BACTIVEC® AND GRISELESF®
BIO-LARVICIDES FOR MOSQUITO CONTROL

IDEASS CUBA

Innovation for Development and South-South Cooperation

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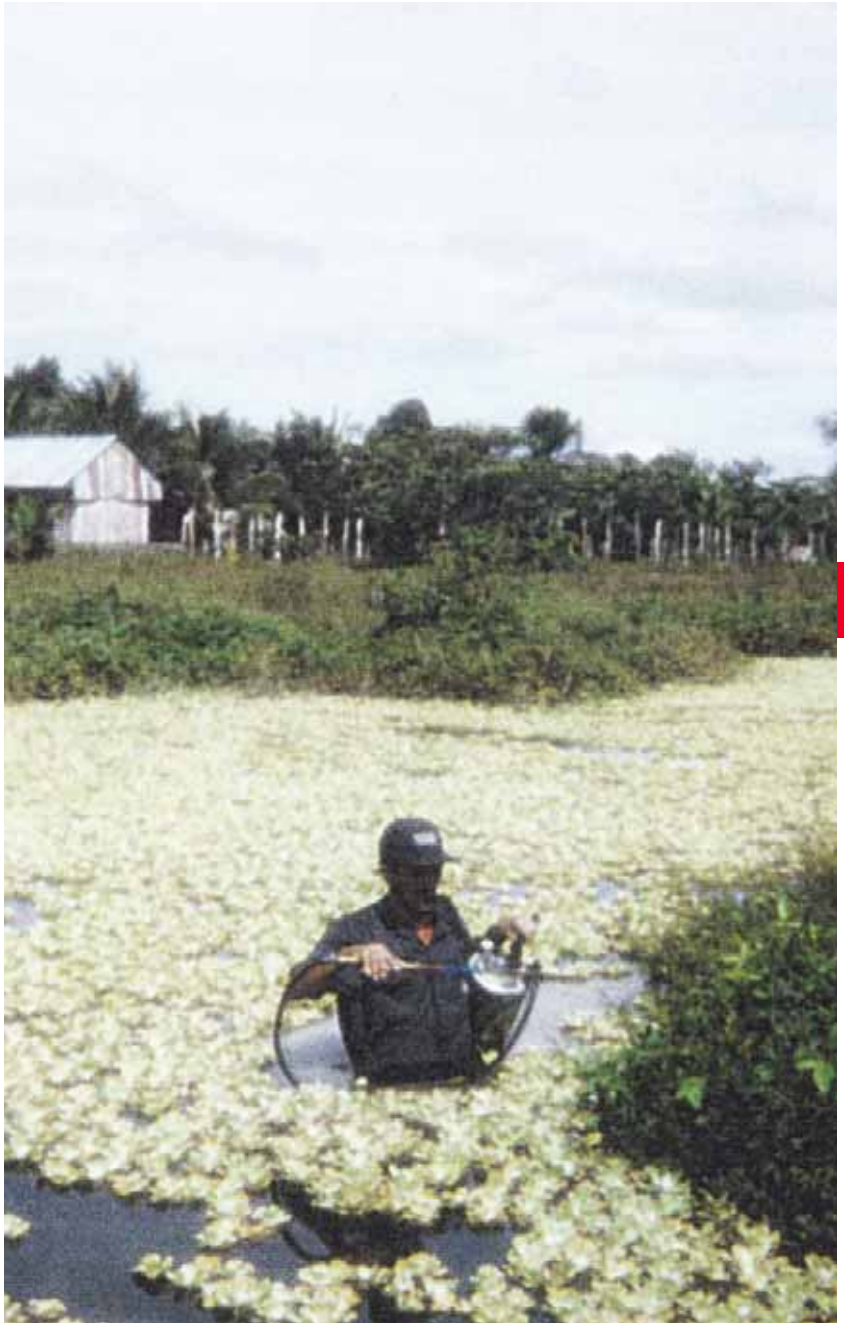


