
CENTER FOR GENETIC ENGINEERING
AND BIOTECHNOLOGY
Sharing experiences on international supply and PQ
BIOTECHNOLOGY IN CUBA

BioCubaFarma

BIOCUBA Farma
GRUPO DE LAS INDUSTRIAS BIOTECNOLÓGICA Y FARMACÉUTICA

CIM

CENIC

CIGB

I. FINLAY

Lab Carlos J. Finlay

Lab 8 de Marzo

Lab Medsol

38 Empresas

21 613 Trabajadores

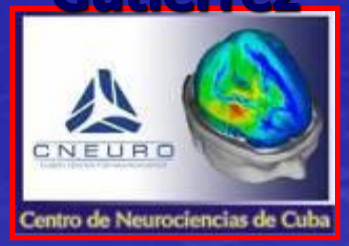
CIDEM

CQB

Lab Hemoderivados

Lab Reinaldo Gutiérrez

BioCen



Lab. Roberto Escudero

New York says that today's tensions and conflicts are characterized less by a 'clash of civilizations', than by larger groups feeling threatened and its end-users meant that h might otherwise have been the

Cuba's biotech boom

The United States would do well to end restrictions on collaborations with the island nation's scientists.

For a week after Cuba marked the 50th anniversary of its revolution on 1 January, a celebratory 'Caravan of Liberty' carried 50 people, including many university students and scientists, along the triumphal route that Fidel Castro had taken half a century earlier. These people represented the health-care and educational systems of which Cubans are proud, however much they

Castro's interest in the fledglin with Randolph Lee Clark, the fo Cancer Center in Houston, Texa to a lab in Finland to learn how cells. The knowledge gleaned fr an industry that developed the 1985, and subsequently a vaccin B — the world's first human va

Unfortunately, Cuba's biote limitations of the top-down the Soviet Union fell apart an

... Cuba marked the 50th anniversary of its revolution on 1 January, a celebratory 'Caravan of Liberty' carried 50 people ...

... These people represented the health-care and educational systems of which Cubans are proud, ...

... And in no small measure the scientists in the caravan symbolize the foundation of that health-care system in the developing world's most established biotechnology industry, which has grown rapidly even though it eschewed the venture-capital funding model that rich countries consider a prerequisite.

et.

s old; the regime will not last much d America's cold-war perspective on . In August, the state of Florida over- d researchers at its universities from the island. And President-elect Barack ess to talk to his country's enemies. uld be wise to start that conversation January inauguration as possible. The h, of course, and the advantages could s the global centre of biotech, and with s contiguous with Cuba's, the United ith which cross-fertilization of ideas

Strategy of Cuban Biotechnology

- **Cuban Government: a Huge Investment**
- **Based on Cuban scientists and professionals**
- **National Health System as first priority**
- **"Closed cycle" strategy: fully integrated institutions,** from research to post-marketing follow-up
- **National collaboration instead of individual competition**; coordination between institutions doing R & D and institutions applying results
- **"Spin off" companies** derived from scientific or production institutions
- **Gaining international competitiveness:** quality, production volumes, cost, novelty, joint ventures
- **Intensive building capacity:** R & D, Production

THE OUTPUT

PRODUCTS/PROJECTS/PATENTS/IMPACTS

- 33 Vaccines against infectious diseases
- 33 Oncological products
- 18 Cardiovascular products
- 7 Products for other diseases

PATENTS

- 230 patents registered in Cuba and 1800 international patent applications

IMPACT IN PUBLIC HEALTH
IMPACT IN FOOD PRODUCTION
ECONOMIC RESULTS

Commercial products launched by the Cuban Biotechnology Program

1981 – 1990

3

1. Anti-meningococcus BC vaccine
2. Heberon alfa N
3. HIV Diagnostic system

1991 – 2000

18

1. Hepatitis B vaccine
2. Heberkinasa
3. Heberon alfa r
4. Hebermin
5. Gavac
6. SUMA System
7. DIRAMIC
8. Hebertrans
9. Culture media
10. Policosanol
11. Trofin
12. Natural products
13. Neurodiagnostic systems
14. Anti-CD3 monoclonal antibody
15. Surfacen
16. Generics
17. Melagenina
18. Neurological restoration services

2001 – 2012

41

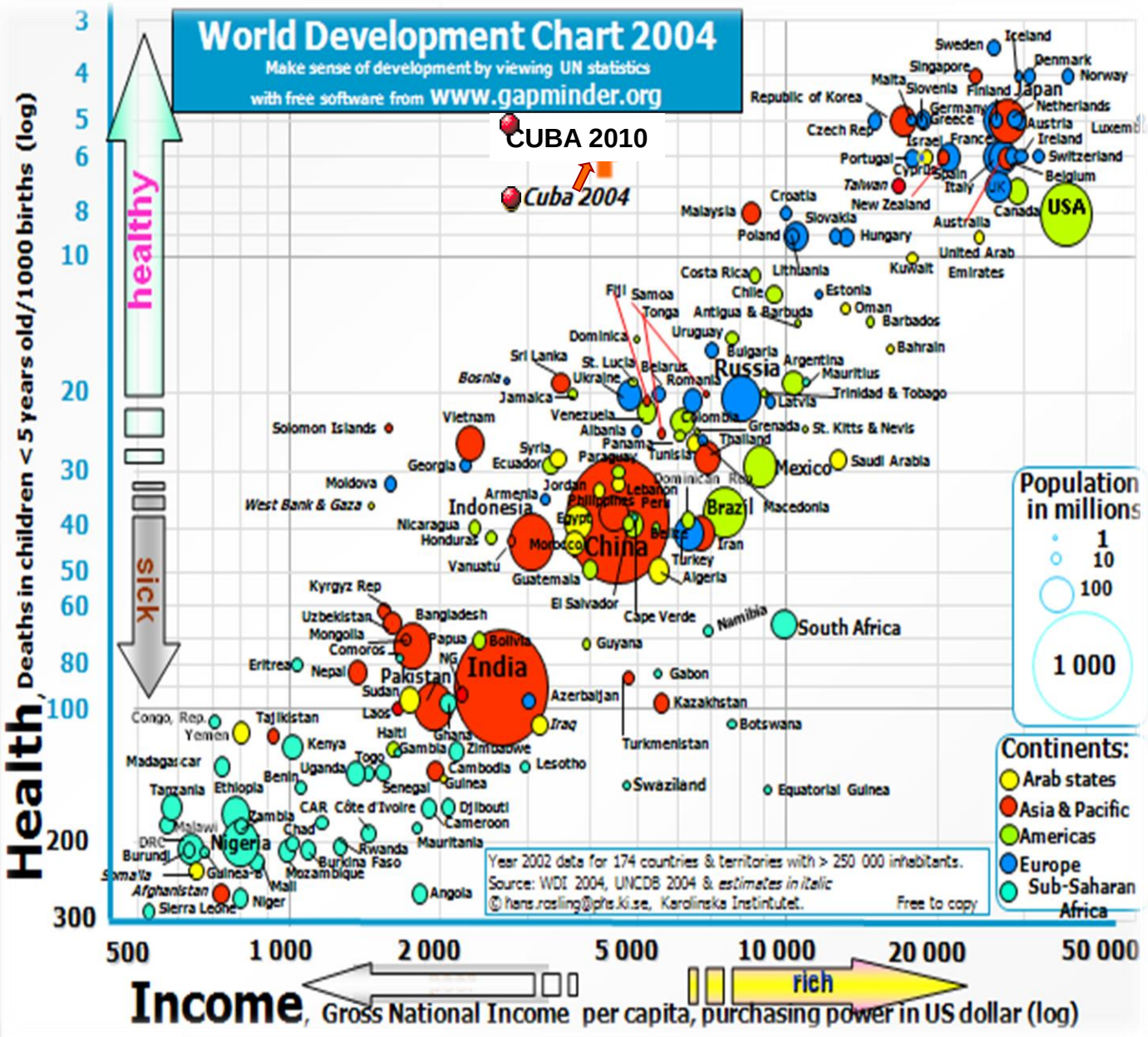
1. Haemophylus B vaccine
2. Tetravalent (DPT-Hib).
3. MAbs for cancer therapy
4. DPT vaccine
5. Meningococcus ACYW135 vaccine
6. Heberpenta 4+1
7. Heberpenta L
8. EPO (CIM, CIGB)
9. Equipment for Neurophysioloy and Neuroinformatics
10. New diagnostic systems
11. Streptokinase (w/o HSA)
12. Neurological restoration services
13. Leptospirae vaccine
14. Salmonella vaccine
15. Tetanus Toxoid
16. G-CSF
17. Allergens
18. New Trofin
19. Interferon (liquid, w/o HSA)
20. Interferon (liophylized, w/o HSA)
21. Interferon + ribavirine
22. Gamma Interferon
23. Interleukin-2
24. PPG-plus
25. Humanized anti EGF-receptor antibody
26. New SUMA system
27. Hebernem
28. Acuabio1
29. Heberprot-P
30. Hebertrans
31. Microbilogy culture media
32. New advanced generics drugs
33. Cytostatics
34. Technology transfers
35. Melagenina plus
36. Coriodermina
37. EPO plus
38. EGF viscous solution
39. Audix
40. PEG-IFN
41. Cancer vaccine

Science

30 APRIL 2010 VOL 328
SCIENCE

Despite the embargo, Cuba has produced better health outcomes than most Latin American countries and they are comparable to those of most developed countries.

