Thailand's perspective on the benefits of collaborating with a large pharmaceutical company

Morakot Tanticharoen
National Center for Genetic Engineering and Biotechnology (BIOTEC), Thailand

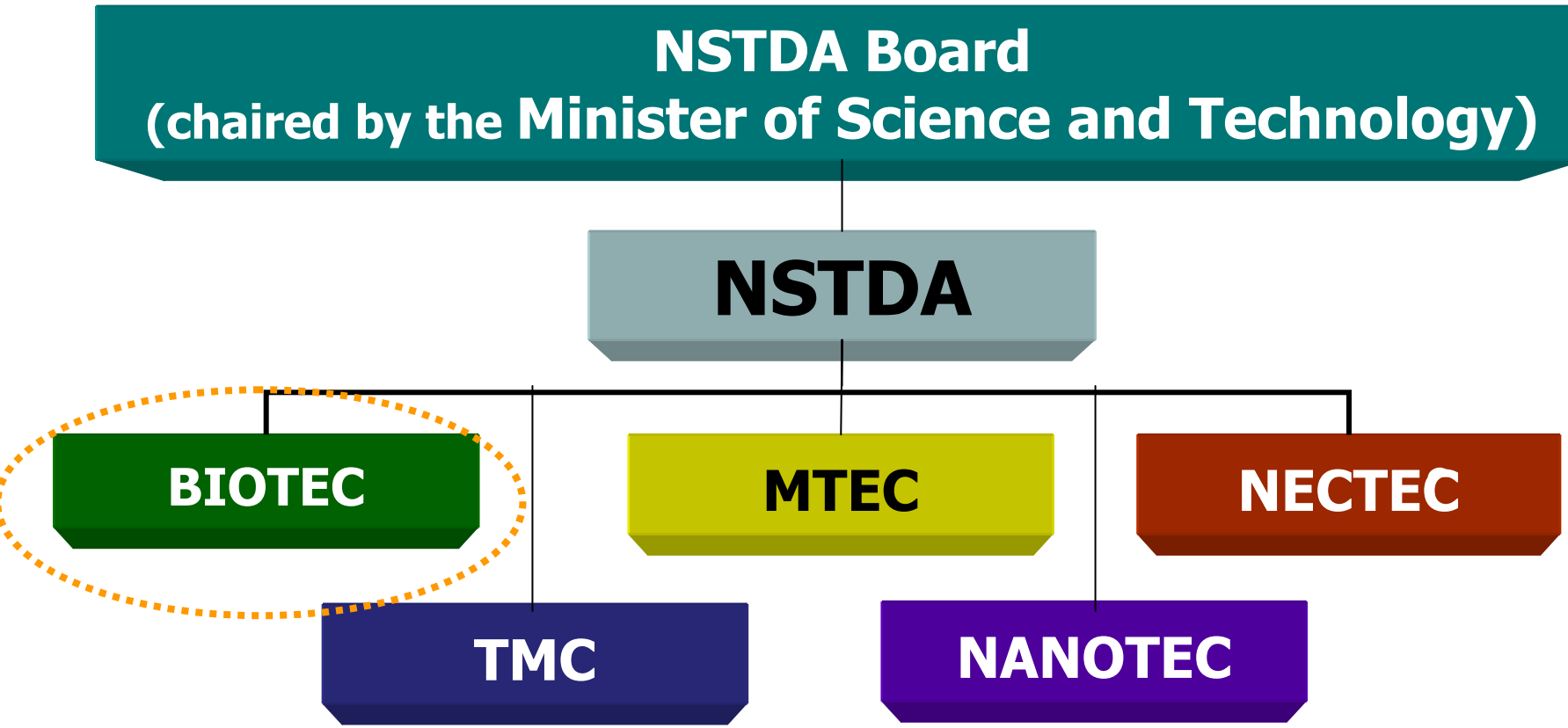
Geneva, Switzerland 23 January 2008

BIOTEC





NSTDA Organization
(established by a special law in 1991)

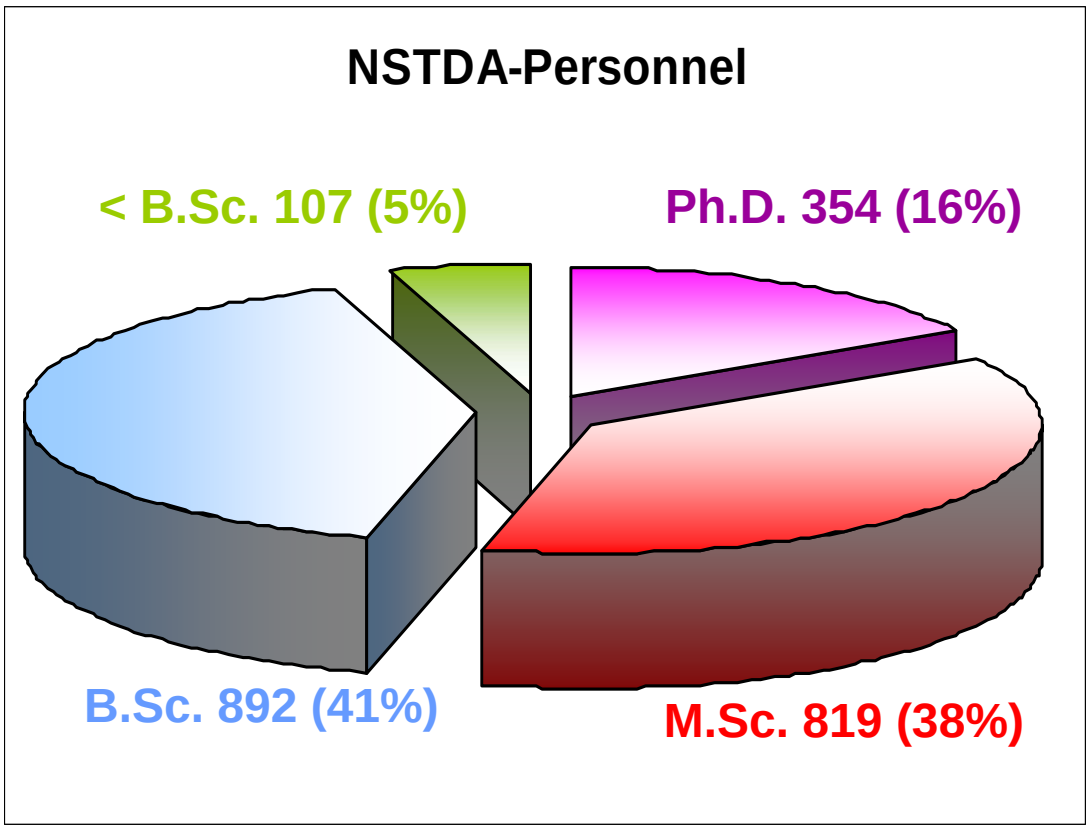


NSTDA : National Science and Technology Development Agency
BIOTEC : National Center for Genetic Engineering and Biotechnology
MTEC : National Metal and Materials Technology Center
NECTEC : National Electronics and Computer Technology Center
NANOTEC: National Nanotechnology Center
TMC : Technology Management Center

BIOTEC

Roles of NSTDA

Personnel



Staff 2,172

As of May, 2007

Mandate by Law

- RD&E
- Human Resource Development
- Technology Transfer
- Infrastructure Development

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Agricultural Biotechnology Research and Development Programs