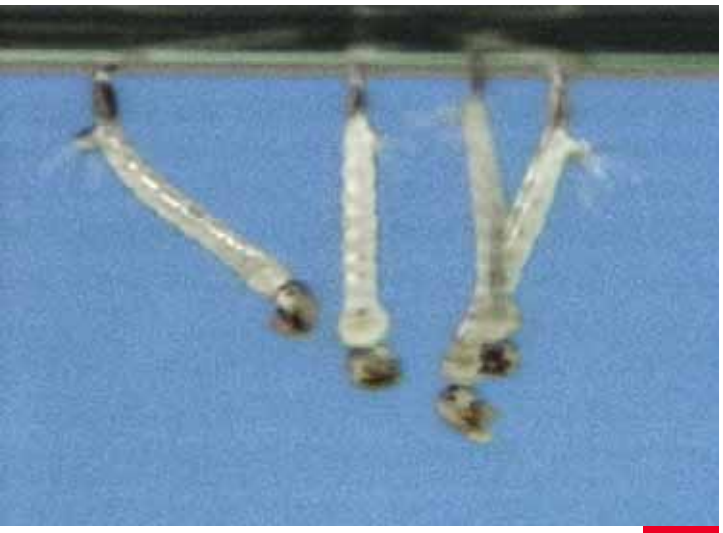
by Agustín Navarro Ortega

Introduction

GRISELESF® and BACTIVEC® are natural, highly effective mosquito bio-larvicides. Since the beginning of history, the development of human settlements has been accompanied by the presence of these blood-feeding insects. Apart from the discomfort their bites produce in humans, mosquitoes can transmit a variety of deadly diseases which have always affected a great number of people. Mosquito infestations are especially harmful when human settlements are located in ecosystems with inadequate environmental health conditions, or with poor or insufficient primary health care structures, or both.

Mosquitoes are very adaptable and so have spread indiscriminately to almost every latitude of the planet, but most successfully in tropical regions. It is there that the most favourable conditions are to be found for them to develop their greatest potential for disrupting human life. The epidemiological consequences brought by these insects have been made more serious by human migrations in the natural quest for better living conditions, so that mosquito species that fed only on animals also started to feed on human blood. This in turn has produced ecological imbalances in the natural centres of infections affecting man.

Over the years, a variety of methods and substances have been used to control mosquito larvae, which represent the early stages of the life cycle of these insects and which always develop in an aquatic habitat. Although these methods include physical control, such as the employment of larva-eating fish in the breeding areas, the method which has gained most ground is the uncontrolled use of chemical substances. Chemical products were most popular in the 20th century, when they were seen as almost the only form of effective control. Still in the 21st century they are being used without adequate technical supervision, despite the recommendations of the World Health Organisation. This situation has led to an increasingly inefficient fight against disease-carrying mosquitoes, provoking a rise in mortality rates as well as an ever more polluted environment, causing even more harm to humans, animals and plants.



In response to this problem the Laboratorios Biológicos Farmacéuticos LABIOFAM de CUBA developed two biological larvicides: BACTIVEC® and GRISELESF®. The active ingredients used are bacteria specific to the mosquito larvae, the israelensis variety of the bacterium Bacillus thuringiensis H-14, and Bacillus sphaericus 2362. The former was isolated by Golberg and Margalit in 1977 in the Negev desert in Israel, and the latter by Kaduna in Nigeria in 1981.

The biological larvicides BACTIVEC® and GRISELESF® developed by LABIOFAM guarantee:

- highly effective control of the larvae of different species of mosquito in urban, rural, industrial and tourist development areas, and under the most varied climates and application conditions;
- totally harmless effects on other animal and plant species present in the various aquatic habitats where mosquitoes develop.
- environmental friendliness, because the are highly biodegradable;
- effective integration with environmental health programmes to control diseases transmitted to man by mosquitoes. BACTIVEC® is also effective in combating other carriers of the tropical illness Onchocerciasis;
- broad acceptance on the part of the community, because they are seen to be effective, harmless and easy to use. Bactivec has proved effective in small doses against the larvae of the aedes aegypti mosquito. The products can easily be applied by health workers, and can be sprayed even by inhabitants themselves, inside and outside the home.