Paul K. Drain and Michele Barry*



CUBAN NEONATAL SCREENING PROGRAMS

By June 2010

Condition	Newborns studied	Diagnostics	Frequency
Congenital Hypothyroidism	3 150 856	782	1: 4 029
Phenylketonuria	2 545 690	49	1: 51 704
Congenital Adrenal Hyperplasia	548 838	35	1: 15 681
Biotinidase Deficiency	532 017	4	1: 133 004
Galactosemia	495 264	2	1: 247 632

ALL CHILDREN WITH NORMAL GROWTH AND NEUROCOGNITIVE DEVELOPMENT

Centro de InmunoEnsayo

CUBAN IMMUNIZATION PROGRAM IMPACT
1962 - 2011

Adopting some of Cuba's successful health-care policies may be the best first step toward normalizing relations.

Congress could request an Institute of medicine study of the successes of the Cuban health system and how to best embark on a new era of cooperation between U.S and Cuban scientists.

30 APRIL 2010 VOL 328
SCIENCE

Paul K. Drain and Michele Barry*

DISEASES	Year of Intervention	Year of Impact	Impact Achieved
Poliomyelitis	1962	1962	Eradicated
Neonatal Tetanus	1962	1972	Eradicated
Diphteria	1962	1979	Eradicated
Measles	1971	1993	Eradicated
Rubella	1982	1995	Eradicated
Mumps	1986	1995	Eradicated
Whooping cough	1962	1997	Eradicated
Congenital Rubella Syndrome	1986	1989	Eradicated
Post Parotiditis Meningitis	1986	1989	Eradicated
Tetanus	1962	1992	Rate<0,1 x 10^3 Inh.
H. influenzae type B	1999	2001	Rate<0,1 x 10^3 Inh.
Hepatitis B<25 years old	1992	2001	Rate<0,1 x 10^3 Inh.
Meningococcus Meningitis	1988	2001	<98% Mortality <93% Incidence

Cuba, best conditions for motherhood among developing countries, according to ***Save the Children's State of the World's Mothers 2010 report***

The report, made public Monday, examines 160 countries - 43 developed and 117 developing ones - and analyzes the best and worst places to be a mother based on 10 factors such as the educational status, health, economic circumstances of the mothers, as well as the basic well-being of children.

Among developed countries, Norway is in first place in the rankings, followed by Australia, Iceland and Sweden. **USA appeared in position 28th.** Cuba is in first place on the list of best developing countries

Center for Genetic Engineering and Biotechnology

Personnel: 1 400

Facilities: 70 000 m^2

Research Focus: Vaccines, pharmaceuticals, diagnostics, plant and animal biotechnology

Products:

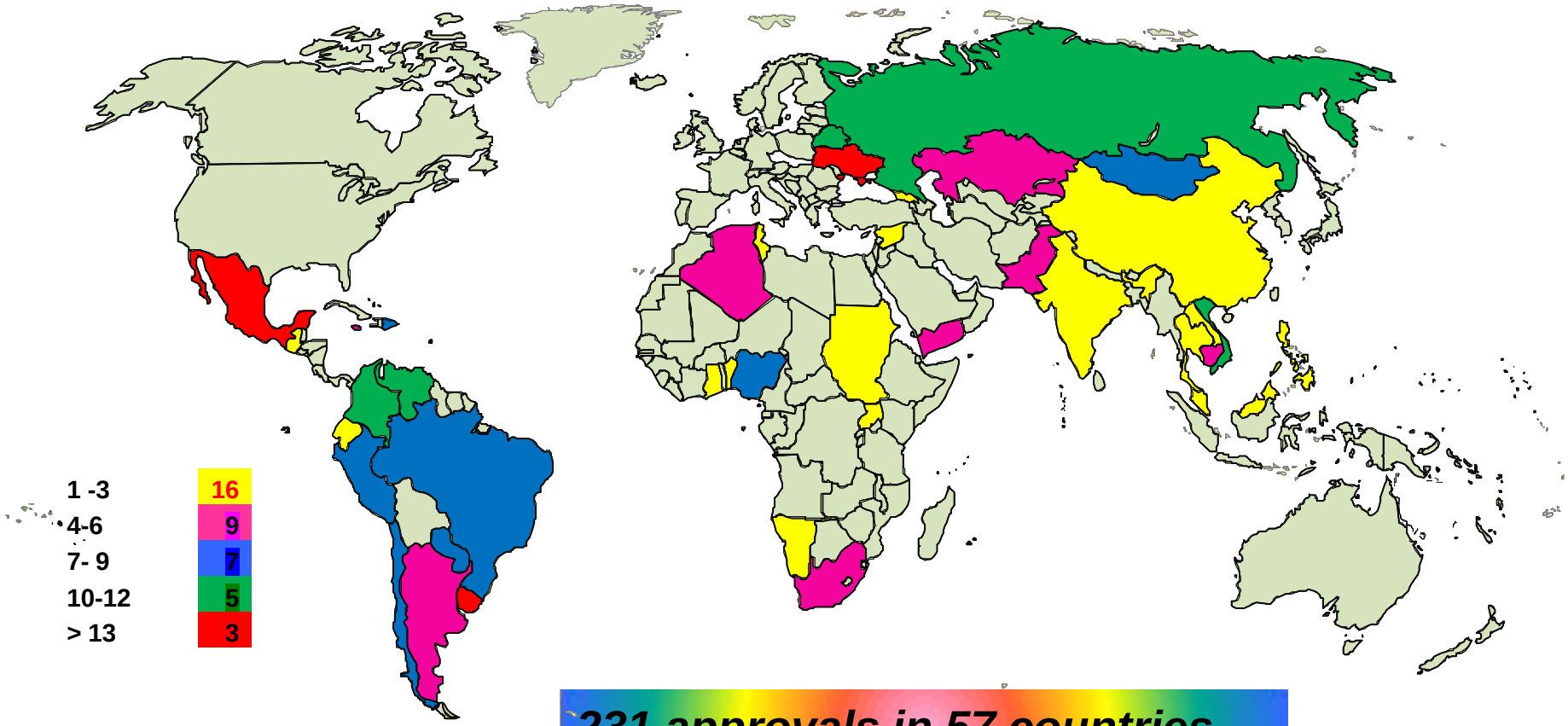
- Pentavalent vaccine
- Rec. Hepatitis B vaccine
- Rec. IFN Alpha-2b
- Rec. GCSF
- Rec. EGF
- Rec. tick vaccine
- Rec. Erythropoietin
- Heberprot P
- Conjugated Hib vaccine
- Rec. IFN gamma
- Rec. Streptokinase
- Transfer Factor
- Diagnostic kits
- Bionematicide

Los productos del CIGB contribuyen al diagnóstico, la prevención y el tratamiento de 26 enfermedades en Cuba

- Hepatitis B
- Hepatitis C
- Meningitis por Hib
- Leucemia mieloide crónica
- Mieloma múltiple
- Melanomas
- Carcinoma basocelular de piel
- Linfomas cutáneo y no-Hodgkin
- Cáncer de riñón
- Cáncer de vejiga
- Hemangioma de la infancia
- Neutropenia
- Anemias no ferriprivas

- Papilomatosis respiratoria recurrente
- Conjuntivitis hemorrágica
- Infarto Agudo del Miocardio
- Ulceras del pie diabético
- Inmunodeficiencia celular
- Herpes zoster
- Herpes simple
- Quemaduras
- Diagnóstico del HIV
- Diagnóstico de la HC
- Diagnóstico de embarazo
- Diagnóstico de rotavirus
- Diagnóstico enfermedad celiaca

Registration approvals abroad



231 approvals in 57 countries

Product	No. Reg		Product	No. Reg		Product	No. Reg
Heberbiovac HB	67		Hebervital	11		Heberprot-P	14
Heberon Alfa R	61		Heberitro	7		Trivac HB	4
Heberkinasa	22		Quimi-Hib	16		Acuabio 1	1
Hebermin	14		Gavac	4		Heberpenta-L	4
			Heberpenta	7			

ACEPTABILIDAD OMS

World Health Organization

20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – TEL CENTRAL +41 22 791 2111 – FAX CENTRAL +41 22 791 3111 – WWW.WHO.INT

Tel. direct: +41 22 791 4050
Fax direct: +41 22 791 4971
E-mail : woodd@who.int

In reply please refer to: QSS-CAR/rs (2009-04-14)

Your reference:

TO WHOM IT MAY CONCERN

15 APR 2009

This is to certify that the Center for Genetic Engineering and Biotechnology (CIGB), Cuba, is a supplier to UN agencies of Hepatitis B vaccine. As such, this product is reassessed by WHO for continued acceptability, in principle, for purchase by UN agencies, at regular intervals. This reassessment includes file review, monitoring compliance with specifications through testing, and facility site visits.