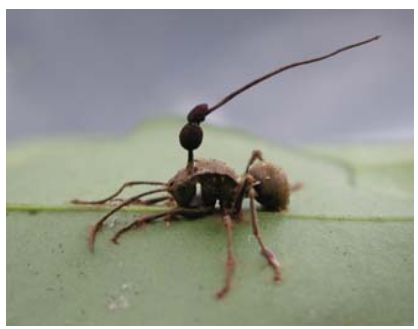
Shrimp-Breeding/ Diseases/Diagnosis

Rice Biotechnology

Seed Technology

Cassava biotechnology

Biodiversity/Bio-pesticides



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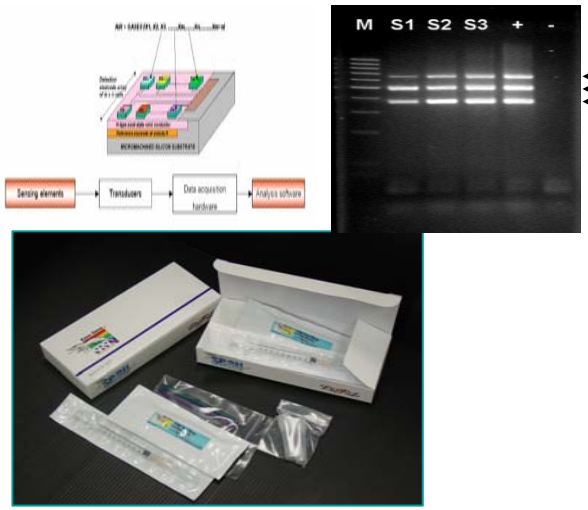
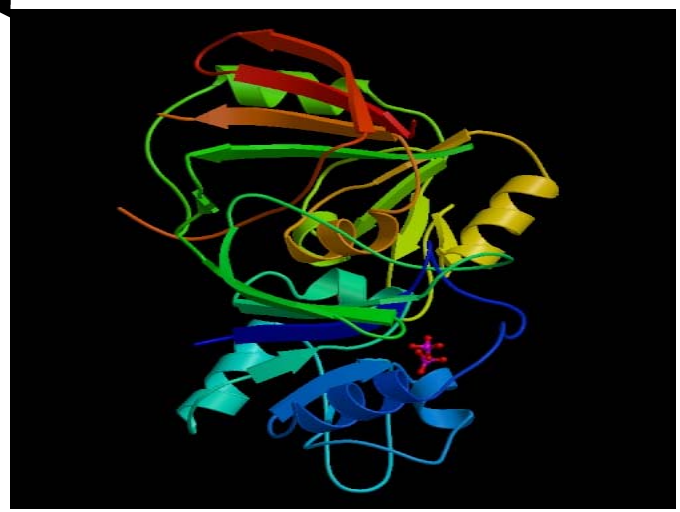
Medical Biotechnology

Sensors/Diagnostic kits

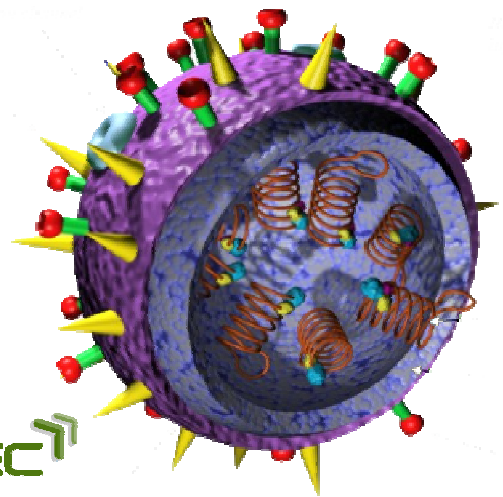


Emerging/Tropical diseases



Genomic Medicine

Avian Influenza



Biodiversity/Drug Discovery

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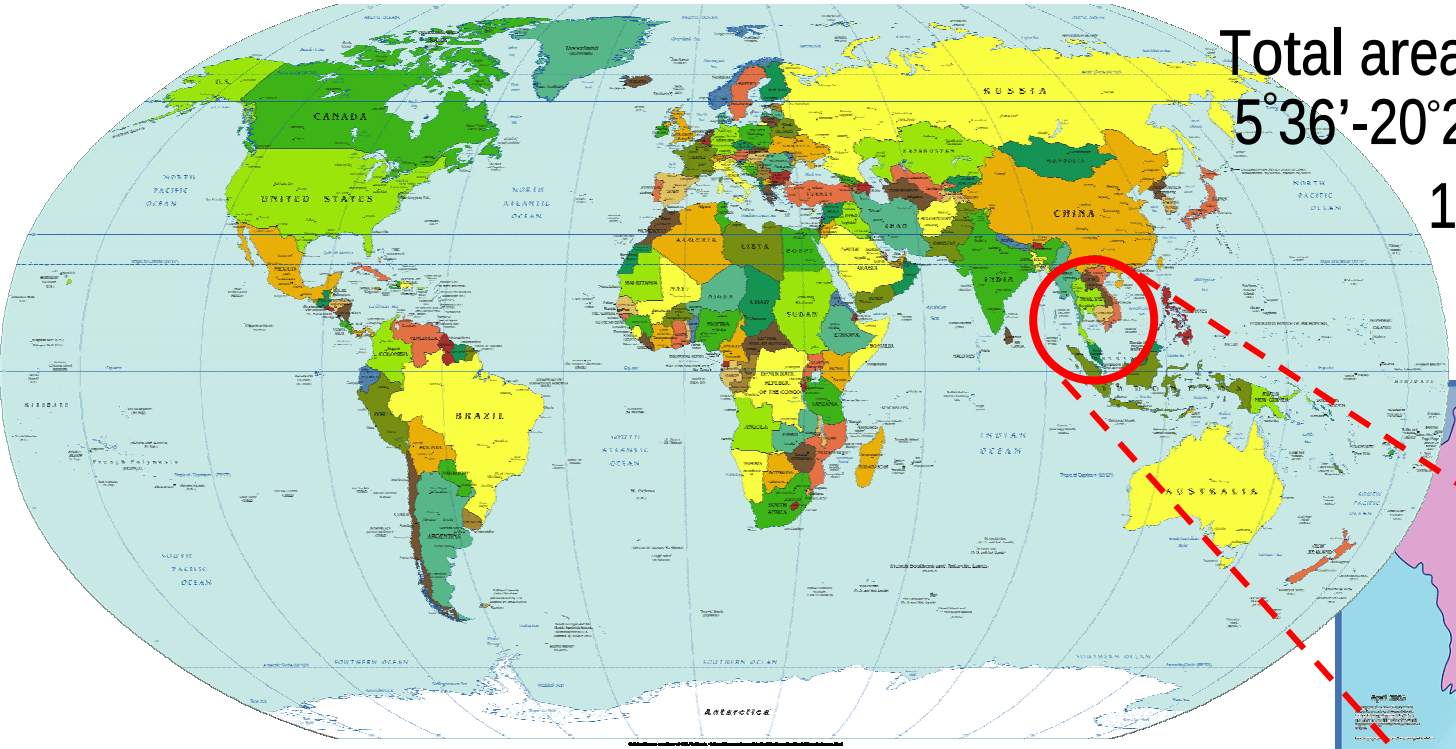
Thailand location