These products have been effectively used in different parts of Latin America, Africa and Asia. They have been used to successfully combat disease-bearing mosquitoes both preventively and as parts of integrated control programmes. They have also proved useful in epidemics of serious illnesses such as Yellow Fever, Dengue, Malaria, Human Filariasis, various types of Encephalitis and Onchocerciasis or River Blindness . They are also used to control infestations of other species of blood-feeding diptera, whose bites cause discomfort to man both in communities and tourist areas.

BACTIVEC® has been used in Cuba since 1980, and GRISELESF® since 1990. In Cuba these products have been recognised by the Cuban industrial property office and various national ministries. Abroad, these products are recognised by public health and agricultural institutions, private enterprises and United Nations agencies such as PAHO/WHO and UNDP.

In terms of industrial property , BACTIVEC® is registered in 9 countries, while GRISELESF® is registered in 13 countries. Both products have been validated by:

- the "Pedro Kourí" Institute of Tropical Medicine;
- the UNESCO Collaborating Centre;
- the WHO Collaborating Centre for Research and Training in Medical Malacology and Biological Control of Vectors and Intermediate Hosts of Diseases Transmittable to Man;
- the WHO Collaborating Centre for the Study of Viral Infections;
- the WHO Collaborating Centre for the Study of Tuberculosis and Mycobacteria;
- the National Reference Centre for Vector Monitoring and Control Activities directed by the Vector Monitoring and Control Unit of the Cuban Public Health Ministry;

Complete documentation is available on clinical, laboratory, field and semi-field tests that have been carried out on each product.

What problem do they solve?

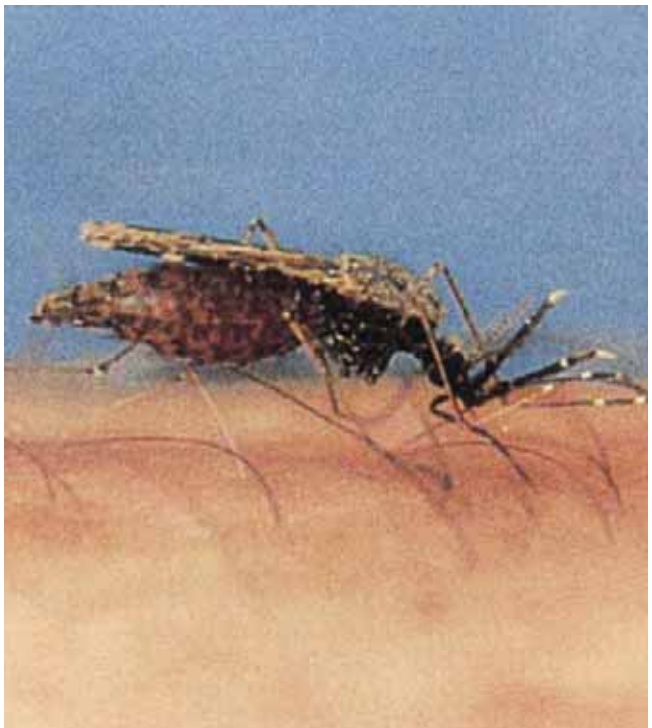
One of the world's main problems in controlling carriers of tropical diseases is the development of resistant populations of carriers due to the indiscriminate use of chemical insecticides. In 1992, the World Health Organisation reported resistance to chemical insecticides in 56 species of anopheles. Of these, 54 were resistant to DDT, 28 to organophosphates and 19 to insecticides derived from carbamates and pyrethroids.

As well as proving ineffective in many programmes for the control of the carriers of the above mentioned diseases, use of chemical products has been so widespread and irrational as to have become highly toxic for humans and to have reached such levels of persistence in the environment that accumulations have been found in animal and human fat.

