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IMPACT OF *B.T.I.* ON BLACK-FLY CONTROL IN THE ONCHOCERCIASIS CONTROL PROGRAM IN WEST AFRICA

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ABSTRACT

Formulations of *Bacillus thuringiensis israelensis* have become the *Simulium* larvicide of choice in the dry season for the Onchocerciasis Control Programme. This amounts to the use of several hundred thousand litres per year. Water dispersable concentrates are used exclusively, with application by helicopter and fixed-wing aircraft. *B.t.i.* has the advantages of being effective against populations resistant to temephos, and of being very selective. On the other hand, the volume to apply is large, which limits use to lower river discharges. Carry is rather limited. Also, algae and turbidity can interfere with efficacy. In order to increase cost-effectiveness, efforts are being made to increase efficacy of the formulations in collaboration with the manufacturers. Also, a method for optimizing treatments based on a mathematical model of transport and susceptibility is being tested.

INTRODUCTION TO THE ONCHOCERCIASIS CONTROL PROGRAM

A. Goals, methods, costs

Created in 1974 and now operating in 11 West African countries, the Onchocerciasis Control Program (OCP) of the World Health Organisation has as its objectives: the reduction of Onchocerciasis or river blindness to a level where the disease is no longer a public health and socioeconomic problem; and the prevention of its recrudescence. In practical terms, this means protecting 2-3 million people scattered along 50,000 km of river, improving their lives and allowing settlement of abandoned zones along rivers.

In the absence of drugs suitable for mass distribution, the approach chosen was interruption of transmission by control of vector black fly, *Simulium damnosum.* This is achieved by weekly larvicide application to thousands of river breeding sites, using approximately 10,000 flying hours and 800,000 litres of insecticide per year at a cost of about $29 m per annum. Transmission is thus broken in a few weeks after starting vector control, and new cases prevented. However, the adult parasite in the human body lives about 12 years so that very effective vector control must continue for about that length of time to reduce the parasite load of those people already infected and to reduce the total parasite reservoir. It is hoped in this way to have a long-term effect on the disease even after the flies are allowed to return, since neither the countries themselves nor the international donor community can support a $29 million a year activity indefinitely. What is hoped for is a situation where relatively inexpensive action could contain the localised and relatively slow recrudescence. The Programme has now operated for 12 of the 15 years in its original plan.

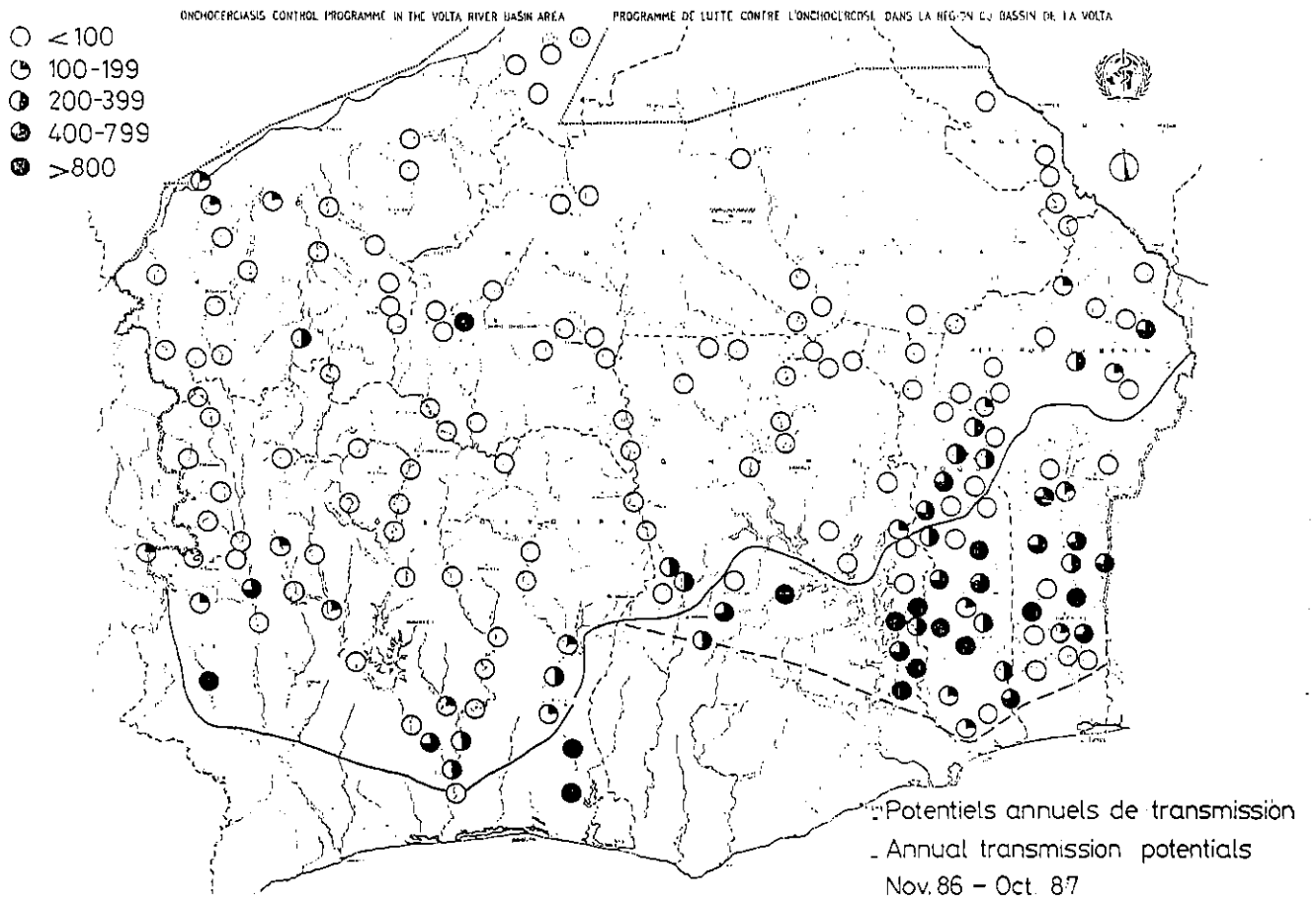

Fig. 1. Annual transmission potentials registered at OCP fly-catching stations from November, 1986 to October, 1987. The area south of the solid line was not subject to continuous larvicide treatments during this period.