Total area = 514,000 sq. km

5°36'-20°27' North latitude

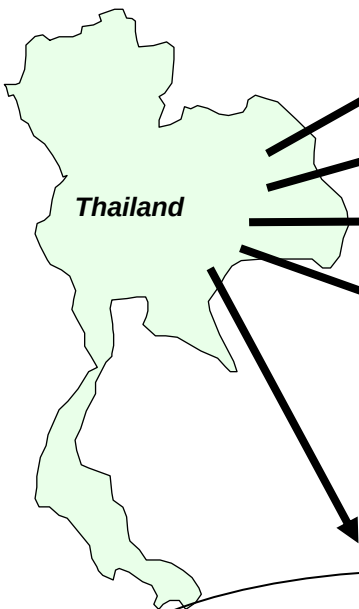
100° East

Protected areas cover 24% of the country's land area

- 139 National Parks
- 59 Wildlife sanctuaries
- 41 Non-hunting areas

A country rich in biodiversity

Species richness of Thailand
ca 7-10 % of the world's described species



Birds
World = 9,8201
Thailand = 980

Plants
World = 250,000
Thailand = 12,000

Mammals
World = 4,260
Thailand = 282

Fungi
World = 80,000
(Expected No. = 1,500,000)
Thailand = 6,000
(Expected No. = 150,000)

Other microbes
World = 84,000
(Expected No. = 1,600,000)
Thailand = 300
(Expected No. = 100,000)

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Diverse habitats

7-10% world biodiversity

Junction between Himalayas and Malayan peninsular

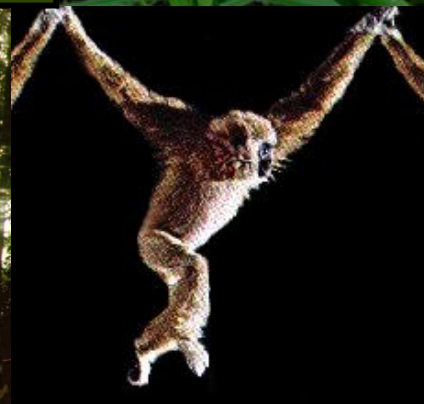




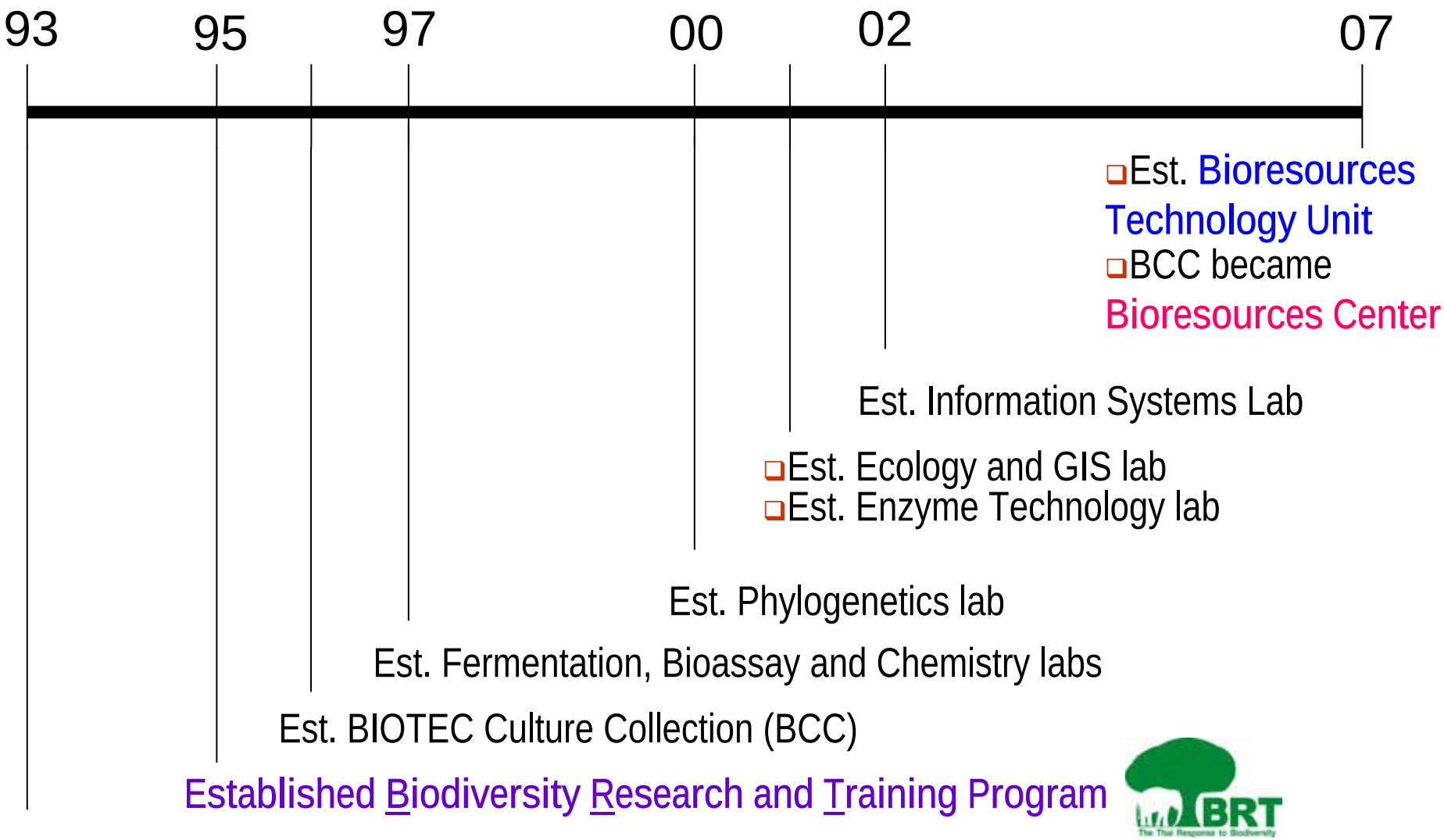
No resources,
no research







Timeline of BIOTEC Biological Resources Research Program



BCC
BIOTEC Culture Collection

SEARCH QUICK ORDER CART

- About BCC
- Deposit of Strains
  - For Public Access
  - Safe Deposit
  - Patent Deposit
- BCC Services
  - BCC Cultures
  - Culture Preservation
  - Purification and Identification
  - Training
- On-line Catalogue
  - Bacteria
  - Fungi
  - Yeasts
  - All Cultures
- Research
- Download Forms
- Contact Us
- Disclaimer

About BCC

BIOTEC Culture Collection

BIOTEC Culture Collection (BCC) was established in 1996 at the National Center for Genetic Engineering and Biotechnology (BIOTEC), National Science and Technology Development Agency (NSTDA) to support the national biodiversity policy in conservation and sustainable use of microbial resources in Thailand. The principle practice of the collection is to preserve and collect microbial cultures isolated in Thailand and the accompanying data in a standard system.

Currently, BCC holds over 16,000 microbial isolates, majority of which is fungal samples isolated from insects, decayed wood, plant seeds, fresh water, soil and leaf litter, lichen, and alkaline sources. Almost all strains in the collection are cryopreserved at –80°C waiting for screening of bioactive compounds and enzymes. Freeze-drying or storage over liquid nitrogen vapor is used for safe, for strains with special characteristics such as those that produce bioactive compounds, and for safe deposit strains. Duplicate collection of safe deposit strains and strains with special characteristics is held at a different location.

Strain data as well as data regarding storage and supply of cultures are recorded in computers using a program called Microbial Information Management System (MIMS) developed by BIOTEC staff. The program allows rapid searching and retrieving of information relating to the cultures BCC holds.