For these reasons, and after more than three decades, the regional offices of the World Health Organization joined forces to find alternative ways of controlling carriers, especially in tropical or subtropical regions of the world, where illnesses such as malaria, human filariasis, dengue, and other arboviruses, each year affect more than 500 million people (Priest, 1992).

In Cuba, as a biological alternative for the control of larvae of disease-bearing mosquitoes, initial studies were carried out on the active ingredients of the bio-larvicides BACTIVEC® and GRISELESF® by the Cuban Academy of Sciences. Further research was carried out in the following Cuban research centres: the National Institute of Hygiene, Epidemiology and Microbiology, and the "Pedro Kourí" Tropical Medicine Institute, of the Ministry of Public Health. These technologically innovative studies on the active ingredients of BACTIVEC® and GRISELESF® led to the industrial production of the bio-larvicides in the Laboratorios Biológicos Farmacéuticos, LABIOFAM.

The National Vector Monitoring and Control Unit of the Vice Ministry of Hygiene and Epidemiology of the Cuban Public Health Ministry (MINSAP) integrated these products into programmes for the control of disease-bearing mosquitoes in 1995. Since then, they have been used throughout the country, through municipal monitoring and control units, to combat mosquitoes carrying dengue, encephalitis, human filariasis and malaria. They are also used to fight other species that cause great problems in tourist areas.



What is GRISELESF®?

GRISELESF® is a water based suspension made up of the following ingredients:

COMPOSITION	GRAMMES PER LITRE OF PRODUCT	CONCENTRATION (%)
Active ingredient: Spores and toxic crystals of Bacillus sphaericus 2362	5	0.5
Inert Ingredients	994.9	99.49
Preservatives	0.1	0.01

The active ingredient is a specific pathogenic agent consisting of the spores and toxic crystals of the strictly aerobic gram variable bacterium Bacillus sphaericus 2362 serotype H5a5b. Effects begin 48-72 hours after ingestion, causing intestinal paralysis in the larvae and poisoning due to the toxic crystals produced by the spores, which are highly specific to mosquito larvae. The product causes no harm to hot blooded vertebrates, amphibians or other aquatic animals.

GRISELESF® provides the following advantages in the biological control of mosquito larvae:

- Just one application kills mosquito larvae in stages I-III and the beginning of stage IV, through ingestion.
- It does not lead to resistance.
- It is effective in all cases, including mosquito populations resistant to chemical products.
- It has no effect on man or domestic animals, so no antidote is need if accidentally ingested.
- Since it is biodegradable, it does not harm the environment.
- It is very cost effective: it remains in mosquito breeding habits for longer than chemical larvicides since activity increases after spores germinate from the remains of dead larvae. It is very effective in breeding areas with a large water surface area, where mosquitoes carrying malaria, human filariasis and encephalitis generally breed. Two applications a year are enough to control outside mosquito breeding areas.
- As opposed to chemical products, which are also deadly for other living creatures, it can be safely used with other bio-larvicides present in aquatic habitats, such as larva-eating fish and other aquatic insects.

What is BACTIVEC®?

BACTIVEC® is a water based suspension made up of the following ingredients:

COMPOSITION	GRAMMES PER LITRE OF PRODUCT	CONCENTRATION (%)
Active ingredients: Spores and toxic crystals of Bacillus thuringiensis israelensis H-14	6 993.9	0.6 99.39
Inert ingredients	0.1	0.01
Preservatives		

The active ingredient is a specific pathogenic agent consisting of spherical spores and toxic crystals of the strictly aerobic gram variable bacterium Bacillus thuringiensis israelensis type H-14. Effects begin 24 - 48 hours after ingestion, causing intestinal paralysis in the larvae and poisoning due to the toxic crystals produced by the spores. The product can be used safely because it is highly specific to the larvae of mosquitoes and other carriers. The product causes absolutely no harm to hot blooded vertebrates, amphibians or other aquatic animals.