B. Evaluation

From the entomological side, long-term evaluation is by fly catches on human bait, and dissections of the flies to determine the number of parasite larvae present. From this information, an Annual Transmission Potential (ATP), equivalent to the number of infective parasites received is calculated. Study of pre-control data fixed this at a maximum of 100 for interruption of transmission.

Figure 1 shows the situation near the end of 1987. In 1974, the ATP at practically all these points was above 200 and most points were above 800. Very few points remain above the limit, and practically all the problem areas are near the edge of the operational area where immigrant flies bring in infection. Some of this will be stopped when the Programme extends to the southeast in 1987. The black dot in the left center is a tiny pocket of about 10 km of river and a few hundred people which was left untreated by oversight for 2 years after several years of successful work. Other than a few such small omissions due to the necessarily rather sparse evaluation network, another potentially serious problem is insecticide resistance. Resistance to organophosphate compounds has occurred but was countered by alternation of insecticides before any epidemiological repercussions occurred.

For evaluation on the medical side, the primary tool is the longitudinal follow-up of sample villages. The skin biopsy is used to determine the incidence in children born since the operation began, the prevalence or percentage of people carrying the infection. And the community microfilarial load which is a measure of parasite density. Visual acuity is also measured. In a smaller number of villages the prevalence and progression of specific eye lesions is also followed.

The results are excellent. First, incidence in children dropped to 0 very quickly over most of the area. In a sample of 9364 children born since the Programme began only 9 were found infected (in 4 of 129 villages) against 837 expected based on the pre-control situation. Results have been less good near the edges or in some small local areas, corresponding to the ATP results.

In Fig. 2, the upper curve shows the prevalence which did not change appreciably for the first 6–8 years, but since then has been falling rapidly, agreeing with a force-of-infection model of the

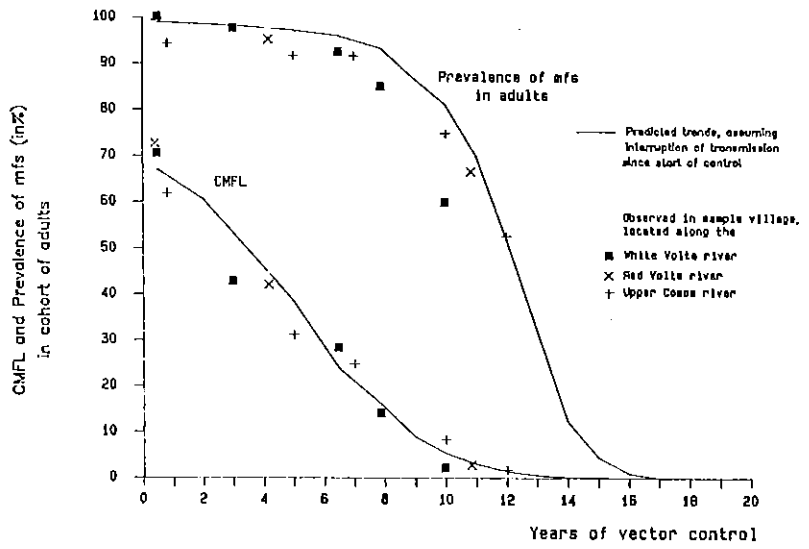

Fig. 2. Fall in prevalence of Onchocerciasis and community microfilarial load (CMFL) in longitudinal studies of hyperendemic villages in the area subjected to larviciding.

disease without transmission. The lower line shows the decline in microfilaria, more linear and very slow, but again agreeing with predictions. The situation is also improving as regards eye damage, with some improvement even in those already badly infected.

C. Outlook for the future

The problem now is to decide when to stop vector control, i.e., when the parasite reservoir has reached a residual level due to fly and human migrations, and small treatment failures, and further vector control will not improve the situation. Our current decision is to continue for 1–2 years beyond 1987.

What will be the possibilities for intervention after massive vector control stops? The drug Ivermectin is a safe, effective, microfilaricide suitable for mass distribution and with some cumulative effect on adult worms. However it seems unlikely that one can break transmission with this drug. There is still hope of finding a new macrofilaricide but at least 6 years in the future. Improvements are being made in immunodiagnostic methods to detect new cases sooner. National teams are being set up to take over surveillance activities.

An important question is what will happen when the flies return. In the end this will be learned empirically, but to help understand the possibilities, a man-fly disease mathematical model will soon be available. Using this model, one can trace 3 possibilities arising out of the conditions of a small disease reservoir and increasing fly numbers which will exist when general vector control ceases. In the best case, the disease will not recover. Long experience shows that this is a very optimistic view.

In the worst case, where the disease's capacity to re-establish itself surpasses our estimations, the disease could return in less than a human generation, perhaps requiring a massive return to vector control. This also seems unlikely.

The most likely outcome is intermediate, with some mild recrudescence in local areas. This can be met by medical surveillance and drug treatment especially if a macrofilaricide becomes available. In a few areas, local vector control might also be effective. The effect of the Program should continue for many generations.

For general descriptions of OCP and its results see Davies et al. (1978); Walsh et al. (1979); Prost et al. (1980); Remme et al. (1986); Karam et al. (1987); Ba et al. (1987); and Dadzie et al. (1986).