BIOTEC

BIOTEC Bangkok Herbarium (BBH)

Address:
BIOTEC Bangkok Herbarium,
113 Thailand Science Park,
Paholyothin Road,
Klong 1, Klong Luang,
Pathumthani 12120, Thailand

Tel: 662-5646666-94 **ext.** 3700
Fax: 662-5646707
E-mail: herbarium@biotec.or.th or

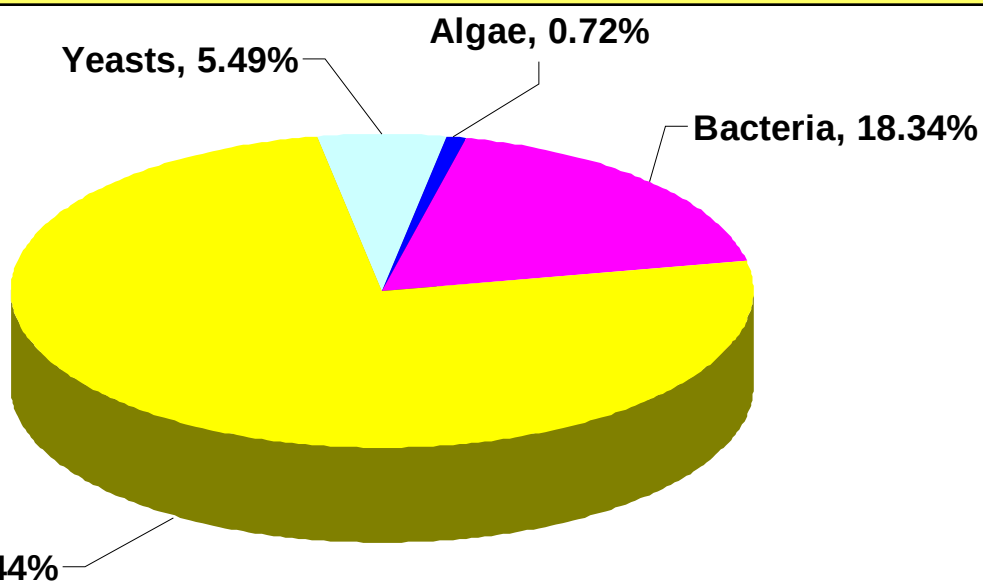
http://www.biotec.or.th/bbh/

The BIOTEC Bangkok Herbarium (BBH) was established in 1999 and is registered with the New York Botanical Garden (NYBG)

BIOTEC

Number of microorganisms preserved at BCC (as of DEC 2007)

Type	Total
Algae	201
Bacteria	5,091
Fungi	20,939
Yeasts	1,524
Total	27,755



BIOTEC

Marine and Mangrove Fungi

Seed and Leaf-litter Fungi

Freshwater Fungi

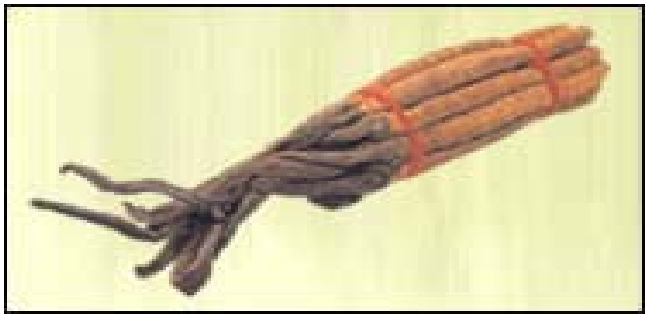
Basidiomycota

BIOTEC
a member of NSTDA

Insect (Entomo) Pathogenic Fungi

NSTDA

PRODUCTS

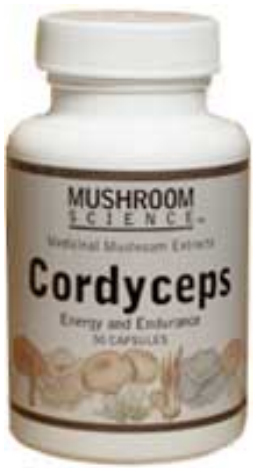


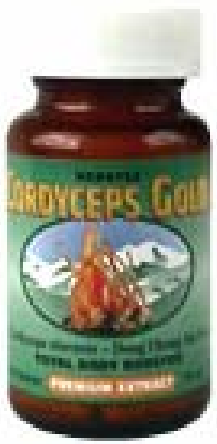
Cordyceps sinensis Extract

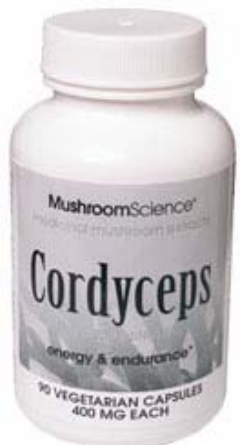
For Energy and Endurance

"You Could Feel Like a Champion in 30 Days"

"Discover how you can improve your Stamina and Endurance with the natural source for energy in Cordyceps."







What is an insect (pathogenic) fungus ?

Cuticle invasion → Infection → Mycelium → Producing metabolites

Parasite
(insect's remain = source of food)

- To inhibit insect's immune system
- To act as antibiotic (against competing microorganisms)
- To modify insect's behavior

Cordyceps unilateralis on ants

BIORESOURCE SCREENING PROGRAM (ADDED VALUE)