David Wood

Dr David Wood
Coordinator
Quality, Safety and Standards

World Health Organization

20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – TEL CENTRAL +41 22 791 2111 – FAX CENTRAL +41 22 791 3111 – WWW.WHO.INT

Tel. direct: +41 22 791 2779/4612
Fax direct: +41 22 791 4227
E-mail: okwobelej@who.int

In reply please refer to: QSS-CAR/rs (2010-083)
I8-370-43 AMRO

Your reference:

Ms Shanelle Hall
Director
Supply Division
UNICEF (Denmark)
Unicef Plads
Freeport
Copenhagen 2100
Danemark

26 APR 2010

Dear Ms Hall,

Acceptability, in principle, of *Haemophilus influenzae* type b vaccine (Quimi-Hib), produced by CIGB, Cuba, for purchase by United Nations Agencies

We are pleased to inform you of the positive decision on the acceptability, in principle, of the *Haemophilus influenzae* type b vaccine (Quimi-Hib) for purchase by United Nations Agencies. This decision is based on appropriate review of the submitted Product Summary File including clinical data, evaluation of the consistency of final product characteristics, site visit of the manufacturing facilities, and follow-up of implementation of recommendations made by WHO reviewers during the evaluation. This decision applies to the Quimi-Hib vaccine filled in a one dose vial presentation with a VVM14 and with a shelf life of 36 months at 2-8°C. The vaccine is supplied in the following packaging presentations:

Box containing 25 vials with a dose of 0,5 mL each one

Vials per inner pack: 25

Inner pack/carton specs: 2,7 x 2,7 x 5,5 cm

Volume per dose: 0,5 mL/ dose

Export packing (Shipper pack profile)

Dimensions (cm): length 54 ± 0,25, width 40 ± 0,25 and height 51 ± 0,25

No. of doses per export packing: 900

cc: Dr I. El-Ziq, UNICEF Supply Division
Dr L. Herrera Martinez and Mr Y. Quinones Maya, CIGB
Dr C. Campa-Huergo, Finlay
Ing A. Agraz, Biocen
Dr R. Perez Cristia, CECMED
WR-Cuba
Ms H. Scaramuzzi, PRS
QSS - Attention: Dr D. Wood and Ms L. Brown

Certificación

ISO 9001: 2008

Certificado del Sistema de Gestión de la Calidad

AENOR ER Empresa Registrada UNE-EN ISO 9001

ER-1355/2008

AENOR, Asociación Española de Normalización y Certificación, certifica que la organización

CENTRO DE INGENIERÍA GENÉTICA Y BIOTECNOLOGÍA

dispone de un sistema de gestión de la calidad conforme con la Norma UNE-EN ISO 9001:2008

para las actividades: A. La investigación, el diseño, el desarrollo, la transferencia de tecnología y la producción de principios activos y productos farmacéuticos y biotecnológicos para uso humano.
La realización de ensayos físico-químicos, microbiológicos, inmunoquímicos y biológicos para el control de productos biotecnológicos.
El uso y manejo de animales de laboratorio con fines de experimentación en vivo y estudios preclínicos.
El diseño, el desarrollo y la impartición de actividades de formación en el área de la biotecnología.
B. El diseño, desarrollo y la gestión de la ejecución de ensayos clínicos de productos farmacéuticos para uso humano.

que se realizan en: A. AVE 31e/ 158 y 190.. - CUBANACAN - PLAYA 10600 (CIUDAD DE LA HABANA - Cuba)
B. CALLE 134 E/23 Y 25. - CUBANACAN - PLAYA 10600 (CIUDAD DE LA HABANA - Cuba)

Fecha de emisión: 2008-11-05
Fecha de renovación: 2011-11-05
Fecha de expiración: 2014-11-05

AENOR Asociación Española de Normalización y Certificación

Avelino BRITO MARQUINA
Director General de AENOR

AENOR Asociación Española de Normalización y Certificación | Génova, 6. 28004 Madrid. España Tel. 902 102 201 – www.aenor.es

ANVISA BRASIL

15. CONSIDERAÇÕES GERAIS / AVALIAÇÃO DE RISCOS / RECOMENDAÇÕES

Durante a inspeção foram encontradas algumas não conformidades, as quais foram prontamente acatadas pela empresa, assim como foram propostas ações corretivas para as mesmas. Dentre as não conformidades encontradas, foi dada ênfase para o gerenciamento do sistema de controle mudanças, o qual verificou-se possuir falhas. Sobre o sistema de controle de mudanças a empresa está avaliando algumas melhorias, as quais devem tornar o gerenciamento das mudanças mais robusto. Desta forma em uma próxima inspeção, o sistema de controle de mudanças da empresa será auditado com maior ênfase para verificação de suas melhorias.

De forma geral as não conformidades encontradas não foram consideradas criticas e não apresentam risco ao processo produtivo e conseqüentemente ao produto.

A equipe inspetora avaliou que a empresa cumpre com as normas de BPF vigentes tanto no Brasil quanto na OMS.

As recomendações e ações corretivas de acompanhamento descritas no corpo deste relatório serão verificadas na próxima inspeção.

16. CONCLUSÃO

(x) SATISFATÓRIA PARA: Insumo: Alfainterferona 2b humana recombinante.

17. EQUIPE INSPETORA

1- Anderson Vezali Montai (COINA/GIMED/GGIMP/ANVISA)

2- Lucia Sciortino Giorgis (GIMED/GGIMP/ANVISA) Lucia S. Giorgis

Data: 29/03/2011.

MCC Sudáfrica

health

Department:
Health
REPUBLIC OF SOUTH AFRICA

MEDICINES CONTROL COUNCIL
The Registrar of Medicines, Private Bag X828, PRETORIA, 0001
Tel (012) 312 0000 Fax (012) 312 3105
Tel: 012 312 0230
Fax: 012 312 3165
Inquiries: DR J GOUWS
Reference: B7.1 CPA39 Point 9.4 Part 1 (Pg116-118)

25 March 2010

The Responsible Pharmacist
The Biovac Institute SA
Private Bag x3
Pinelands
7430

Fax: 021 551 3962

Attention: Mr JM Jellin

COUNCIL RESOLUTION: CENTER FOR GENETIC ENGINEERING AND BIOTECHNOLOGY (CIGB): CUBANACAN, HAVANA CITY, CUBA

This letter serves to inform you that the inspection report and company response for the GMP Inspection conducted at Center for Genetic Engineering and Biotechnology (CIGB): Cubanacan, Havana City, Cuba has been tabled at the recent meeting of the Medicines Control Council of 19 March 2010.

Council resolved that:

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection reflected in the observations listed in the inspection report and the company response, the Council IS satisfied that Centre for Genetic Engineering and Biotechnology (CIGB): Cubanacan, Havana City, Cuba is operating at an acceptable level of compliance with the principles and guidelines of Good Manufacturing Practice as prescribed by the SA Guide to GMP and RECOMMENDS registration of medicines (API for Anti Hepatitis B vaccines and Heberbiovac HB vaccines) in terms of quality.

Should you require any further information, please do not hesitate to contact the inspectorate.

Yours faithfully

REGISTRAR OF MEDICINES

Auditoria cGMP Consultoría Española CESIF

CESIF consultoría

ESTATUS DE CUMPLIMENTO

CONCLUSIONES GENERALES

Cumplimiento de Normas Correctas de Fabricación (N.C.F.)

Se considera que, actualmente, el grado de cumplimiento global de las N.C.F. del CIGB, en relación específicamente con la fabricación de sustancias activas y, en particular, de la fabricación del Factor de Crecimiento Epidérmico (EGF), **es satisfactorio** a todos los niveles.

Es opinión de los auditores que el CIGB, con el personal, instalaciones, equipos, sistema documental y servicios auxiliares con los que cuenta actualmente, algunos de los cuales se encuentran en proceso de remodelación, reestructuración o actualización, es capaz de alcanzar los niveles de calidad adecuados para asegurar la fabricación consistente y repetitiva de lotes de sustancia activa con las características fijadas en las especificaciones.

Como complemento a los resultados de la auditoria realizada, es muy interesante saber que el CIGB ha conseguido las siguientes certificaciones de calidad:

1. Certificado ISO 9001:2000, emitido por IQNet y AENOR.
2. Certificado NC-ISO 9001:2001.
3. Certificado de Buenas Prácticas de Fabricación, emitido por ANVISA (Brasil) (2008)
4. Certificado de Buenas Prácticas de Fabricación, emitido por el CECMED (Cuba) (2009).
5. Certificado de Buenas Prácticas de Fabricación, emitido por la OMS, para la fabricación y análisis de la vacuna de la Hepatitis B (2009).
6. Certificado de Buenas Prácticas de Fabricación, emitido por la OMS, para la fabricación y análisis de la vacuna Quimi - Hib (2009).

Firmado:

Dr. Fernando Pérez Vallejo
Farmacéutico Especialista en
Farmacia Industrial y Galénica
Director de la Sección Industrial

Dra. Teresa Crespo Garcés
Farmacéutico Especialista en
Farmacia Industrial y Galénica
Consultor de CESIF Consultoría

Auditoria cGMP Consultoría Inglesa

aptuit

Statement of GMP Compliance

As part of Clinical Trials Application requirements for Investigational Medicinal Products which are intended to be imported to EU member states, a QP Declaration is required as part of the submission to certify that all sites involved with the production and testing of the IMP operates in compliance with GMP at least equivalent to EU.

In order to facilitate the issue of a QP declaration, GMP audits were performed between 9th November 2009 and 12th November 2009 of the following companies;

Center For Molecular Immunology (CIM)
Calle 216 y 15, Atabey, Playa.
Ciudad de La Habana, Cuba.

Center For Genetic Engineering and Biotechnology (CIGB)
Ave. 31 e/ 158 y 190, Cubanacan Playa
PO Box 6162, La Habana 10600, Cuba.