II. HISTORY OF THE USE OF *B.T.I.* IN OCP

OCP began in 1975 based solely on temephos (or Abate®), which had been chosen to replace DDT primarily for ecological reasons. Because of the possibility of resistance, screening of new compounds, including *B.t.i.*, went on. (Guillet et Escaffre, 1979). Early in 1980, resistance did occur in a limited area in southern Ivory Coast (Guillet, 1980). The first response was a change to chlorphoxim, another organophosphate which luckily did not show cross-resistance immediately. It took another year to develop a second resistance to this product (Kurtak et al., 1982). In the mean time, *B.t.i.* was rapidly developed (Lacey et al., 1982). The Teknar® WDC formulation was found to be effective against *S. damnosum*, but at a relatively high dose. It could only be used economically at discharges of 25 m^3/sec and below. In the absence of other products, it was used at discharges of several hundred cubic meters per second, but at very great increases in cost (3–4 X) including using large helicopters costing $1000/hr to operate. Since that time, active collaboration with the manufacturers (and competition between them!) has improved the product and reduced its price. Table 1 illustrates the progress that has been made in the last 7 years. Several other manufacturers, including Solvay, have provided small samples with superior qualities, but have not yet been able to produce large quantities. Table 2 shows the relative costs of the different insecticides used in OCP. It can be seen that the Abbott product is now very competitive with temephos at lower discharges. Based on experimental samples, it seems possible to have products at least three times more active, as shown

TABLE 1
Improvements in B.t.i formulations

Year	Product	Manufacturer	Dose mg/l–10 min	Vol. per m^3/sec (litres)	Dilution	Price/liter F.O.B. ($U.S.)	Limit for use (m^3/sec)
1980–1985	Teknar®	Sandoz	1.6	1.2	20%	3.50	25
1986	Teknar HPD®	Sandoz	1.2	0.72	none	6.50	50
1987	Vectobac® 12 AS	Abbott	1.2	0.72	none	3.50	50
1988–	"6000®* and/or Vec-	Sandoz	0.4	0.24	none	$12 approx.	125
1989?	tobac®* 24 AS	Abbott	0.4	0.24	none	$7 approx.	125

*Experimental products

on the last two lines of Table 1. Such products have been produced on a small scale, but not yet successfully on an industrial scale. With these improvements, *B.t.i.* now has a very important place in OCP, as shown in Table 3. Resistance to chemical insecticides is now very widespread, and *B.t.i.* is used universally in the dry season. In the wet season, combinations of temephos, chlorphoxim, permethrin, and carbosulfan are used depending on susceptibility, risk of resistance, price, and ecological impact. To date, this strategy has prevented resistance from having any impact on the epidemiological results. More complete reviews of the resistance situation can be found in Kurtak *et al.* (1987).

TABLE 2
Relative costs of *Simulium* larvicides operational in the onchocerciasis control programme

Compound	Relative cost/km of river treated (temephos = 1.0)	
	Dry season (10 m^3/sec)	Wet season (500 m^3/sec)
Temephos	1.0	1.0
Chlorphoxim	0.7	1.3
Carbosulfan	0.9	2.3
Permethrin	0.6	0.7
B.t.i. (Sandoz HP–D)[1]	1.4	4.3
B.t.i. (Abbott Vectobac 12AS)[2]	0.9	2.5

[1]$6.50/litre.
[2]$3.50/litre.

III. ADVANTAGES OF *B.T.I.* FOR OCP NEEDS

A. Efficacy against organophosphate resistant strains

Because of its completely different mode of action, *B.t.i.* can overcome organophosphate resistance in *Simulium damnosum.*

B. Low potential for developing resistance

Although *S. damnosum* cannot be colonised easily enough to allow selection experiments to be carried out, experiments with mosquito larvae (Georghiou, 1982, 1983, 1984; Goldman et al., 1986) have shown relatively low levels of resistance (2X to 16X) in mosquito populations subjected to intense selection pressure. Goldman (*loc. cit*) expressed the opinion that resistance to microbial insecticides requires concerted change of two gene loci, thus slowing the process considerably.

TABLE 3
Use of larvicides by OCP (litres) 1975–1987

Year	Product					
	Temephos 20 EC	Chlorphoxim 20 EC	Permethrin 20 EC	Carbosulfan 25 EC	*B.t.i.*	Total
1975	75,631	–	–	–	–	75,631
1976	129,947	–	–	–	–	129,947
1977	155,615	–	–	–	–	155,615
1978	215,879	–	–	–	–	215,879
1979	263,377	–	–	–	–	263,377
1980	184,517	–	–	–	–	184,517
1981	132,497	81,462	–	–	7,990	221,949
1982	162,750	6,700	–	–	232,986	402,436
1983	74,762	35,782	–	–	303,290	413,834
1984	77,849	56,783	5,300	–	256,860	396,792
1985	130,117	9,856	3,200	5,000	198,944	347,117
1986	92,032	17,356	9,800	7,000	381,230	507,418
1987[1]	125,000	65,000	14,800	21,000	651,000	876,800
1988[1]	65,000	75,000	20,000	12,500	750,000	922,500

[1]Forecasts

C. High selectivity

The product is only active against *Similium* and other Diptera, basically Chironomidae, in the habitats treated by OCP. Drift is limited to about 10% of the non-target fauna in gutter tests (see Troubat, 1982 for method), very similar to controls, even with overdoses (Table 4). Effects of field applications are also very slight (Déjoux et al., 1980). By comparison, temephos destroys 20–30% of the non-target insects, and permethrin destroys 50–75%/ (OCP, unpublished data).

TABLE 4
Effect of *B.t.i.* formulations on non-target insects in Africa

Product	Concentration mg/l	Percent detachment for various groups in 24 hours following a 10-minute exposure in troughs				
		Ephemeroptera	Trichoptera	All Diptera	Chironomidae	Total
Teknar HPD (Sandoz)	1.2*	1.3	0	19.0	18.1	3.3
Vectobac 12 AS (Abbott)	1.2*	10.1	2.2	13.0	1.7	10.1
"6000" (Sandoz)	0.8*	17.4	7.7	50.9	50.5	18.3
"6000" (Sandoz)	2.4	6.7	5.5	16.9	17.7	6.7
"6000" (Sandoz)	4.0	4.6	1.4	44.5	44.7	10.8
Vectobac 24 AS (Abbott)	0.8*	2.8	1.0	9.6	8.0	0.1
Vectobac 24 AS (Abbott)	2.4	7.0	0	15.2	15.4	5.3
Vectobac 24 AS (Abbott)	4.0	2.1	0.8	19.0	19.5	3.9
Control	–0–	8.1	5.4	14.3	13.8	10.0

*Operational doses 100% effective against *S. damnosum*

D. Low mammalian toxicity

There is very little risk to the riverine human population or OCP and Aerial Contractor personnel handling the product.