Culture Collection

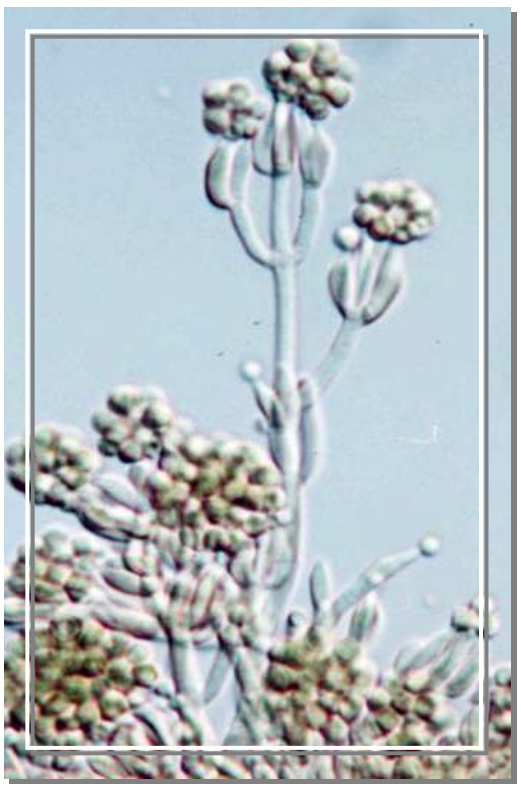
Fermentation

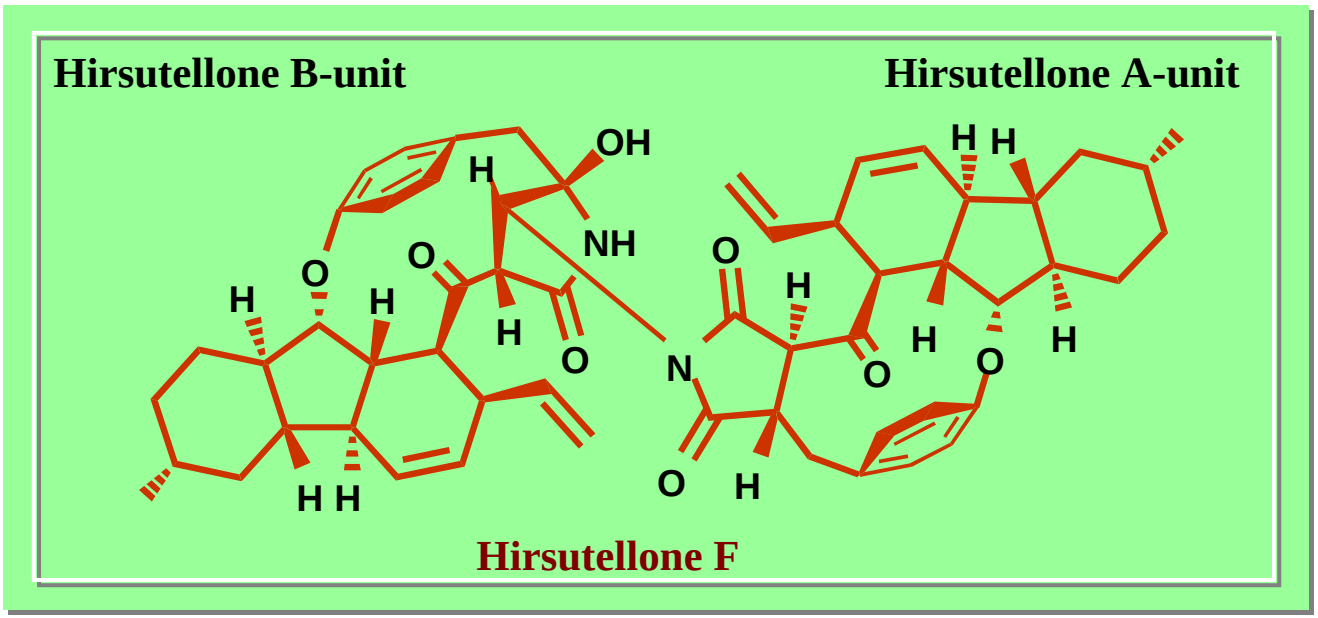
Bioassay

Bioorganic Chemistry

Hirsutellone F from *Trichoderma gelatinosum* (BCC 7579)

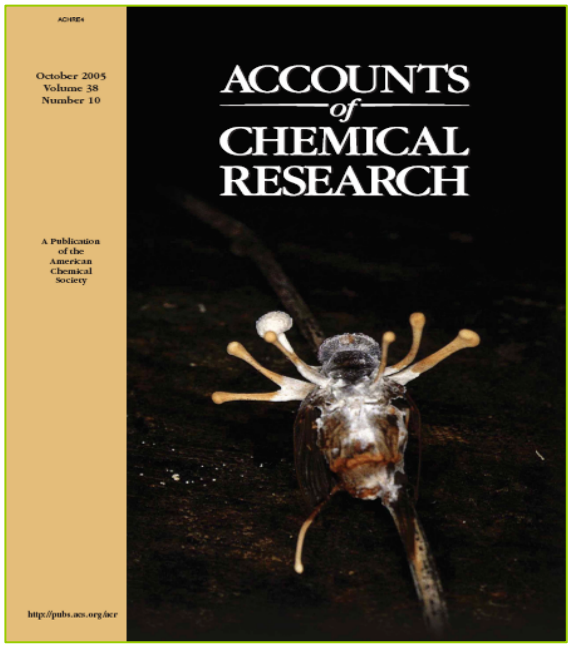
- Isolated from seed of *Entada persetha* ฝักสะบ้า
- Novel compound: Hirsutellone F
- Anti-mycobacteria (MIC 3.12 microgram/ml)
- Anti-malaria (IC_{50} 4.2 microgram/ml.)





Isaka, M., W. Prathumpai, P. Wongsa & M. Tanticharoen. 2006. Hirsutellone F, a dimer of antitubercular alkaloids from the seed fungus *Trichoderma* species BCC 7579. Organic Letters 8(13): 2815-2817.

Significant Publications



- In search of cycloxygenase inhibitors, *anti-Mycobacterium tuberculosis* and anti-malarial drugs from Thai flora and microbes.

Pharmacology and Therapeutics 2007; 115: 307-351.

Miraikan

BIOTEC

National Museum of Emerging Science and Innovation, Japan (Miraikan) used content from BIOTEC's research on bioactive substances from Thai insect pathogenic fungi for an exhibition entitled "Science News! from Asia - Power of Asia, Power of Science" on 2 June - 2 September, 2007

Screening for compounds against insect pest and plant pathogen

Evaluating fungal extracts first in insect cell lines

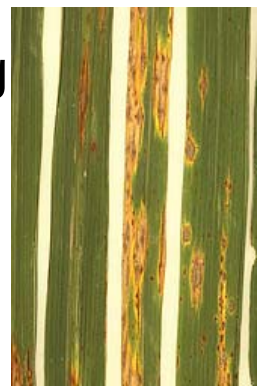
Se. = *Spodoptera exigua*
Sf9 = *Spodoptera frugiperda* pupal ovarian tissue cell line
C6/36 = Mosquito larvae, *Aedes albopictus* cell line

in vivo testing

1. *Myzus persicae* (aphid)
2. *Bemisia tabaci* (white fly)
3. *Thrips palmi* (thrips)
4. *Spodoptera exigua*

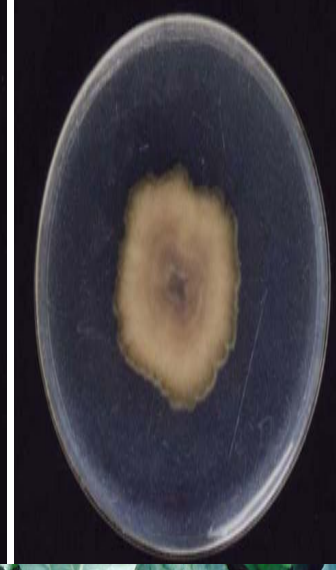
Plant pathogens

Magnaporthe grisea causing rice blast disease

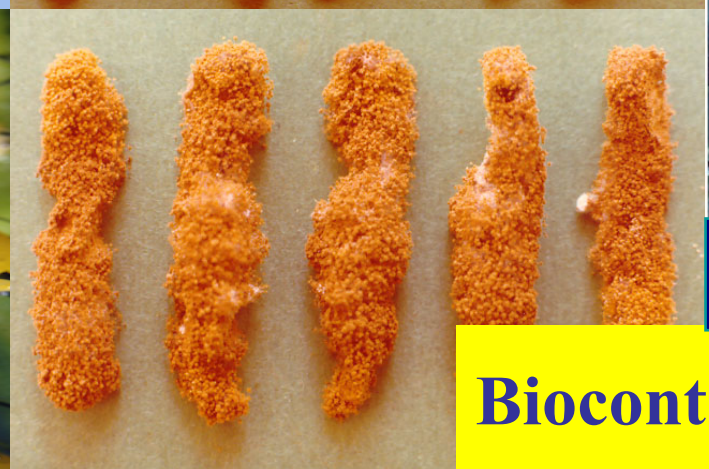


Curvularia lunata causing dirty panicle disease in rice and sorghum, and leaf spot disease in gladiolus