BACTIVEC® offers the following advantages in the biological control of mosquito larvae:

- Just one application kills Mosquito larvae in stages I-III and the beginning of stage IV through ingestion.
- It does not lead to resistance.
- It is effective in all cases, including mosquito populations resistant to chemical products.
- It has no effect on man or domestic animals, so no antidote is needed if accidentally ingested.
- Since it is biodegradable, it does not harm the environment.
- It produces rapid results (24 - 48 hours) and affects a great number of mosquito species including the carriers of Dengue. It is suitable for small breeding areas (less than one hectare) and can be used in emergency epidemiological situations. Effective control is maintained by applications every 15-60 days outside and inside mosquito breeding areas.
- As opposed to chemical products, which are also deadly for other living creatures, it can be safely used with other bio-larvicides present in aquatic habitats, such as larva-eating fish and other aquatic insects.

BACTIVEC® and GRISELESF® bio-larvicides in practice

The action of these bacterial insecticides is entirely preventative, since by eliminating the larvae they prevent the emergence of adult insects, which are the direct agents of the transmission of the illnesses to man. Because of their preventative action, these products should be included in national vector control programmes. The programmes should make use of integrated entomological monitoring systems which, by keeping a check on community risks of contracting diseases transmitted by the said carriers, can decide when to intervene and assess the impact they have. In Cuba these products have been part of the following MINSAP Vice Ministry of Hygiene and Epidemiology programmes since 1995:

- National programme for the eradication of the aedes aegypti mosquito.
- Programme for the control of other culicidae.
- National surveillance programme for priority areas.
- Surveillance programme for tourist areas.

The need for controls on these carriers depends on the samples taken by the control systems of each of the above mentioned programmes. The following table shows the infestation tolerance levels of the programmes.

MOSQUITO INFESTATION TOLERANCE LEVELS OF MINSAP PROGRAMMES IN CUBA

PROGRAMME	INFESTATION TOLERANCE LEVEL
• National programme for the eradication of the aedes aegypti mosquito	No infestation level > 0 is permitted
• National surveillance programme for priority areas	1 adult mosquito per room
• National programme for the control of other culicidae (except aedes aegypti)	< 5 adult mosquitoes per room < 20 mosquito larvae per square metre
• National surveillance programme for tourist areas	< 1 adult mosquito per room (In urban areas in adjoining rooms in a radius of no more that 100 metres) < 1 mosquito bite /hour/man < 10 mosquitoes larvae/metro^2 < 2 mosquitoes/hour/light trap

STAGES IN A GENERAL CONTROL PROGRAMME FOR HUMAN DISEASE-BEARING MOSQUITOES

STAGE 1 – PRE-TREATMENT

Gathering basic information (1 month)

The necessary information needs to be gathered in collaboration with health authorities in each target area. The information will then be used to give a hygienic – epidemiological – carrier profile of each target area and then to remove the insects.

Examples of information:

- Number of homes and population.
- Number of temporary and permanent breeding areas.
- Species present and density levels before treatment.
- Profile of breeding areas.
- Maps and sketches of the target areas or municipalities.
- Epidemiological data from the target areas for the past 5 years.
- Weather data.

Logistics

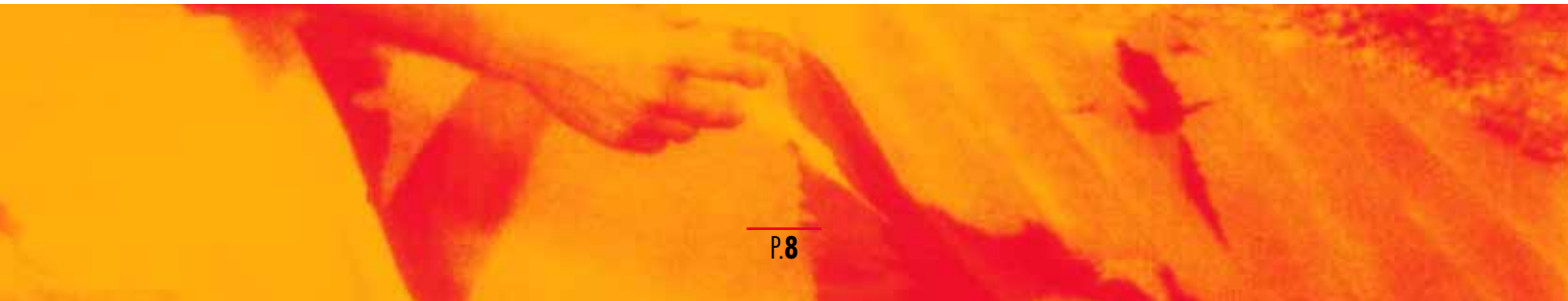
Logistics are fundamental to the success of the programme. Unforeseen circumstances may, depending on specific aspects, affect programme costs by between 5-10% of the total.