E. Stability of active ingredient

The toxin is stable for at least two years under field storage (Guillet et al., 1982 a). This is important because under OCP conditions, with large yearly variations in rainfall, it is often impossible to rotate stock every year.

IV. DISADVANTAGES

A. Relatively low specific activity and carry

Table 5 compares the performance of larvicides currently operational in OCP (unpublished OCP data). For current *B.t.i.* formulations, 720 ml per m^3/sec of river discharge is used. This is 2.4 to 16 times more than with classical chemical compounds. Carry (distance with 100% effect) is also less than for the chemical compounds, especially temephos, which has a tremendous carry at high discharges (up to 50 km). Fig. 3 shows a detailed diagram of *B.t.i.* carry used as a guideline in operations.

TABLE 5
Comparison of performance of operational OCP products

Compound	Dosing rate mg/l–10 min.	Carry		Effects of fauna
		Low discharge	High discharge	
Temephos	0.05 to 0.1	1–3 km	50 km	acceptable for long-term use in all seasons
Chlorphoxim	0.05	1–3 km	15 km	acceptable for long-term use in wet season
Carbosulfan	0.05	3–6 km	10–15 km	acceptable for short-term use in wet season
Permethrin	0.015	1–3 km	15 km	acceptable for short-term use in wet season
B.t.i. (Sandoz HP-D)	1.2	1–2 km	10 km	acceptable for long-term use in all seasons

B. Difficulties in application

Being rather viscous fluids with complex fluid behavior, *B.t.i.* water dispersable concentrates are rather difficult to pump. To get good dispersal in the river, it is necessary to apply them as a coarse spray. Typically, a short boom applying 2–3 l/sec through 5 BX50 cone jet nozzles at 40 psi. is used.

Since the product is applied at very nearly the minimum dose and does not spread on the water like an emulsifiable concetrate placement must be quite precise. This means that inattention by pilots very easily leads to treatment failures and in general *B.t.i.* treatments are somewhat less reliable than treatments with classical chemical compounds. It will take several cycles longer to achieve zero fly catch when commencing treatments, for example.

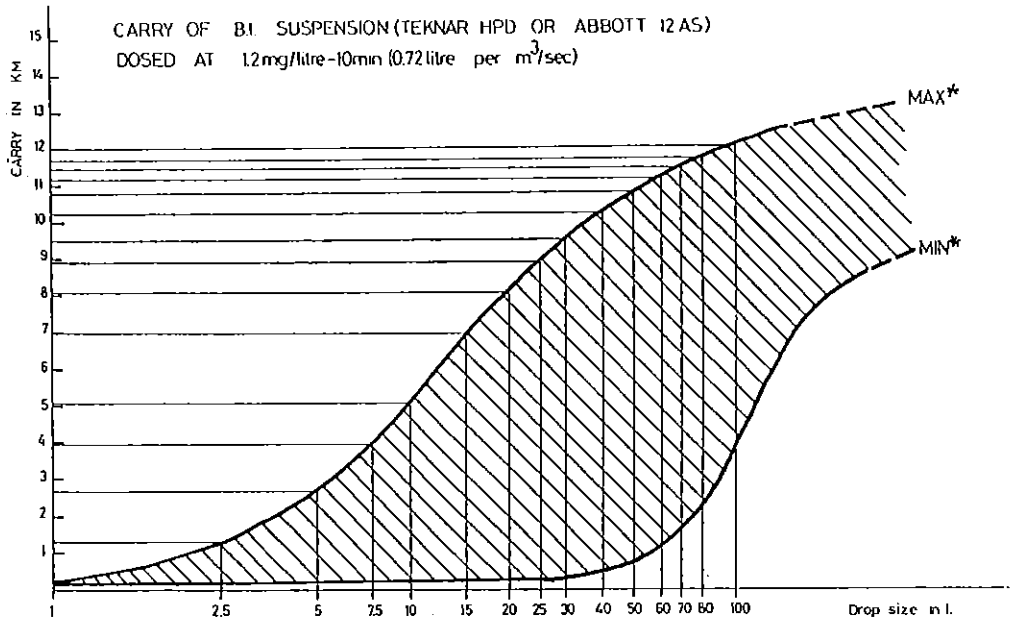

Fig. 3. Diagram showing estimated carry of *B.t.i.* suspension when used against *Simulium damnosum* in West African rivers. Maximum carry is to be expected under optimum river transport conditions, i.e. relatively narrow, deep, straight, smoothly flowing rivers without much turbulence and without many islands and channels. Carry will be reduced towards minimum under poor transport conditions, i.e. wide, shallow, sinuous, turbulent rivers which are broken into many channels.

C. Sensitivity to environmental conditions

The efficacy of *B.t.i.* formulations is reduced in the presence of turbidity (100 JTU or more) and in the presence of algae (if more than 1500 cells/ml present). The former is rather rare in OCP during the period of the year when *B.t.i.* is used. The latter is quite frequent in the dry season, as sections of river stagnate. Algal blooms are particularly well developed where some organic pollution occurs, as from sugar cane processing plants. This can be overcome to some degree by increasing the dose 2 to 3 times. The mechanism seems to be adsorption of the *B.t.i.* on algal cells.

D. Degradation of the formulation in storage

In storage, there is very little loss of activity of the toxin itself, even after several years storage in the open where temperatures can reach 40°C inside the drums. On the other hand, quite serious problems have been encountered with precipitation of mineral crystals (from 1 mm up to 1 cm) from the residue of the culture medium. When the spraying system was not protected by filters, these crystals wore out pump shafts very quickly. When filters were used, there was frequent clogging and attendant delays. This problem has been eased by storage and refiltering at the factory before shipment.

Also, problems were encountered with drums which continued to ferment, sometimes cracking the drums and causing loss of product. Drums are now equipped with automatic gas vents and stronger inhibiters of fermentation are added to the formulation.

Sedimentation can also occur, especially in formulations with larger particles. This results in a considerable loss of active ingredient into a heavy sludge at the bottom of the drum which can only be recovered with powerful agitation, which is difficult in a wide-spread field operation.

