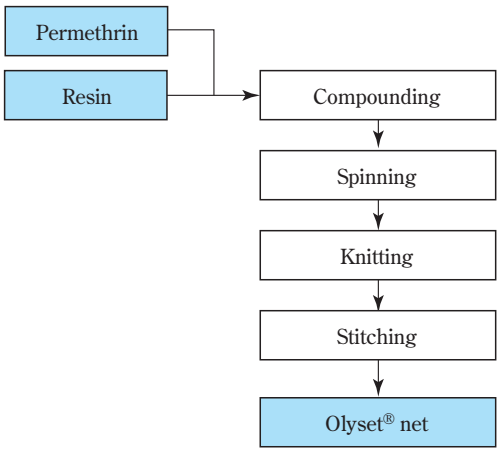

Fig. 11 Manufacturing process of Olyset® net

4. Overseas Production of Olyset® net

The production of Olyset® net was initially on a small scale and was carried out at a plant that would be very difficult to say had good efficiency, but what was most frequent among the demands of the localities concerned with the production was supplying the product at an affordable price so that it could be purchased by people in less-developed countries. It was necessary to have local production in areas and at sites that had competitive strength in costs to respond to these needs related to the production of the labor intensive Olyset® net. In particular, the cutting, sewing and inspection of the finished product, which are very labor intensive elements, were a problem. Therefore, the authors took on the challenge of carrying out the compounding process which governs the basic performance for the quality of the product, in an efficient system with concentrated production and producing it with processes for creating the product (spinning process, weaving process, cutting and sewing process), which are labor intensive, overseas where labor is inexpensive.

From the technical aspects and the cost competitiveness aspect, the first production location used was China. At the time, there were no production facilities nor production technology and quality control technology suitable for the manufacturing of Olyset® net in China, but as a result of daily technical guidance and tenacious cooperation of the local staff, it was possible to achieve Olyset® net production with the target productivity and economy in an extremely short period of time, and the production and shipment of the first 20,000 nets was achieved in 1999. **Fig. 12** shows a photo of the local plant in China.

With the start of the Roll Back Malaria campaign, the demand for Olyset® net suddenly increased, and in 2002, WHO requested that Sumitomo Chemical Co., Ltd. carry out mass production. Along with strengthening the production plant in China and strengthening the capacity after receiving this request, Sumitomo Chemical Co., Ltd. was also successful in introducing local facilities in China and was able to establish technology for producing Olyset® net with superior productivity and costs. Furthermore, 5 million Olyset® nets were produced and shipped in 2005.

Fig. 12 Olyset® net Factory in China-I

5. Technology Transfer for Production of Olyset® net in Africa

To suppress malaria over the long term and make progress in economic development in Africa, WHO proposed production of Olyset® net by African laborers

in Africa. In response to this WHO proposal, Sumitomo Chemical Co., Ltd. decided to transfer the production technology for Olyset® net to A to Z Textile Mills Ltd., which is a local African company, without licensing fees.

In this technology transfer, the basic technology that was born in Japan and the facilities technology and production management technology that were established at manufacturing plants in various locations were transferred to A to Z Textile Mills Ltd., which eventually succeeded in producing the qualified products that were required, **Fig. 13** shows a photo of the local plant in Africa.

Fig. 13 Olyset® net Factory in Africa

6. Development toward Global Production

Along with further developments in the Roll Back Malaria campaign, the demand for Olyset® net increased after that. Along with further increasing of the production at the Olyset® net plants in China and Africa to respond to the rapid increase in demand, Sumitomo Chemical Co., Ltd., started production at two new plants in Vietnam (**Fig. 14**) and Dalian(**Fig. 15**), China in 2006.

Fig. 14 Olyset® net Factory in Vietnam

Fig. 15 Olyset® net Factory in China-Ⅱ

As of the present in 2006, a total of four plants, two plants in China, one plant in Vietnam and one plant in Africa, are producing Olyset® net, and further, a new plant will start up production in Africa. The plan is for a global production system of 20 million nets.

Conclusion

If products utilize the technique of incorporating insecticides into resin and are designed so that only the effective amount of the insecticide for the target pest insects is present on the surface of the product through slow bleeding, consumers will not be exposed to any more of the insecticide than is necessary. In addition, the effect of continuously releasing small amounts can be a reduction in the amount of insecticide used because it is released over a long period of time. Furthermore, when it is a problem, the product itself can be removed along with insecticide.

On the other hand, the control of vectors is converting from the conventional top-down system to the direction of incorporating community, such as the use of mosquito nets. Because of this, it is easier for the community to participate because spray treatment techniques and special equipment are not necessary for treatment with insecticides with products where insecticides are incorporated into a resin.

WHO focused on these advantages and has requested that Sumitomo Chemical cooperate in the development of protective materials for various vectors as a means for fundamentally changing conventional vector protection methods. At present, having received this request, we are exploring various new products based on the technology of fusing insecticides and resins as alternatives to indoor residual spray (method of treating the walls of houses with insecticides in

advance for killing blood feeding mosquitoes resting on the treated wall for digestion of the blood that has been ingested).

Fig. 16 Photograph appeared on the TIME issued on November of 2004

The U.S. magazine *Time* selected Olyset® net as one of the Coolest Inventions of 2004 in the November issue of 2004. **Fig. 16** is the photograph that appeared in the magazine In addition, as part of Sumitomo Chemical's corporate social responsibility, the fact that Olyset® net is being supplied inexpensively to prevent malaria is being brought forth in active participation in various societal events centered on public relations.

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