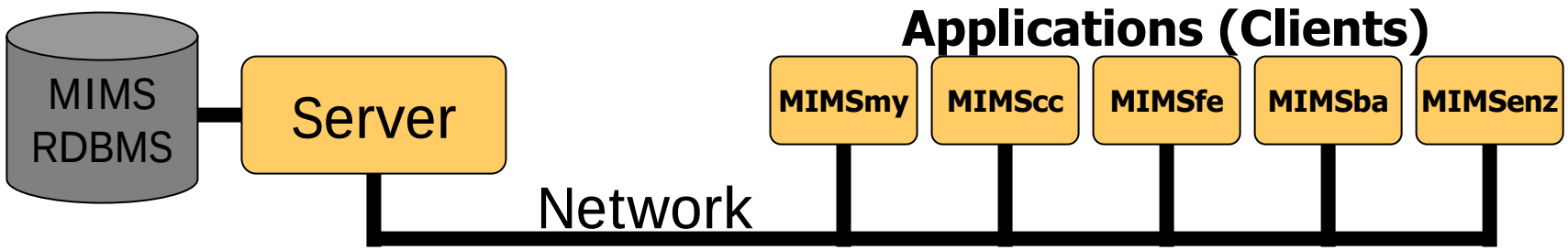



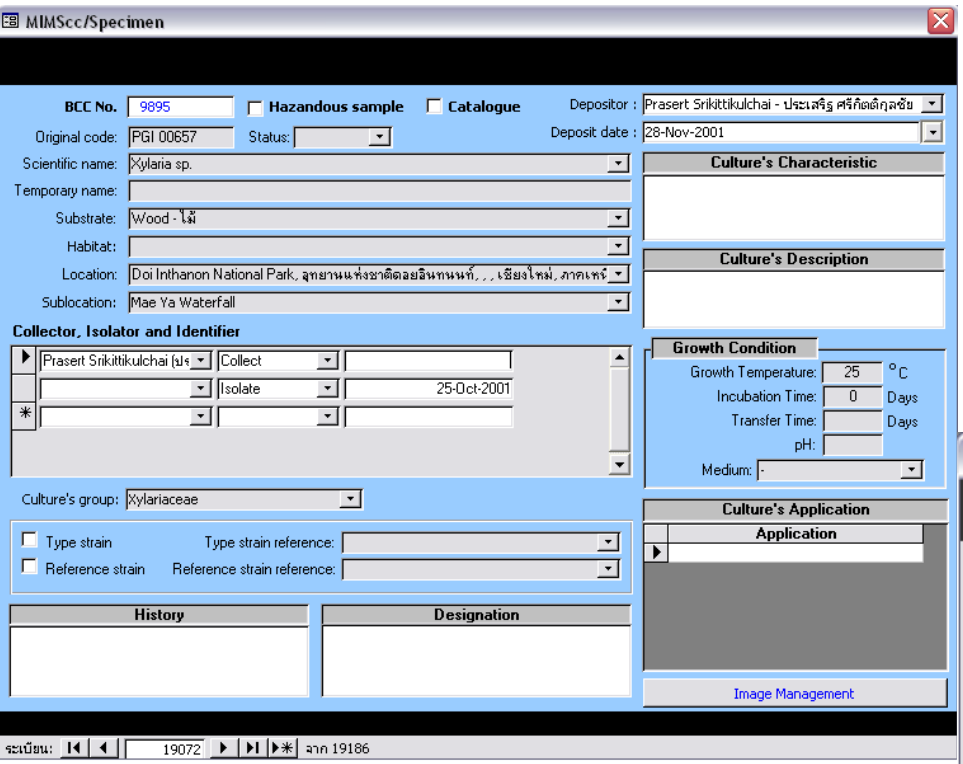


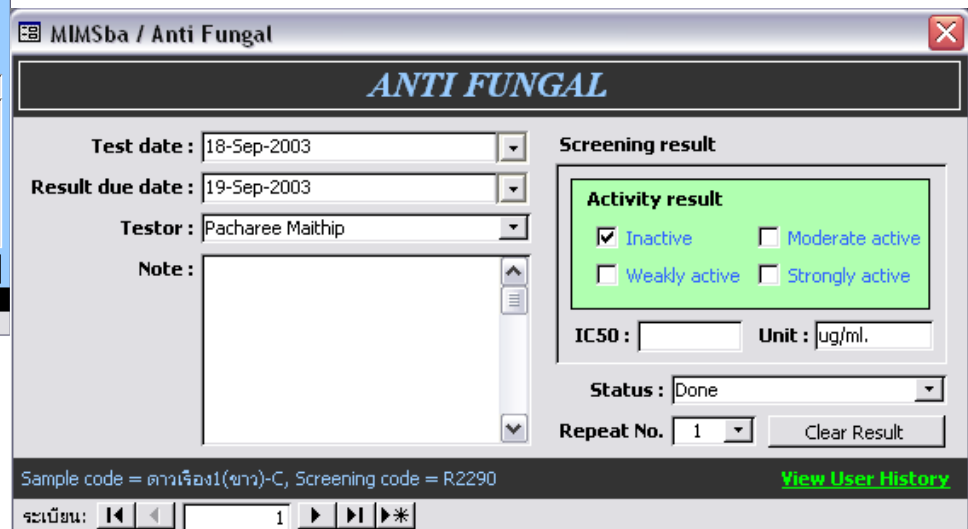


Biocontrol/Biopesticides

Microbial Information Management System





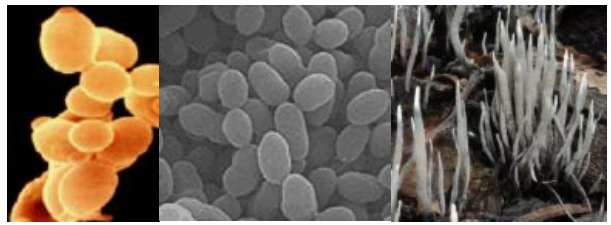


BIOTEC

Department of Biotechnology, National Institute of Technology and Evaluation (DOB-NITE)

BIOTEC-NITE MOU Signing, Feb 2005

Workshop in Thailand Oct 2004



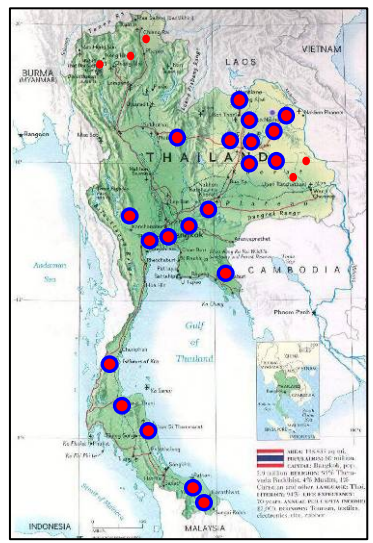
Joint research on taxonomy of acetic acid bacteria, xylaria and yeast, 2005-2008