Most *B.t.i.* formulations react with aluminium spray equipment, probably due to their high mineral salt content. Aluminium is corroded, and crystals form inside aluminium pumps and pipes which later break off and clog filters. We advise only stainless steel and plastic to be used for parts in contact with *B.t.i.* formulations.

V. PROSPECTS FOR IMPROVEMENT

If one takes results with Institut Pasteur IPS primary powder in minigutters as a base, it does not seem unreasonable to eventually hope for a formulation operational at 0.2 mg/l–10 min or 120 ml/m^3/sec of river discharge. This would be equivalent to classical chemicals in volume. This can be achieved by a combination of improved fermentation yield, recovery, and possibly adjustment of particle size. The price would probably also be competitive. The carry on the other hand seems limited by the particulate nature of the product and there is no immediate hope for improvement.

VI. SCREENING PROCEDURES AND SPECIFICATIONS

In the past 8 years, considerable experience has been gained in screening techniques (Guillet and Escaffre, 1979; Guillet et al., 1985 a, b)[1]. The mosquito bioassay is a poor indicator of activity against *S. damnosum* although these bioassays are done to confirm information provided by the manufacturer. The basic screening bioassay is the minigutter test, where field-collected larvae are placed in flowing water in small troughs, the candidate formulation dripped in over 10 min., and mortality observed after 24h. Probit analysis of the results with mature larvae (young larvae are somewhat more susceptible) gives a good indication of field activity. Temperature, inherent susceptibility of the larval population, and other factors influence the results to a considerable degree (±50%) and it is necessary to test candidate products in parallel with a standard.

When natural conditions permit, the testing is repeated with turbid and clear water. Attempts to use tests with kaolin as an artificial turbidity to predict results in muddy water were not successful.

For samples which show an improvement in activity over the operational product, physical analysis is carried out to determine if the product is suitable for operational field use. First, viscosity is measured with a Brookfield LVT viscometer. Experience has shown that products with a viscosity of 900 or more CPS at 30°C with a No. 3 spindle at 30 rpm cannot be easily applied. They will be slow to load, cause cavitation in the tank, and be difficult to spray. In operational use, the limit is fixed at 500 CPS. For a quick, inexpensive check, this corresponds roughly to a flow-out time of 10 secs with a No. 3 Zahn Cup at 30°C. Second, dispersal or suspendability is tested by dropping the product into still water. A detailed protocol is attached in Annex I. In the simplest form, dispersal is evaluated visually as very good, fair, or poor. Very good means a dense cloud of fine particles is formed spontaneously and poor means that the drop of concentrate falls to the bottom of the test cylinder without breaking up at all. The suspension is evaluated again after agitating the cylinder.

In a more quantitative method, the proportion of product in suspension after 10 minutes, after 60 minutes, and immediately after agitation is measured by turbidometry. The data are used to calculate a suspension index. Experience has shown that this value must be superior to 0.7 (70 % remaining in suspension after 60 min) for a product to be successful in the field. For the formulator, this means that the product must contain a very energetic surfactant system capable of "blooming" without agitation when it falls on the water surface in coarse droplets. Some early formulations were so poor in this regard that they required pre-dilution and sometimes sank to the bottom of the river in blobs 5–10 mm in diameter to be eaten by fish (harmlessly it seems!).

[1]Screening for OCP is a collaborative effort of WHO and the Institut Pierre Richet in Bouaké, Côte d'Ivore. Personnel of WHO, Organisation de Cooperation et de Coordination pour la lutte contre les Grandes Endemies (OCCGE), and the Institut Français pour le Développement en Cooperation (ORSTOM) all participate.

If the sample qualifies physically, river tests are undertaken. In this case, a series of rapids are examined before the application, and natural supports with *S. damnosum* larvae are marked and evaluated. The stretch of river may be from 1 to over 20 km depending on how far the effect is expected to extend. The treatment is carried out above the first rapids of the series. For a small river, application may be by hand sprayer. For larger rivers, a helicopter with operational equipment is used. The treated area is revisited 24 hours after the application and the mortality (detachment) is evaluated at different distances below the application point. The carry is defined as the maximum distance where 100 % effect was achieved. Several tests of this type will be done, at different water levels, and different water qualities (turbid versus clear water). If the performance represents a clear-cut advantage over the operational product, a full-scale operational trial is organised. In this case an entire stretch of river is treated for several months, and evaluation is carried out not only in the larval breeding sites, but with fly catches and estimates of transmission. On the basis of these results, plus price, a decision will be made to introduce a new product or not.

In this way, several hundred samples have been screened, although only a handful have reached the stage of an operational trial.

OCP accepts samples of *B.t.i.* from any source, as long as the product can eventually be produced commercially and is formulated as a water-dispersable concentrate. Wettable powder formulations are not suitable because pre-mixing must be avoided in the widely dispersed field depots.

VII. SUSCEPTIBILITY MONITORING

Susceptibility is monitored by the use of agitator-type bioassay devices (Guillet et al., 1985 c, d) which can be transported into the field. To date, no significant changes in susceptibility have been seen, even in areas where *B.t.i.* has been used 7 years. However, continuous use in any one year is usually limited to about 8 months, with other compounds being used when the rivers are flooding. Table 6 presents typical data. There are no significant differences between mean baseline values and values obtained after 1, 2, or 7 years of *B.t.i.* application.