Upon completion of the audits, I have found that both CIMAB and CIGB operate within standards equivalent to EU GMP and have found no observations which would prevent issuance of a QP Declaration in support of a Clinical Trials Application.

12 NOV 09

Andrew Michalkiewicz
Manager, Quality (QP)
Aptuit, Unit 107 Tenth Ave, Deeside, UK. CH5 2UA

Date

12/11/09

Name: Antonio Vallin Garcia
Quality Manager
Calle 216 esq 16. Atabey, Playa, Ciudad Habana. CP 11600.

Date

Auditoria cGMP Nobelpharma Japón

Summary Report of Site Visit

Sep. 2, 2011
Prepared by CMC-GMP Manufacturing Group

Acknowledgement

First of all, we greatly appreciate your perfect coordination for the audit. Regardless of such a short time, we could see everything we wanted during DD, and we owe it all to your kind cooperation.
Thank you very much!

Summary

CMC-GMP Manufacturing Group performed this site audit of CIGB Group's three manufacturing facilities to overview the state of compliance to Japanese GMP regulations and expectation for the manufacture of Hib vaccine and the facilities' readiness to host a PMDA inspection.

Our feeling is that your GMP systems comply with global GMPs' expectation on the whole, and the product quality is sufficiently assured.

Although a couple of issues have arisen, which are described a bit more in detail below, they could be overcome with extensive discussion and cooperation between CIGB and Nobelpharma.

It should be noted that the time for the audit was so limited that this report dose represent just a snapshot in time of the sites.

Signed by:

Takako A

Ms. Takako Aburada
(Nobelpharma Co., Ltd.)

白木澤 治

Mr. Osamu Shirokizawa
(Pharma Solutions Co., Ltd.)

Auditoria c GMP PHARMAQ Noruega

PHARMAQ

We make aquaculture progress

Harbitzalleen 5
P.O.B.267 Skoyen
N-0213, Oslo. Norway

Summary Report of Site Visit

November 2, 2011

Acknowledgement

First of all, we greatly appreciate your perfect coordination for the visit. Regardless of such a short time, it was possible see everything we wanted, and we owe it all to your kind cooperation.

Thank you very much!

Summary

Product Development and Manufacturing Group performed this visit to Camaguey CIGB facilities to overview the state of compliance to Norwegian GMP regulations and expectation for the manufacture of Sea Lice vaccine and the facilities readiness to host a European NRA Audit.

Our feeling is that your quality system for Product Development and Manufacturing are in place.

On request from PHARMAQ for certain documents we were provided those documents verifying that quality systems were implemented in those cases.

Some issues risen during the visit was discussed and options were proposed between CIGB and PHARMAQ. This was specially connected to the lay out of the new production facility.

Due to reconstruction of the new facility PHARMAQ was not able to evaluate the process line and equipments. As this is an important part of the GMP concept this has to be performed later.

It should be noted that the time for the pre audit was so limited that this report does represent just a snapshot in time of the sites. A PHARMAQ audit is proposed to take place in Q1 2012.

Signature by

Edel Anne Norderhus, PhD
Director Product Development, R&D

Arne Marius Fiskum, PhD
Director Manufacturing

Resumen de Auditorias/Inspecciones externas recibidas en el CIGB.

- **2009**
  CECMED: 8
  Otros: 5
- **2010**
  CECMED: 12
  Otros: 6
- **2011**
  CECMED:12
  Otros: 8
- **2012**
  CECMED:7
  Otros: 7

Almacén

Cuarto de Muestreo

Almacén

Áreas de Microbiología y Biología Molecular.

CIGB, GMP MANUFACTURING PLANTS

Áreas de producción

Áreas de producción


APV
STERIVESSEL

Reactores

Autoclaves y Hornos

Centrifugas

Sistemas cromatograficos

SISTEMA CRITICOS

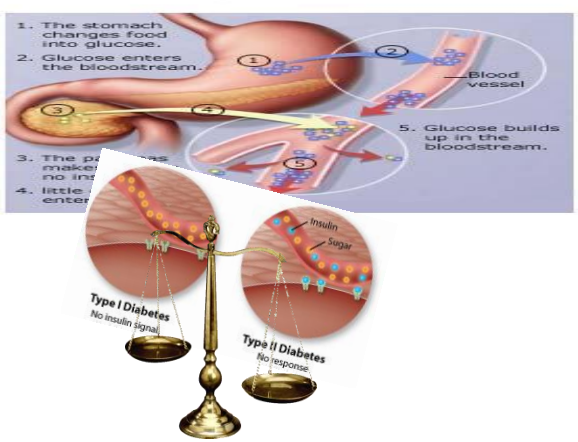
GENERADOR DE VAPOR PURO

AGUA PARA INYECCIONES

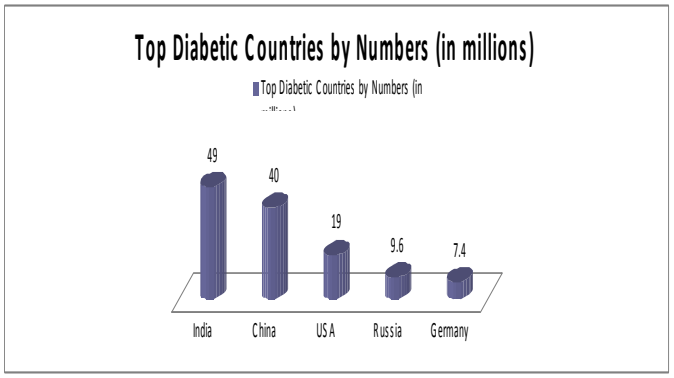
AGUA PURIFICADA

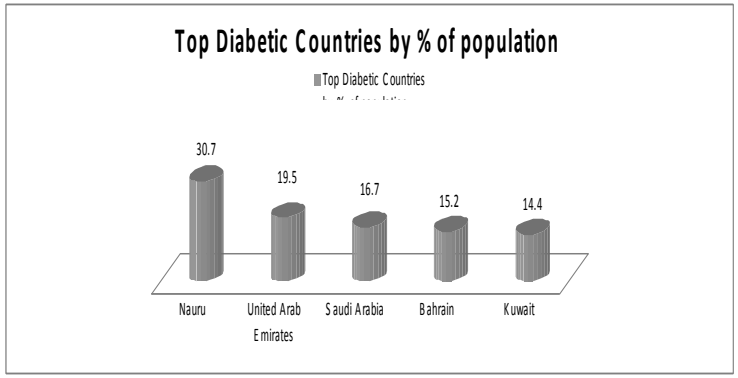
SISTEMA HVAC

DIABETES:
The problem



230 million people have diabetes
More than 230 million people worldwide are estimated to have diabetes — nearly an eightfold jump since 1985 — and nearly 4 million died of the blood sugar disorder in 2007, according to the World Diabetes Foundation.

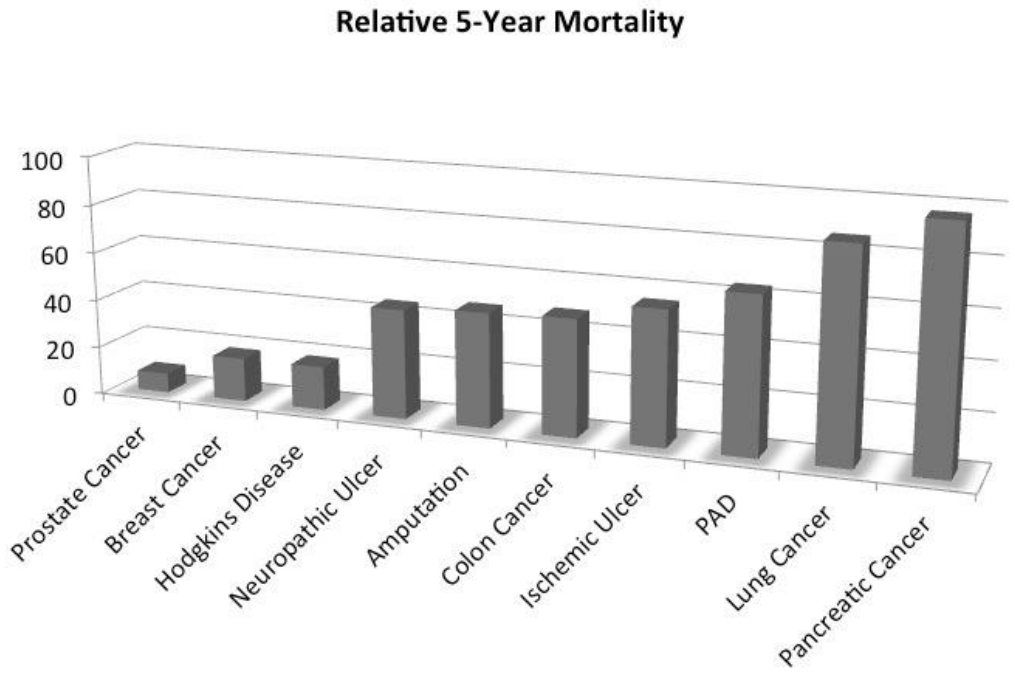




Natural History of Diabetic Foot Ulcer (DFU)

15% of diabetic patients would be affecting by DFU
30% of DFU patients never healing the ulcer with standard therapy
15% of DFU patients would be amputated as consequence of the DFU
50% of amputee patients died in 5-year, one of the most severe conditions

Armstrong DG, Wrobel J, Robbins JM: Are diabetes-related wounds and amputations worse than cancer? *Int Wound J* 2007, 4(4):286-287

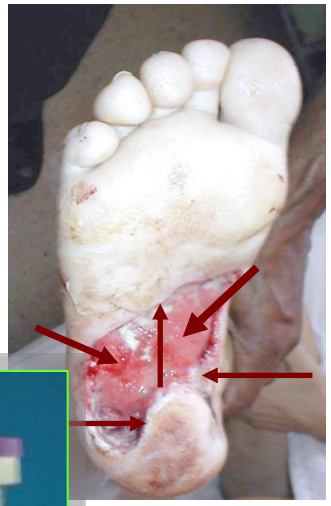


Severe DFU is a limb-threatening and also a life-threatening, among more aggressive types of cancer

KEY TO SUCCESS

THE STRATEGIC ALLIANCE IN CONDUCTING BASIC AND MEDICAL RESEARCH BETWEEN CIGB'S SCIENTISTS AND MEDICAL STAFF FROM THE NATIONAL INSTITUTE OF ANGIOLOGY AND VASCULAR SURGERY (INACV) IN CUBA

Pharmaceutical composition [human recombinant epidermal growth factor (EGFhrec) in an injectable formulation, administered by local intralesional infiltration, three times/week (6-24 doses)].