Joint publications

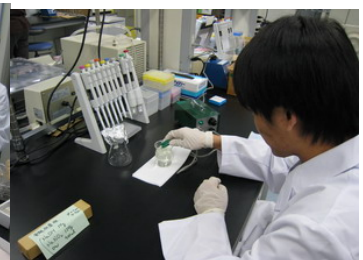
Joint publication

1. Yukphan, P., T. Malimas, M. Takahashi, M. Kaneyasu, W. Potacharoen, S. Tanasupawat, Y. Nakagawa, M. Tanticharoen and Y. Yamada. **2006. Identification of strains assigned to the genus *Asaia* Yamada et al. 2000 based on 16S rDNA restriction analysis**. J. Gen. Appl. Microbiol. Vol. 52 (4): 241-247.
2. Takahashi, M., P. Yukphan, Y. Yamada, K. Suzuki, T. Sakane and Y. Nakagawa. **2006. Intrageneric structure of the genus *Gluconobacter* analyzed by the 16S rRNA gene and 16S-23S rRNA gene internal transcribed spacer sequences**. J. Gen. Appl. Microbiol. Vol. 52 (3): 187-193
3. Malimas, T., P. Yukphan, M. Takahashi, W. Potacharoen, S. Tanasupawat, Y. Nakagawa, M. Tanticharoen and Y. Yamada. **2006. Heterogeneity of Strains Assigned to *Gluconobacter frateurii* Mason and Claus 1989 Based on Restriction Analysis of 16S-23S rDNA Internal Transcribed Spacer Regions. Biosci. Biotechnol. Biochem**. Vol. 70 (3): 684-690.
4. Yukphan P., T. Malimas, Y. Muramatsu, M. Takahashi, M. Kaneyasu, W. Potacharoen, S. Tanasupawat, Y. Nakagawa, K. Suzuki, M. Tanticharoen and Y. Yamada. ***Ameyamaea chiangmaiensis* gen. nov., sp. nov., a polar-flagellated and acetate-oxidizing acetic acid bacterium in the *α-Proteobacteria***. Int. J. Syst. Evol. Microbiol. (submitted)
5. Yukphan P., T. Malimas, Y. Muramatsu, M. Takahashi, M. Kaneyasu, S. Tanasupawat, Y. Nakagawa, K. Suzuki, W. Potacharoen and Y. Yamada. ***Tanticharoenia sakaeratensis* gen. nov., sp. nov., a new osmotolerant acetic acid bacterium in the *α-Proteobacteria***. J. Gen. Appl. Microbiol. (submitted)

More isolates, new species found



HRD through exchange of researchers and experts



BIOTEC

Vinh University, Vietnam

MOU Signing, Oct 2006

Joint research & HRD on insect fungi, July 2007-2009

BIOTEC organized the Training Course for 27 lecturers and technicians from Vinh University, Oct 2006

Institute of Tropical Biology, Vietnam

MOU Signing , July 2005

Joint research & HRD on insect fungi, 2006-2007

Starter culture for fermented meat

Nham Biotech Co. Ltd.

Vicchi Consolidate Co. Ltd.

BIOTEC

Paecilomyces lilacinus

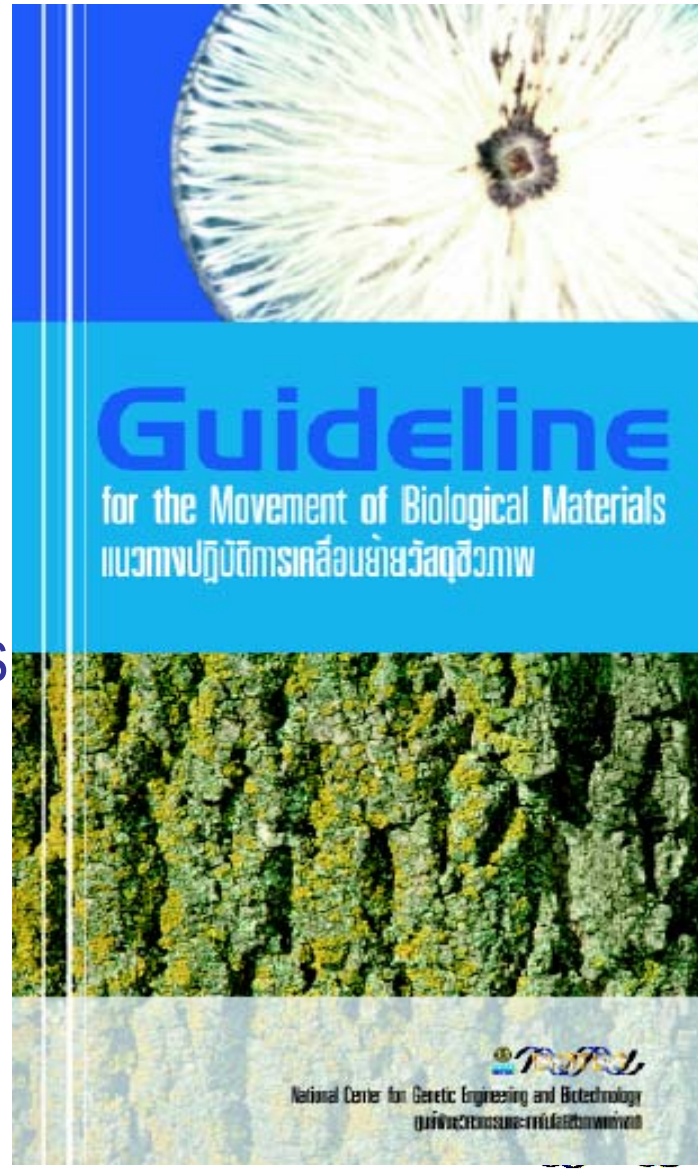
Access to Biomaterials vs Benefit Sharing

- **Biodiversity vs biotechnology**
- **IP vs local rights**
- **Collaboration and partnership**
- **Sharing benefits, values of genetic resources, institutional arrangements, Capacity building**
- **Monetary vs non-monetary**

BIOTEC

Bioresources management at BIOTEC

- Established Dept. of Business Development and BioLaw (IP lawyers and techno/business analysis personnel)
- Developed Material Acquisition Agreements (MAA)
- Developed Material Transfer Agreements (MTA)
- Guidelines for Movement of Biological Materials



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Bioresources management at BIOTEC

BIOTEC Guidelines

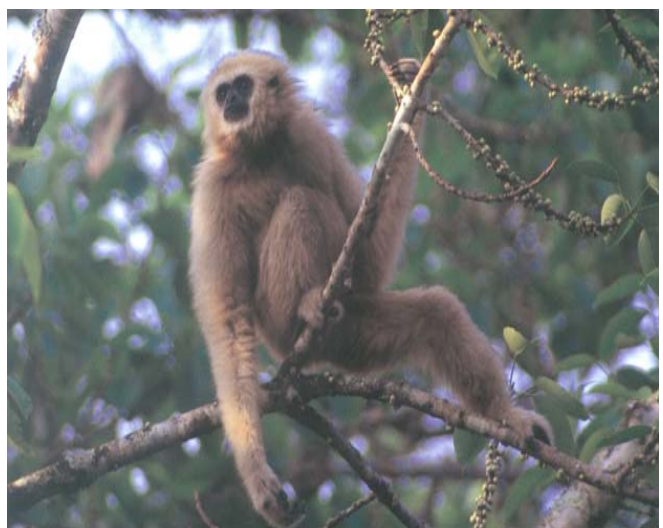
- All access to biological material must comply with all applicable laws and regulations
- Imported microbial resources should be deposited at BCC (BIOTEC Culture Collection)
- Transfer of biological material from BIOTEC must be accompanied with a MTA

NUTRITIONAL DIETS OR MEDICINAL PURPOSES

CONSUMED A SMALL PORTION OF THE FRUIT/BARK

COMSUMED ONLY FEW SPECIES

CERTAIN TIME: BREEDING SEASON OR SICKNESS



BIOTEC

International Cooperation

Background of the collaboration with NOVARTIS

The President of Switzerland and CEO of NOVARTIS came to Thailand and invited the Minister of Science and Technology to visit NOVARTIS

June 04 BIOTEC's Director visited NOVARTIS in Basel with the Thai Minister of Science and Technology

Sept 04 Novartis team visited BIOTEC at Science Park

Jan 05 First draft of proposed Term Sheet for a cooperation agreement between BIOTEC and NOVARTIS

March 05 Finalizing the Term Sheet

BIOTEC

Background of the collaboration

31 March 2005 MOU signing and press conference

BIOTEC

Aims clearly established from the beginning

From BIOTEC, NOVARTIS was interested in:

-Microorganisms to be evaluated in drug screening program at NOVARTIS

-Pure characterized compounds from BIOTEC's library and newly characterized compounds that are novel

Service fees and milestone payments were agreed upon

What BIOTEC was searching for:

-***Enhance capability*** of bioresource utilization to the next level by partnering with an experienced organization in drug discovery and development

-***Capacity building*** of its human resources

BIOTEC

MODE OF OPERATION: EQUAL PARTNERSHIP

A joint steering committee between BIOTEC and NOVARTIS has been established.