TABLE 6
Susceptibility of *Simulium damnosum* (mature larvae) to IPS 82 preparation of *B.t.i.* before and after operational use of *B.t.i.* formulations

Population	LC 50 (95% conf. int.)	LC 95 (95% conf. int.)	LC 100 (observed)	No. of tests
Untreated (highly susceptible)	0.0087 (0.0028–0.015)	0.11 (0.078–0.22)	1.0	2
Untreated (least susceptible)	0.044 (0.034–0.053)	0.44 (0.32–0.68)	1.0	1
Untreated (average)	0.027 ±0.017 (S.D).	0.19 ±0.12 (S.D.)	0.125 to 2.0	43
1 year of treatment	0.065 (0.051–0.080)	0.35 (0.26–0.52)	1.0	2
2 years of treatment	0.050 (0.039–0.060)	0.24 (0.16–0.52)	0.5	2
7 years of treatment	0.039 (0.028–0.050)	0.26 (0.19–0.40	2.0 (1.0 = 99.2%)	2

VIII. OPTIMISATION OF USE

A. History of project

Due to the problems mentioned in IV., above, and the large and expanding scale of *B.t.i.* use, OCP judged it useful to undertake careful scientific study of how it should be used in the field. As a result, in 1985 a research collaboration was initiated with the Research Group on Biting Flies of Trois-Rivières University in Québec. The objective of this collaboration was to establish means of predicting the carry of *B.t.i.* in OCP operations. The strategy of the project was the following:

- establish a model of susceptibility of black fly larvae to *B.t.i.*;
- establish a model of *B.t.i.* transport in rivers;
- integrate both models in a prediction model of *B.t.i.* carry for operational treatments.

B. Experimental approaches

Approaches had to be developed to tackle the problem of analysis and prediction of *B.t.i.* carry in rivers. The experimental protocol was based on two basic techniques, bioassays in minigutters for the susceptibility model, and tracing experiments in rivers for the transport model.

— Bioassay results obtained in minigutters with *B.t.i.* reflect accurately those observed in actual river treatments. By using probit analysis, the effect of different factors on mortality was measured: intrinsic factors (species and age of larvae); insecticide exposure factors (time and concentration), and water parameters (temperature, seston concentration).

— Tracing experiments in rivers were the basic technique for the study of *B.t.i.* transport. *B.t.i.* losses, during downstream travel, were measured by reference to a neutral fluorescent tracer, considered as the "ideal" insecticide. To analyze these data, a computer program was developed on the analytical solution proposed by Khalig (1979) for a one-dimensional river transport model. This program can measure the three basic parameters of river transport, speed, dispersion and removal; once these are known, the program can predict the concentration/time curves of insecticide at any distance for any combination of dosage and application time. The process of development of the combined susceptibility/transport model is shown in Fig. 4.

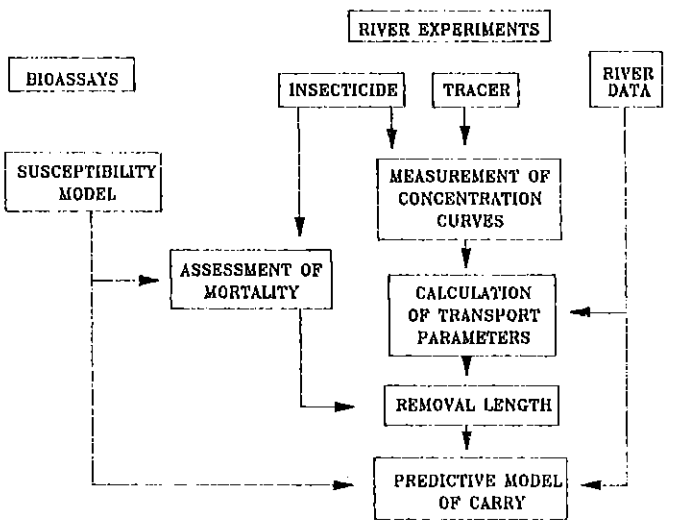

Fig. 4. Process of developing a combined susceptibility transport model for prediction of *Simulium* mortality during river treatment with *B.t.i.*.

C. Results

The models were validated through three years of experiments in Québec and in the OCP area. An integrated model predicting carry from all the forementioned parameters was developed. One immediate application of this model was the planning of control operations. In this context, it was advisable to simplify the model to its essential elements. It was found that for the susceptibility model, only the dose (concentration × exposure time) was important as a treatment parameter, thus leaving removal as the only important transport parameter for the determination of carry. Results showed that removal can be predicted from the discharge and stage of rivers. The susceptibility model was adjusted for mature larvae (the less susceptible to *B.t.i.*) of *S. damnosum*, and for average temperature and seston concentration.

One immediate use of such a model was the establishment of a chart giving the carry of regular treatments at a fixed dosage (Fig. 5). An even more interesting application was the development of

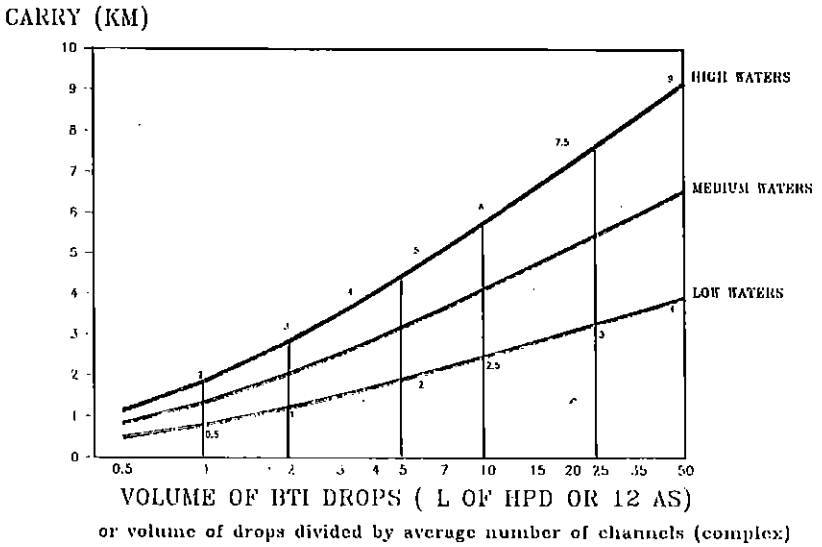

Fig. 5. Diagram giving carry which is reliably achieved by drops of *B.t.i.* formulation of increasing size under different flow conditions. High waters means the river is near its maximum flow. Medium waters implies rainy season conditions, and low waters means that the flow is a small fraction of the rainy season flow.

an optimization program for treatments. The structure of this program is shown in Fig. 6. This implied the computerization of all the treatment planning process. Using operational research theory, A. Chalifour developed an optimization algorithm for planning treatments. A first version optimized the amount of insecticide needed for the control of breeding sites in one stretch of river. Since the integrated model allowed us to calculate the amount of insecticide needed for any treatment strategy along a given stretch of river, the purpose of the optimization was to determine the lowest cost strategy (set of treatment points and doses). For a stretch of river with 50 breeding sites, the number of possible strategies amounts to millions, among which the program finds the best in a few seconds. See Fig. 7 for an example of optimized course. An augmented version of the program was developed, which also took into account the cost of aircraft operation (helicopter or fixed-wing aircraft).