CIGB

INACV

Clinical Summary (Status and trials)

Registration (14): Cuba, Algeria, Argentina, Dominic Republic, Ecuador, Mexico, Paraguay, Uruguay, Venezuela, Libya, Colombia, Guatemala, Georgia, Ukraine.

Patents Granted: United States, European Union, Japan, Canada, Australia, Hong Kong, Singapore, South Korea, South Africa, Russia, China, India, Indonesia, Malaysia, Ukraine, Mexico, Argentina and Cuba. Filed: Brazil, Thailand and Chile.

Clinical trials (Seminal)

1. Phase I: 45 patients, 16 patients in PK trial
2. Phase II: Cuba, 166 patients (4 trials)
3. Phase III: 149 patients
4. National Surveillance in Cuba: 1,851 patients
5. Clinical trials running in Europe, China, Russia, and so on.

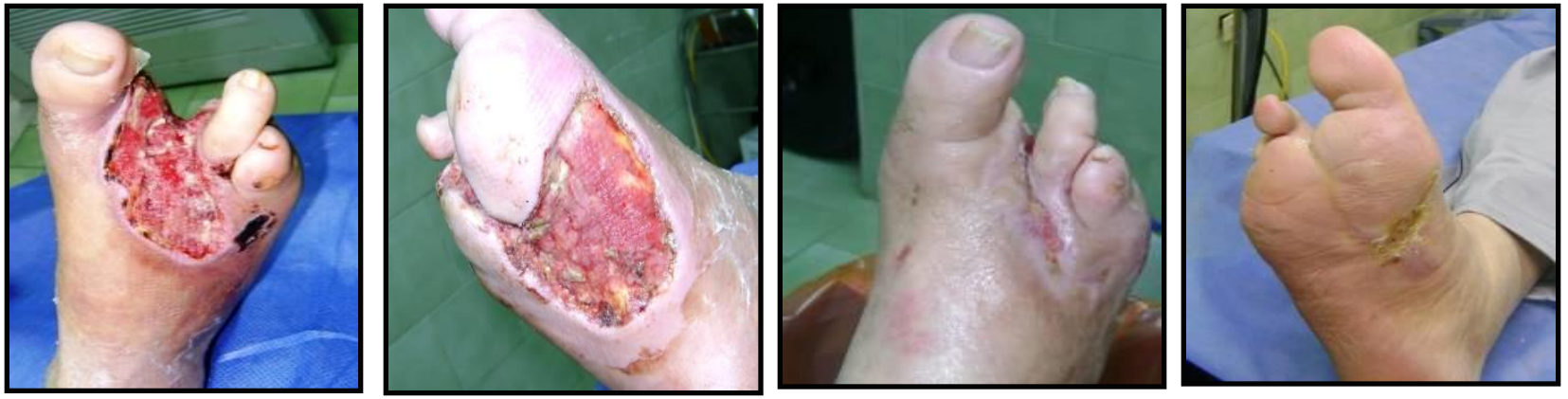
National Application

1. National Program in Venezuela: + 75,000
2. National Program in Cuba: + 15,000
3. Algeria (269), Argentina (360), Libya (159), Angola (18), Dominic Republic (10), others (+200).

Total: + 95,000

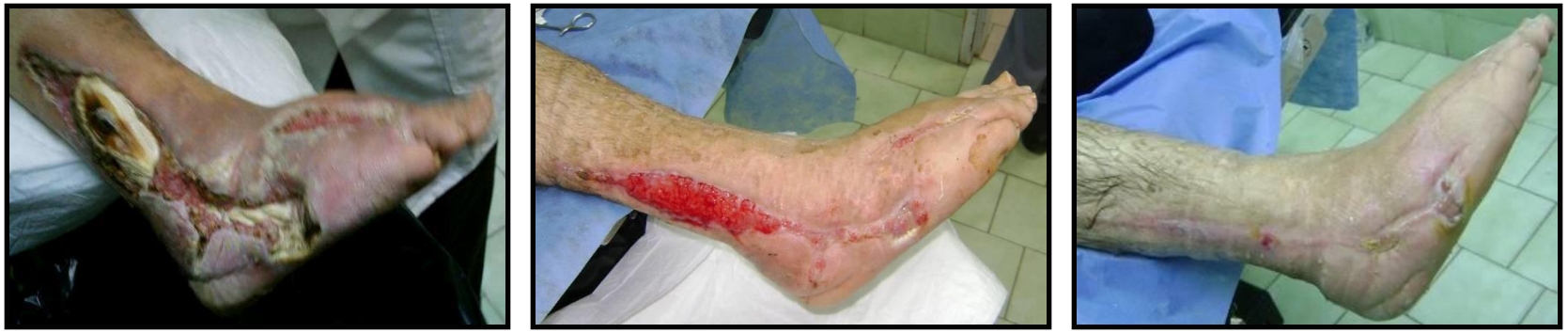
Heberprot P changes paradigms in diabetic foot ulcer management. Examples:

Bone exposed: Before = amputation required



Heberprot-P: Granulation achieved after 18 infiltrations (6 weeks) and wound closure after 51 days. (≥95% efficacy of treated cases)

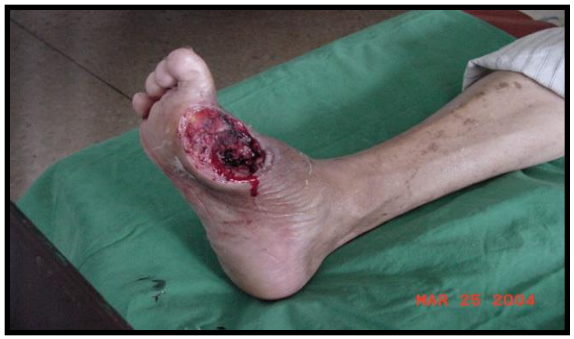
Tendon exposed: Before = removal and dysfunctional foot

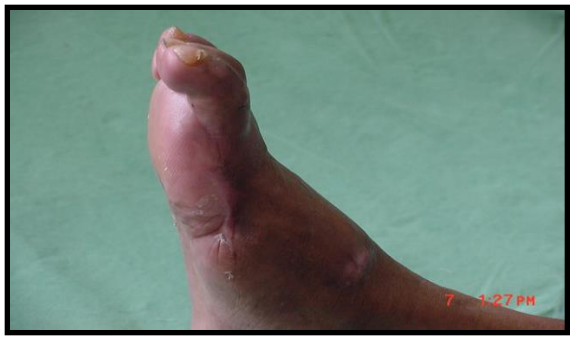


Heberprot-P: Granulation achieved in 4 weeks and wound closure after 52 days. (≥95% efficacy of treated cases)

Heberprot P changes paradigms in diabetic foot ulcer management. Examples:

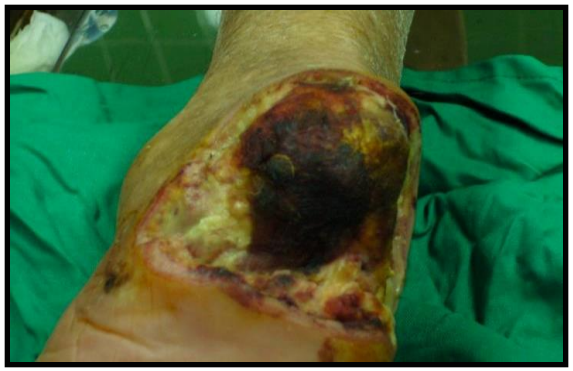
Osteomyelitis without bone seizure: Before = minor amputation required