Capacity building

Those working directly or indirectly in the programme are given a two-week course on the safe use of Griselesf and Bactivec, larvicide action, spraying techniques, control, and monitoring.

Health education and community participation

The media, health talks, publicity, etc. are used to gain the support of the population in implementing the programme, produce changes in community life style that generate a greater awareness of the risks of contracting diseases, and foster participation in the fight against disease carriers.



STAGE 2 – SAMPLING AND APPLICATION OF BIO-LARVICIDES

Pre-treatment sampling
Pre-treatment samples are taken from all existing or potential breeding areas, whether they be natural or artificial, permanent or temporary. In each of these, fixed trapping stations are selected to collect samples. These are used to determine relative larva density before and after periodic bio-larvicide application to find out the percentage reduction of larva populations. Records are kept on special forms. Every three months, experts asses and analyse the progress of the programme.

Treatment of mosquito breeding areas
All existing breeding grounds are treated with Griselesf or Bactivec, depending on the area, mosquito species, population densities and duration of habitat (permanent or temporary), using appropriate equipment.

STAGE 3 – DATA ANALYSIS AND DRAFTING OF FINAL REPORT

This final stage of the programme lasts two months. The final report should contain statistics to show how successful the programme has been and details on setting up an epidemiological monitoring system that gives plenty of warning time for action to be taken so as to give sustainable results.

The practical results that have been obtained in almost two decades of experience in the employment of GRISELESF® and BACTIVEC® depend directly on areas where they have been applied, since this has a decisive influence on the final effectiveness of the application.

Percentage effectiveness of BACTIVEC® in different areas:

AREA OF APPLICATION	EFFECTIVENESS (24 - 48 hours)
Urban areas	100
Semi rural and rural areas	98 - 100
Tourist areas	98 - 100

Percentage effectiveness of GRISELESF® in different areas:

AREA OF APPLICATION	EFFECTIVENESS (48 - 72 hours)
Urban areas	100
Semi rural and rural areas	98 - 100
Tourist areas	98 - 100

Results

Increasing use is made of GRISELESF® and BACTIVEC® larvicides because:

- These products are harmless to other animal species, man and the environment.
- The advanced technological nature of the products provides a greater understanding of biological infestation control mechanisms and methods, both for the personnel involved in the spraying programmes and the people, who can appreciate the beneficial effects of the method.
- They arouse great interest in health authorities and the business sector, since, compared to traditional methods, they are not harmful or so ineffective.
- They win recognition from those concerned because of the benefits they represent for health.
- They protect people working in agricultural areas, stabilising the workforce and making economic successes more sustainable.
- Production is sustainable because they are made up of ingredients that are easy to acquire anywhere in the world.

In terms of cost effectiveness, the employment of these bio-larvicides to treat mosquito breeding areas instead of chemical larvicides such as Temephos and Fenthion produces economic savings of up to 60%. One of the main reasons for this is that the effects of bio-larvicides are longer lasting.

The superiority of bio-larvicides is also clear in terms of the benefits they bring to human health and the biotic environment in general. Chemical larvicides are losing credibility because they produce resistant mosquito populations and harm other aquatic creatures in the ecosystem. In terms of tourism, the use of chemical products is increasingly deplored, because they pollute the environment.