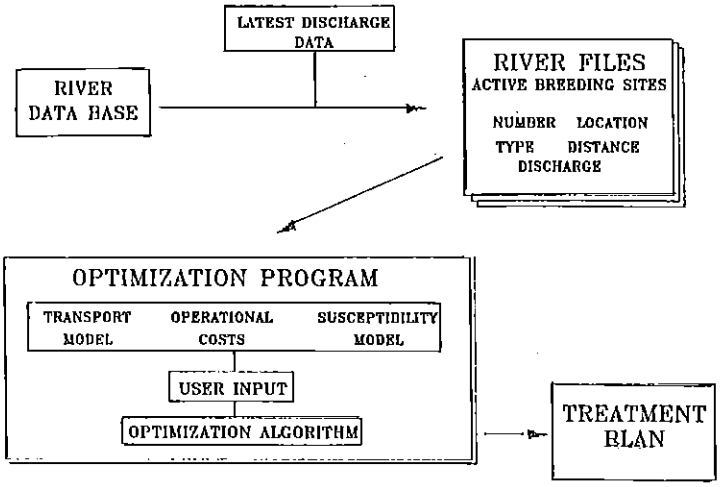

Fig. 6. Structure of treatment optimization program.

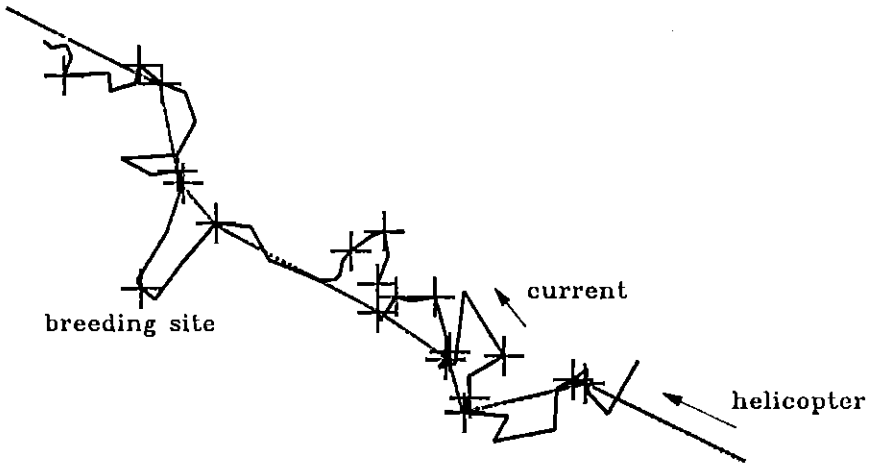

Fig. 7. Example of optimized helicopter path along a river. Solid line represents the river, which flows from the lower right to upper left, while the dotted line represents the path of the helicopter. Crosses represent rapids (breeding sites). The volumes of the drops are adjusted to provide adequate carry around curves.

The input file for the optimization program consists of several elements:

- a digitized map of the river.
- for each active breeding site: number, type, coordinates, and relative distance along the river.
- discharge at each breeding site, automatically interpolated from latest discharge readings sent through satellite network.
- values for susceptibility and transport parameters for chosen insecticide.
- unit costs of insecticide and aircraft operation.
- performance of aircraft.

To this basic input, most of which is fixed or automatically calculated, the person in charge of operations adds the desired mortality level (lowest mortality of mature larvae tolerated at the last breeding site downstream of a treatment point), and the limits of allowed dosage (especially important in the case of chemical insecticides in order to protect the non-target fauna).

In 1987, it was decided to test this optimization program in actual control operations. A circuit encompassing an area of 200 by 400 km and including 5 rivers was controlled for three weeks according to computer-designed treatment plans. Four of these rivers were treated with *B.t.i.* formulations, and one with temephos. This experimental circuit was chosen for its diversity and representativeness.

After three weeks of treatment, a ground survey of selected breeding sites was made to assess the efficacy of dosages suggested by the program. Control was satisfying in almost all breeding sites, except for a few cases where failure was actually due to omission from the list of active breeding sites.

Before the optimization program can be used regularly at the operational level, its limits of application will have to be assessed. For instance, one of the major differences with classical treatment techniques is the frequent change in the size of drops, and the precise determination of treatment points. This may be too demanding of the pilots on some small, meandering and forest-bordered rivers.

Still, the optimization of treatments by computer is promising on several grounds:

- It shows possible savings in aircraft and insecticide costs. For isolated breeding sites, where no carry is needed, the suggested dose of *B.t.i.* was lower by one-third compared to the regular dose; and this was effective. For stretches of river with series of breeding sites, the total amount of insecticide suggested was also lower. This represents not only savings in insecticide, but also increased autonomy for the aircraft, which is often rather short with *B.t.i.* formulations. In the case of the Baoulé, a large meandering river, the optimized flight plan was almost a straight line, thus minimizing maneuvers and allowing treatment in a significantly reduced time.
- The use of computer programs to plan treatments allows direct implementation of recent efforts to determine more accurately the discharge of treated rivers through satellite transmission of readings.
- The calculations of the optimization program take only a few minutes, and their automation can greatly alleviate the task of planning operations weekly.
- The modular, user-controlled characteristics of the program allow for fine-tuning according to treatment conditions (high turbidity, algal blooms, temperature), and for easy readjustment of control level.
- The use of the optimization program gives an automatic way of keeping record of past operations, which compensates for the additional task of maintaining an up-to-date river data base.
- It provides a tool for a fast and accurate evaluation of costs for different insecticides, aircrafts, discharges, control levels.

These results have justified continuing the project in 1988.