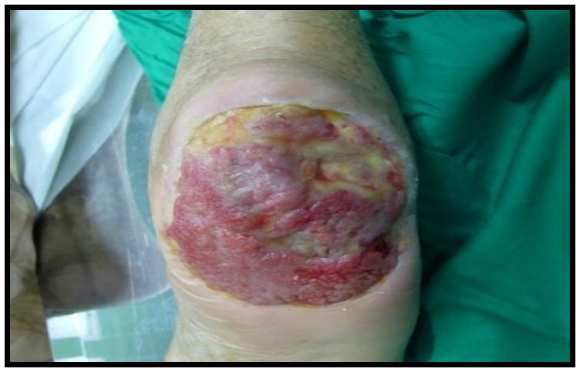


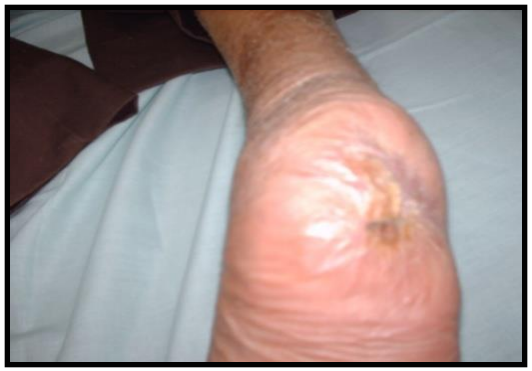


Heberprot-P: Granulation achieved in 8 weeks and wound closure 28 days after. (≥90% efficacy of treated cases)

Osteonecrosis of the calcaneous region: Before = amputation required







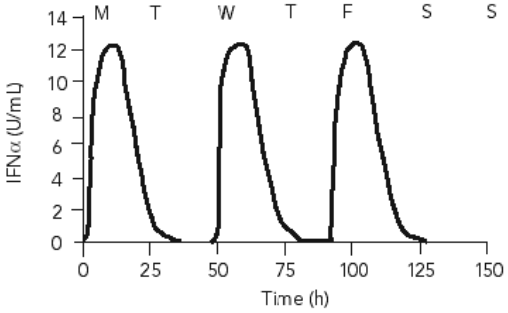
Heberprot-P: Granulation achieved after 32 infiltrations (10 weeks); closure 45 days after. (≥60% efficacy of treated cases)

THE WORLD'S LARGEST MARKET-PLACE FOR INVENTIONS

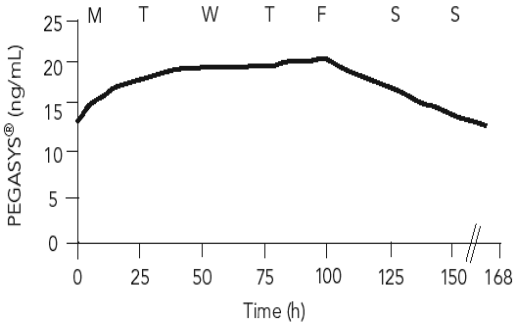
WIPO AWARD FOR BEST YOUNG INVENTOR

39th International Exhibition of Inventions of Geneva

PEGylated Interferon alpha 2b. CIGB results

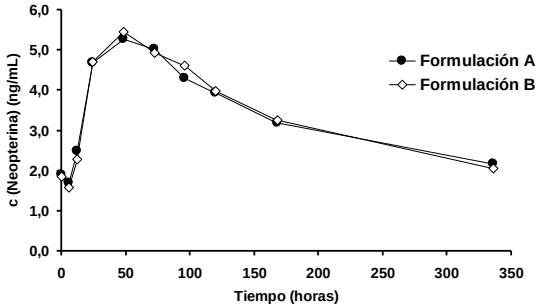


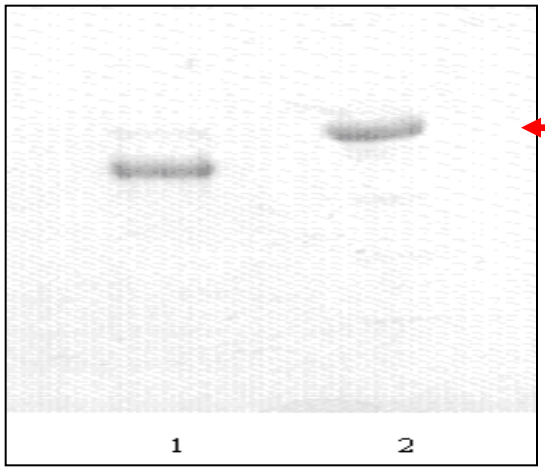
PEGylation enhances pharmacokinetic properties of IFN-α



Thrice weekly administration of conventional IFN-α2b results in peaks and troughs of drug concentration which are associated with side-effects and viral rebound, respectively

IFN-α2a conjugated to a branched PEG (40 kDa).





High purity level of the new IFN-Peg$_{4,48k}$ obtained by CIGB (Patent product)

Analysis of PEG$_{2,40K}$-IFN-a2b (1) and PEG4,12K-IFN-a2b (2) purity by SDS-PAGE:

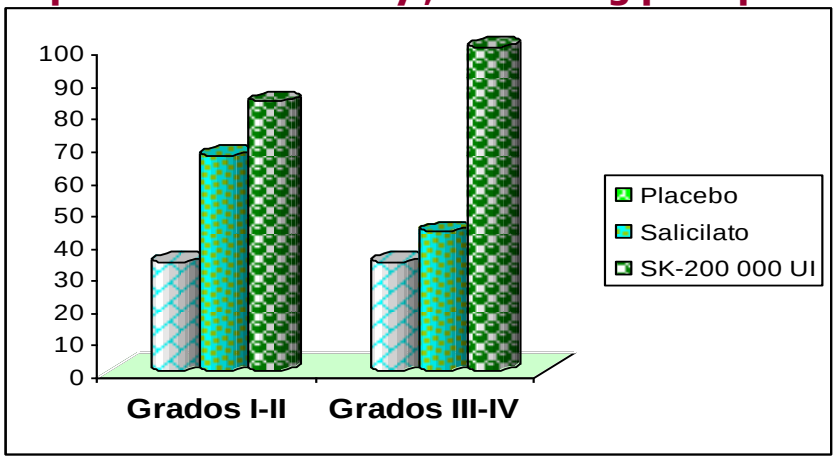
Proctokinase

Treatment of Hemorrhoid with Recombinant Streptokinase Suppository

Hemorrhoids are one of the rectal pathologies with the highest worldwide incidence, 50 % of people with more than 50 years old will develop hemorrhoids.

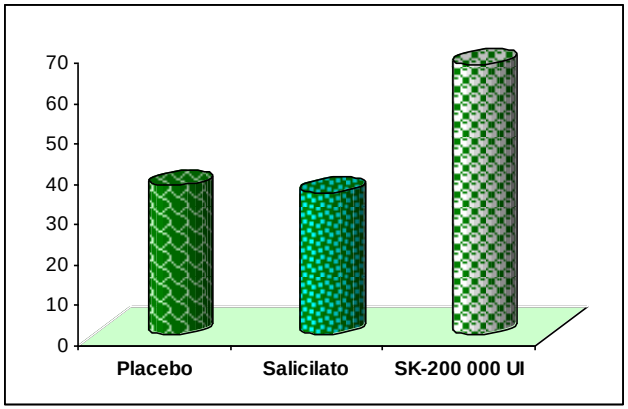
(Johanson JF, Sonnenberg A. Prevalence of hemorrhoids and chronic constipation. An epidemiologic study 1990; 98-380.)

Total response after 5to day , according prolapsus grade



Differences between Proctoquinasa (SK 200 000 UI) vs. Placebo, in III-IV Grades.

Total response at day 5th



Difference between Proctoquinasa (SK 200 000 UI) vs. Placebo.

ANR: C E C M E D

SISTEMA DE PRODUCCION DE VACUNAS

- INSTITUTO FINLAY
- CENTRO ING. GENETICA Y BIOTECNOLOGIA
- BIOCEN
- HEBER BIOTEC S.A.

World Health Organization

WORLD HEALTH ORGANIZATION
IMMUNIZATION, VACCINES AND BIOLOGICALS
STRENGTHENING NATIONAL REGULATORY SYSTEM

Certificate

The World Health Organization certifies that the National Regulatory Authority of Cuba for vaccines, represented by the

Centro para el Control Estatal de la Calidad de los Medicamentos (CECMED)

has been assessed from 23 to 28 November 2008 against the WHO National Regulatory Authority indicators (rev.Dec.2007) as a functional National Regulatory Authority

This certificate is valid until the next assessment that, in principle, will take place, in 2 to 5 years.

Signed: _____
Dr Jean-Marie Okwo-Bele
Director
Department of Immunization, Vaccines and Biologicals
World Health Organization

Relaciones entre los centros

Finlay

CIGB

BioCen

Heber Biotec

SISTEMA DE GESTION DE LA CALIDAD EN EL CIGB

POLITICA DE LA CALIDAD

NC-ISO 9001:2008
Registro No. 117:2009

La calidad es y será la imagen del Centro de Ingeniería Genética y Biotecnología como organización comprometida con su país, con los clientes internos y externos, con la sociedad y el medio ambiente.

Las investigaciones desarrolladas, los servicios brindados, así como los productos desarrollados y elaborados en nuestro Centro se distinguen por su calidad, seguridad y eficacia, mediante el cumplimiento de los requisitos enunciados en las regulaciones de las Buenas Prácticas aplicables, así como los requisitos reglamentarios y legales, todo inmerso en un Sistema de Gestión de la Calidad eficaz basado en la Norma NC-ISO 9001:2008 y en las tendencias internacionales.

El cumplimiento de la política de calidad se garantiza mediante el compromiso de la alta dirección, la gestión de los recursos, de los productos y procesos, la motivación y dedicación de todos y cada uno de los integrantes de nuestra institución y sobre todo, por la aptitud que mantenemos en relación con la calidad y su incesante proceso de mejoramiento.