How GRISELESF® works in practice:

Day 1	Product is sprayed
Days 2-3	Deadly effect develops
General effectiveness	98-100 %
Second application	Between 6 months and 1 year

How BACTIVEC® works in practice:

Day 1	Product is sprayed
Days 2-3	Deadly effect develops
General effectiveness	100 %
Second application	Between 15 days to 2 months

International interest

GRISELESF® is registered and has been employed in 13 countries in Central and South America, Africa and Asia. BACTIVEC® is registered in 9 countries in Central and South America, Africa and Asia.

Due to the indubitable advantages represented by GRISELESF® and BATIVEC® as ecologically safe agents for the control of mosquito larvae, different national and international organisations have promoted the use of these bio-larvicides.

At the national level, use is primarily promoted by the health ministries of the different countries in which they have been applied, at the central, provincial and municipal levels.

Agriculture ministries, too, employ these bio-larvicides to protect people involved in agricultural activities.

It is also of interest to tourism ministries and the tourist industry, since the use of these bio-larvicides controls mosquito infestations without polluting the environment, as was the case with chemical products.

At the international level, GRISELESF® and BACTIVEC® have gained prestige through the backing given to them by PAHO/WHO and the United Nations Development Programme (PNUD), which have recommended integrating them into other methods for combating disease carriers in countries facing emergency epidemiological situations.

The employment of GRISELESF® and BACTIVEC® in other countries

The procedures for employing these bio-larvicides in other countries are similar to those for other biological products.

Importing GRISELESF® and BACTIVEC®

Importing these products to a specific country involves the following steps:

- A national accredited body for importing and registering this type of product is identified and an initial agreement is reached.
- LABIOFAM S.A. and the above mentioned body sign the following documents: Agency agreement; Non-disclosure agreement; Power of attorney to represent LABIOFAM S.A. before the registration authorities.
- LABIOFAM S.A. consigns the necessary documentation to this national body.
- The product is included in the health register and the trademark is deposited in the country concerned. Generally, those responsible for receiving, examining and approving applications are dependencies of the ministry of health, though this can vary from country to country.
- Product is commercialised.

There have been occasions when, because of emergency health needs, governments have granted temporary authorisations for the commercialisation of these products, without having to go through steps 3, 4 and 5.

Producing GRISELESF® and BACTIVEC® in other countries

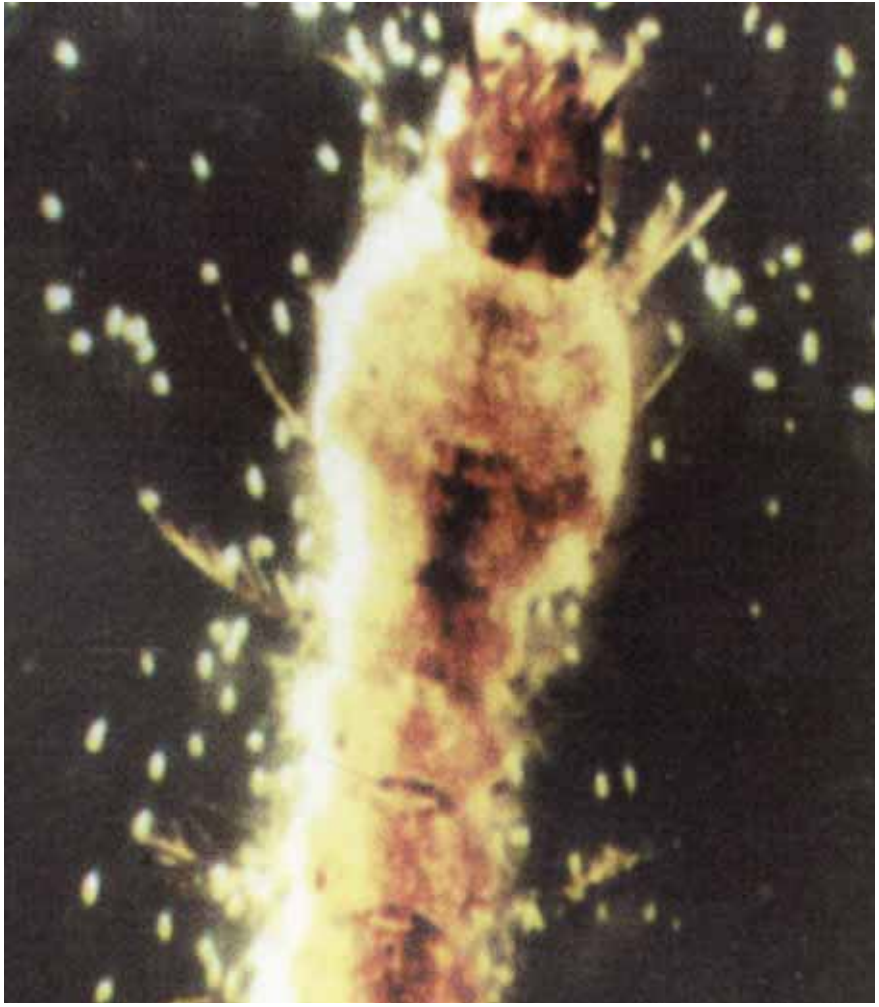
Another possibility is to produce these products in the country itself. Once the above mentioned steps have been taken, some form of economic joint venture needs to be set up with a local organisation, after which the following steps are taken:

- A market study is conducted on the country in which the product is to be commercialised, including details on the size of the production factory and technical requirements.
- An economic feasibility study is conducted to assess viability and capital investment.
- The parties negotiate and agree on their respective contributions to the establishment of the joint venture.
- Legal documents setting up the joint venture are drafted and regulations governing administration, control and management are established.
- Joint venture and investment projects are approved by the competent authorities of the countries concerned, usually involving organisations responsible for foreign investment, science and technology, construction, industrial property and central banks.
- Investment
- New enterprise begins operations.

To learn more

LABIOFAM S.A. possesses an abundance of scientific literature on the work that has gone into the bio-larvicides GRISELESF® and BACTIVEC® over the years, which it can make available to those interested. Documentation includes:

- Clinical studies on the harmlessness of both products, both in man and different animal species.
- Results of laboratory and field tests on both products.
- Results of application campaigns in various countries.
- Recognition certificates from different national and international bodies.
- Scientific documentation on both products.



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The IDEASS Programme – Innovation for Development and South-South Cooperation – is part of the international cooperation Initiative ART. IDEASS grew out of the major world summits in the 1990s and the Millennium General Assembly and it gives priority to cooperation between protagonists in the South, with the support of the industrialised countries.

The aim of IDEASS is to strengthen the effectiveness of local development processes through the increased use of innovations for human development. By means of south-south cooperation projects, it acts as a catalyst for the spread of social, economic and technological innovations that favour economic and social development at the local level. The innovations promoted may be products, technologies, or social, economic or cultural practices. For more information about the IDEASS Programme, please consult the website: **www.ideassonline.org.**

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Innovation for Development and South-South Cooperation

ART - Support for territorial and thematic networks of co-operation for human development - is an international co-operation initiative that brings together programmes and activities of several United Nations Agencies. ART promotes a new type of multilateralism in which the United Nations system works with governments to promote the active participation of local communities and social actors from the South and the North. ART shares the objectives of the Millennium Development Goals.

In the interested countries, ART promotes and supports national co-operation framework programmes for Governance and Local Development - ART GOLD. These Programs create an organized institutional context that allows the various national and international actors to contribute to a country's human development in co-ordinated and complementary ways. Participants include donor countries, United Nations agencies, regional governments, city and local governments, associations, universities, private sector organizations and non-governmental organizations.

It is in the framework of ART GOLD Programmes where IDEASS innovations are promoted and where cooperation projects are implemented for their transfer, whenever required by local actors.