IX. SUMMARY

To summarise, formulations of *Bacillus thuringiensis* var. *israelensis* have been an essential part of the inventory of insecticides used by OCP since 1980. This product offers unique advantages in combating resistance, selectivity, and low mammalian toxicity. However, the relatively large volumes needed and the low carry make it prohibitively expensive at high river discharges. It is likely that improved formulations will be available in the near future to overcome some of these

problems. For OCP use, where a product with a high and very uniform active ingredient content is needed, as well as a high-performance formulation, it is doubtful that local production would be cost-effective, and OCP will continue to purchase from the major manufacturers and benefit from their expertise in improving the product and their competition in keeping the price low.

When Onchocerciasis is no longer a major socio-economic and public health problem in the OCP Area in West Africa, *B.t.i.* will have played an important role in the successful fight against a major parasitic disease.

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ANNEX I

WHO – OCP

PROPOSED PROTOCOL FOR LABORATORY TESTING OF SPONTANEOUS SUSPENDABILITY OF FORMULATIONS OF *BACILLUS THURINGIENSIS* H–14 FOR USE AS *SIMULIUM* LARVICIDES

Objective:

To permit the laboratory evaluation of the suspendability of *Bacillus thuringiensis* H14 formulation under OCP conditions (i.e. aerial application of pure or slightly diluted formulations to rivers).

Method:

1. Preparation of suspensions.
   1.1 The suspensions are prepared in 1000 cc graduated cylinder of the high form (calibrated portion roughly 6.5 cm in diameter by 35 cm high).
   1.2 1 ml of the formulation to be tested is dropped into the water from a glass tube (i.d. = 5 mm; o.d. = 8 mm) held 50 cm above the surface of the water. There is no agitation initially.
   From 0.1 to 0.3 g of the product remains adhering to the tube. It is for this reason that the value found in the cylinder is usually only about 0.7 to 0.8 g and that the suspension index (see 4.3 below) cannot be calculated on the basis of the total amount added. If it is desired to know the exact quantity added, the tube can be weighed before and after release and the amount adhering to its walls obtained by subtraction.
2. Sampling the suspension.
   2.1 The suspension is sampled 10 min and 60 min after adding the product.
   2.2 Samples are taken at 5 cm, 17.5 cm and 25 cm below the surface each time.
   2.3 After the second sampling at 60 min, all but 50 ml are carefully siphoned out of the cylinder and the undisturbed bottom 50 ml analyzed.
   2.4 All the samples and the remaining suspension are then added together and mixed by inverting the cylinder 30 times. A final sample is taken from the middle of the water column.
3. Analysis of the samples
   3.1 The turbidity of the samples is measured by an electronic turbidometer. (The Hach[1] Ratio Turbidometer Model 18700 provides excellent results, although samples over 200 NTU require dilution. We have also successfully used the FIsher DRT 100 Model[2].) The turbidity then converted to concentration in mg/l using a calibration curve established for each product by measuring the turbidity of known concentrations.
4. Analysis of the data.
   4.1 The turbidity units are first converted to concentrations in mg/l.
   4.2 At this point the distribution of the product in the water column and the stability of the suspension can be observed.
   4.3 Then the suspension index at 10 min and 60 min is calculated as follows:

$$\frac{\dfrac{\text{sample concentrations at 5.0, 17.5 and 25 cm}}{3}}{\text{divided by concentration at 60 min after stirring}}$$

This index represents the percentage of the formulation which is suspended without agitation.

Examples of Data

In Table 1 are displayed values in mg/l for a series of *B.t.* H14 formulations, along with the viscosity (flow-out time) measurements. Corresponding suspension indices are given in Table 2.

It can be quickly seen that Teknar W85-27 formulation (designed by the manufacturer to be auto-dispersing) distributes itself uniformly in the water column and stays uniformly distributed on hour later. A very high percentage of the material is suspended (suspension index over 0.9).

Teknar SC93, on the other hand, in its undiluted very viscous form (flow-out time 18.6 sec) suspends poorly and sinks out of the water column. With 20% water, the viscosity is much lower and the suspension indices improve dramatically.

[1]Hach Europe S.A./N.V. B.P. 51 5000 Namur 1 Belgique.
[2]Fisher International, Nottingerst 14 8032 Zurich, Suisse.

TABLE 1 (Annex)
Suspendability of formulation of *B.t.* H14 concentrations in mg/l at various depths in the water column 10 min and 60 min after application (mean for 3 series tests)

		Product					
Time	Depth (cm)	Teknar Commercial Lot 32-241 + 20% water	Teknar W85-27	Teknar SC93	Teknar SC93 + 20% water	Bactimos K83004	Bactimos 14-100-20/5
10 min	5.0	547	667	322	630	464	475
	17.5	552	657	396	615	518	476
	25.0	430	626	430	616	551	480
60 min	5.0	317	640	327	540	312	321
	17.5	482	634	317	530	290	318
	25.0	498	641	321	503	266	306
	Bottom	3075	1915	3000+	2605	3000+	3000+
60 min + mixing	mean for whole column	740	692	723	665	905	798
Viscosity index (flow-out time in sec)		4.7	4.9	19.4	5.6	2.7	4.6

TABLE 2 (Annex)
Suspendability of formulations of B.t H14 suspension indices* after 10 min and 60 min

Product	10 min	60 min	Viscosity Index (run-out time)
Teknar W85-27	0.92	0.91	4.9
Teknar SC93 + 20% water	0.84	0.81	5.6
Commercial Teknar lot 32-241 + 20% water	0.68	0.66	4.7
Teknar SC93	0.55	0.45	19.4
Bactimos 14/100/20/5	0.60	0.39	4.6
Bactimos K83004	0.56	0.31	2.7

$* = \frac{\text{average concentration at 5,0,17.5, and 25 cm before mixing}}{\text{concentration after mixing entire water column}}$

Commercial Teknar is an intermediate case. It suspends reasonably well for ten minutes, but later settles out of the water column (317 mg/l at 5 cm depth after 60 min vs. 547 mg/l after 10 min at the same depth).

The two Bactimos formulation, although very fluid, suspend only moderately well and show a very strong tendency to settle out of the water column (suspension indices after 60 min 0.39 and 0.45).