Sistema de Gestión de la Calidad
Recursos Humanos
Sistema de Materias Primas y Componentes
Aseguramiento en los Procesos de Producción
Aseguramiento de la Calidad
Lab. de Control Analítico

Aseguramiento de la Calidad

- Documentación
- Aseguramiento Metrológico.
- Inspecciones y Auditorias.
- Cambios.
- Sistema CAPA .
- Análisis de Riesgo
- Quejas y Reclamaciones y Recogidas.
- Revisión Anual de Producto.
- Programa de Monitoreo Ambiental.
- Programas de validación.
- Liberación de Lotes.

Impacto de la vacuna contra la Hepatitis B
Cuba 1991 - 2011

Heberbiovac HB

Certificada por la OMS: Dic. 2001
Recalificación de OMS: Oct 2003
Recalificación de OMS: Sept 2005
Recalificación de OMS: Nov. 2008

	91	93	94	96	98	'00	'01	'02	'03	'04	'05	'06	'07	'08	'10	'11
Población	2044	1908	1747	1695	1026	451	243	132	90	61	49	38	17	15	11	21
Niños < 15	304	240	212	144	10	2	1	1	1	1	0	1	0	0	0	0
Niños < 5	72	48	31	17	1	0	0	0	0	0	0	0	0	0	0	0

Source: National Direction of Statistics Ministry of Public Health Cuba

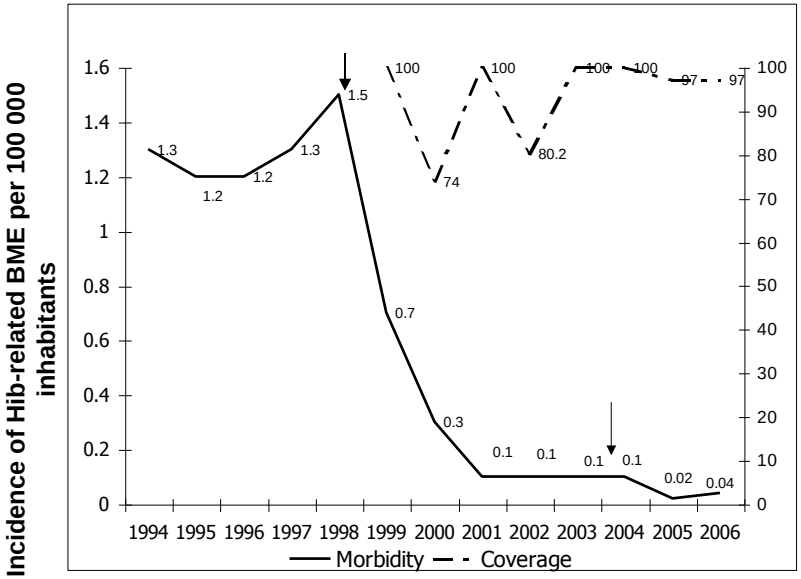
Organización Mundial de la Salud

QuimiHib vaccine vs. *Haemophilus influenzae* type b

Registry in Cuba: November 2003

Sugar shot. Simpler synthesis of carbohydrates has led to a new vaccine for *Haemophilus influenzae* type B.

Quimi – Hib®



Source: National Immunization Program, Ministry of Public Health of Cuba

HEBERPENTA

Combined diphtheria, tetanus, cellular pertussis, hepatitis B and Haemophilus influenzae type b vaccine. Heberpenta was introduced in the Cuban's immunization program in September, 2006. More than 3 millions doses have been applied in several countries

First pentavalent vaccine fully produced in a Developing Country

Heberpenta-L

Fully liquid pentavalent DTP-HB-Hib vaccine

New Formulation

Contains all 5 antigens in a ready-to-use 0.5 mL suspension in a vial

Vacunas Combinadas

Registradas:

- Tetravalente DPT-HB (Trivac HB®)
- Pentavalente DPT-HB+Hib (Heberpenta®)
- Pentavalente DPT-HB-Hib líquida en un solo vial (Heberpenta-L®)

*La nueva vacuna, Heberpenta-L se logró registrar en otros 3 paises en el 2012: Venezuela, Georgia y Argentina.

* Se ha logrado todo el suministro de la vacuna que necesita el PAI cubano

En proyección:

- Pentavalente DaPT-HB-Hib
- Hexavalente DaPT-HB-Hib-IPV

*Se han logrado avances en el proyecto de desarrollo de la pertussis acelular

Proyectos I+D en el campo de las vacunas

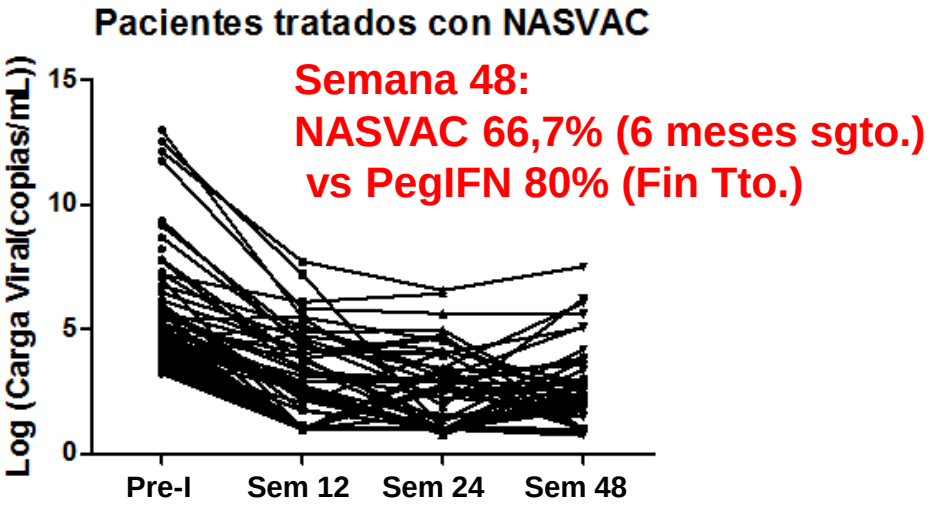
Cartera de proyectos - Enfermedades infecciosas

PROYECTO/PRODUCTO	Laboratorio	Desarrollo	Pre Clínica	Fase E. Clínico			
				I	II	III	Registro
Heberpenta (vacuna pentavalente)	■	■	■	■	■	■	2006
Vacuna pentavalente líquida	■	■	■	■	■	■	2010
Vacuna Hepatitis C profiláctica	■	■	■	■	■		2012
Vacuna terapéutica Hepatitis C	■	■	■	■	■		2013
Vacuna NASVAC contra Hepatitis B	■	■	■	■			2013
Vacuna Pertussis acelular	■	■	■				2013
Vacuna terapéutica SIDA	■	■	■				2015
CIGB 210 – Antiviral SIDA	■	■					2016
Vacuna dengue	■	■					2017
Inhibidores Dengue	■						2017
Antivirales VIH	■						2016

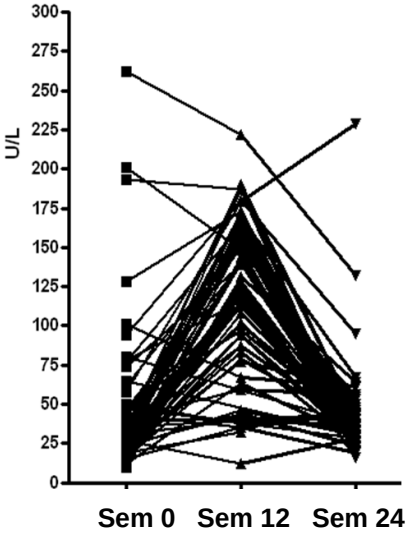
Vacuna terapéutica contra Hepatitis B: NASVAC

- La administración IN y SC de NASVAC fue segura.
- La vacunación terapéutica se relacionó a la disminución de la CV de los pacientes al final del tratamiento y del seguimiento en mas de un 60% de los pacientes inmunizados luego del fin de las inmunizaciones y de 6 meses de seguimiento.
- El incremento de las ALT en la semana 12 evidenció una inmuno-activación generalizada, seguida de una rápida normalización de los valores de transaminasas.

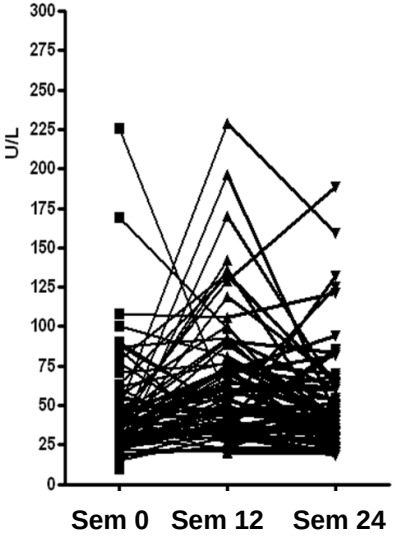
Carga Viral: NASVAC



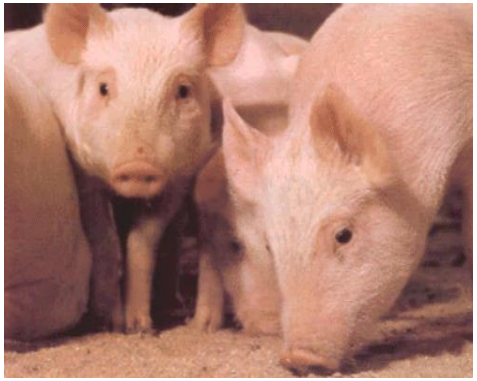
ALT NASVAC

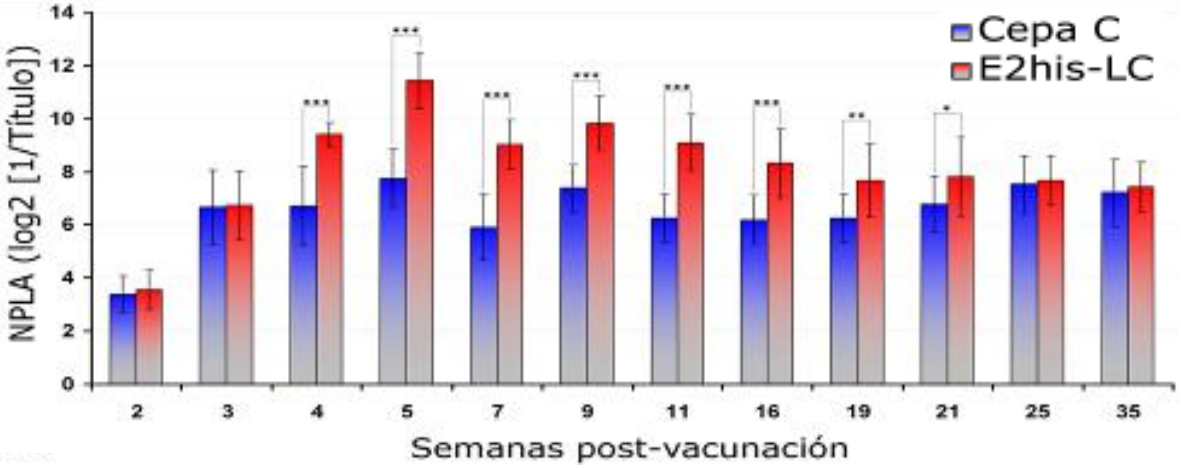


ALT PegIFN

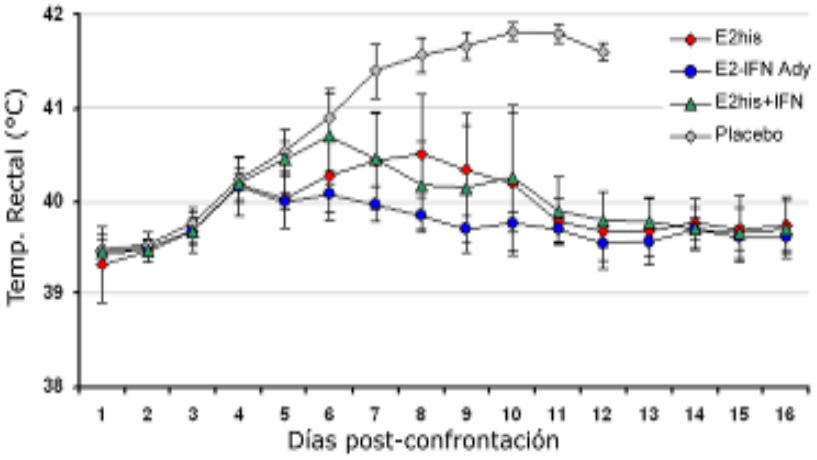


Vaccine against the Classic Porcine Cholera

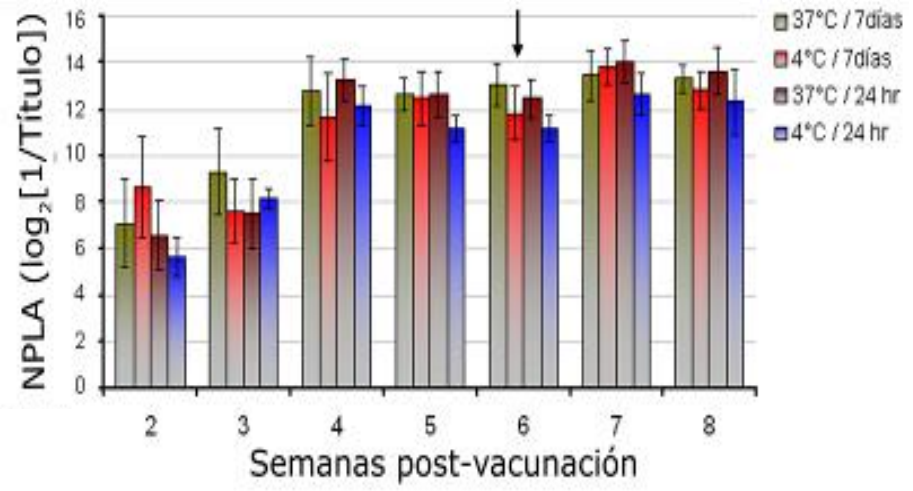




Vaccine formulations protects since a few days after vaccination

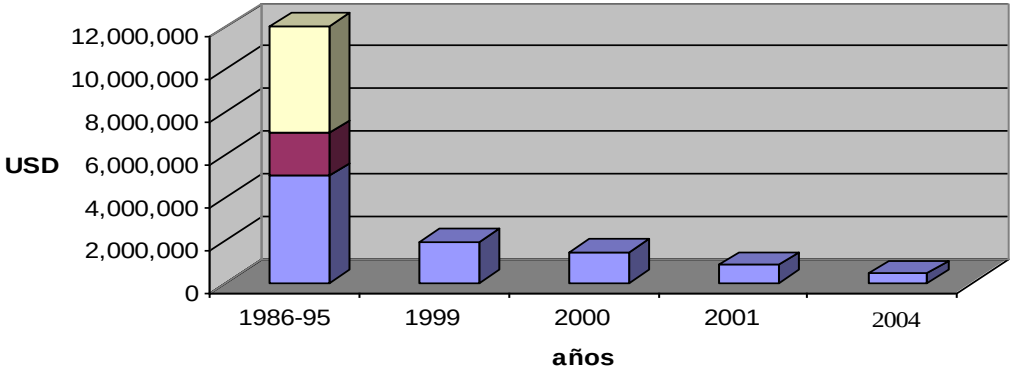


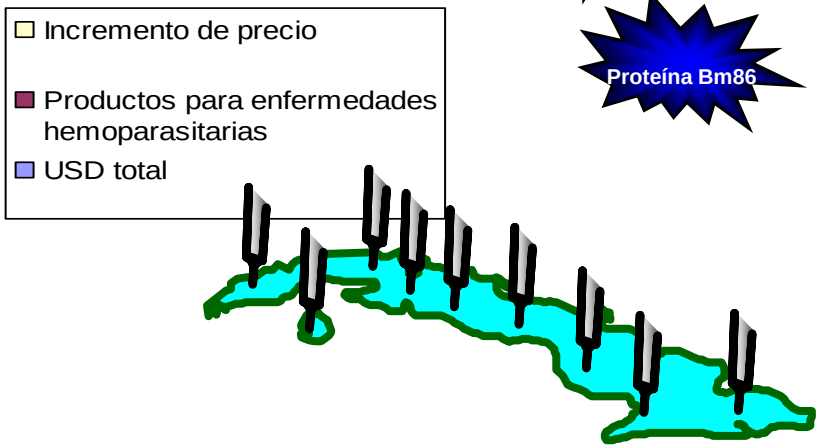
Resistance of the vaccine formulation to thermal stress without modifying its immunogenicity and protective activity .



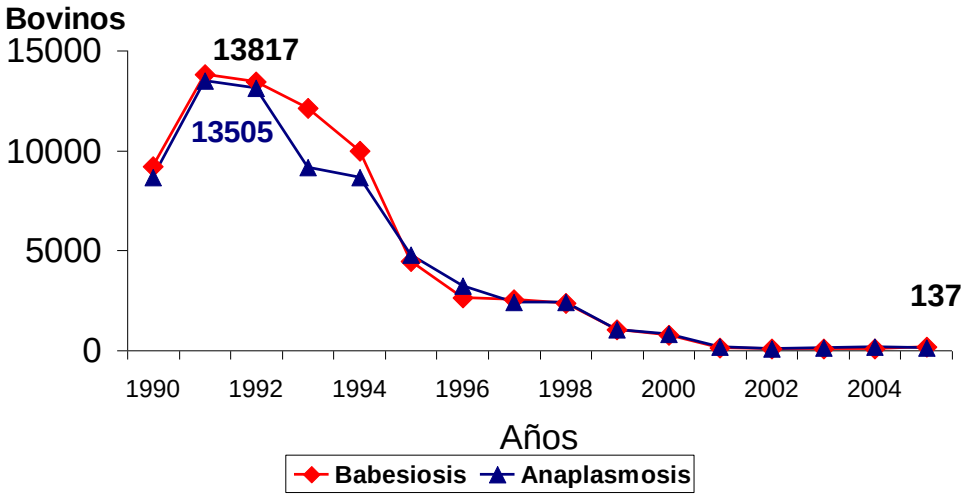
Vaccine against bovine cattle ticks

Gastos en productos químicos para el control de la garrapata y las enfermedades asociadas.





Muertos por Babesiosis y Anasplasmosis




GRACIAS POR SU
ATENCION
Julio 2013