The committee consists of an equal number of members from both sides.

The committee has two co-chairpersons from BIOTEC and NOVARTIS.

The committee meets every 6 months

BIOTEC

Capacity building through training

During the 3-year collaboration period, NOVARTIS provides 9 training slots of 3 months each at NOVARTIS labs

Five have completed training (4 PhDs, 1 MSc)



Chemistry lab

Screening lab

Microbiol lab

BIOTEC

Post-training activities at BIOTEC:

- Modified existing assays to increase performance/ throughput
- Introduced assay quality assessment and validation to the process of assay development
- Set up a microbial extract management system (enable sample tracking & liquid handling automation)
- Set up a chemical screening system using automated HPLC
- Acquired and installed an HPLC-MS-MS as part of a chemical screening system

BIOTEC

Capacity building through training

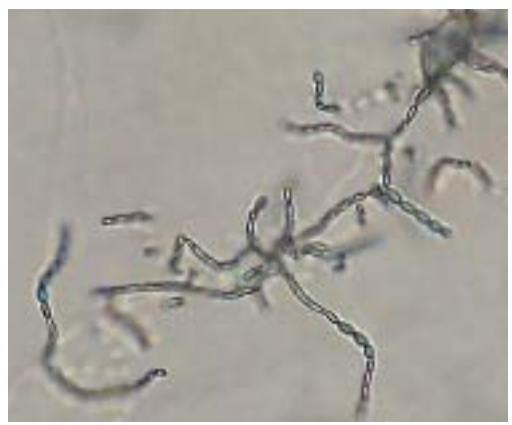
A microbiology expert traveled to Thailand for two short training periods

Objective: Develop isolation and identification skills of Thai scientists

Strengthening capacity of BIOTEC

Improved diversity of the BIOTEC Culture Collection by adding a new group of microbes, Actinomycetes

- ☑ Over 2,000 Actinomycetes from 25 genera were isolated from Thailand
- ☑ Twenty seven isolates are likely to belong to new species or new genera
- ☑ A manuscript describing a new species was generated



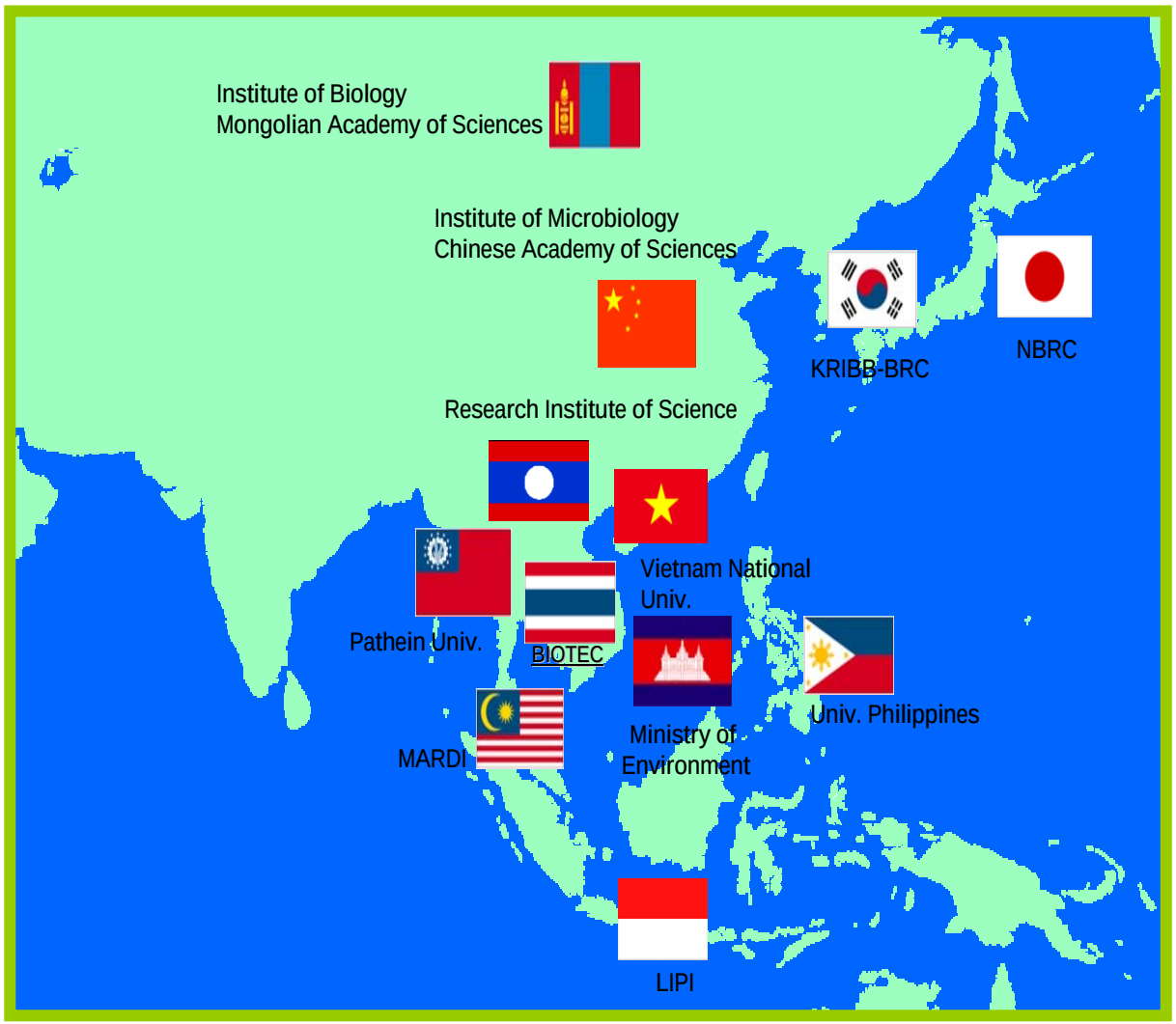
BIOTEC

Additional benefits

- NOVARTIS expert was invited to BIOTEC three more times. Currently he is in Thailand for 1 month to run a 2-week workshop on experimental design

- An MSc staff is enrolling in a PhD program in Thailand with the expert from NOVARTIS as a co-advisor

Asian Consortium for the Conservation and Sustainable Use of Microbial Resources (ACM)



12 member countries: Cambodia, China, Indonesia, Japan, Korea, Laos, Malaysia, Mongolia, Myanmar, Philippines, Thailand, and Vietnam

ACM commenced in 2004

BIOTEC

Aims of ACM

- Framework for international cooperation to encourage microbiological research projects
- Development of microbial resources characteristic of each country
- Construction of mechanisms for academia and industry to utilize microbial resources
- Establishment of a BRC network
- Establishment of international standards for biological material transfers and benefit-sharing
- Improvement and sharing of standardized techniques

Activities of ACM

Action plan

- Annual meeting
- Information exchange through seminars and workshops
- Promotion for public acceptance and social infrastructure

Task Forces

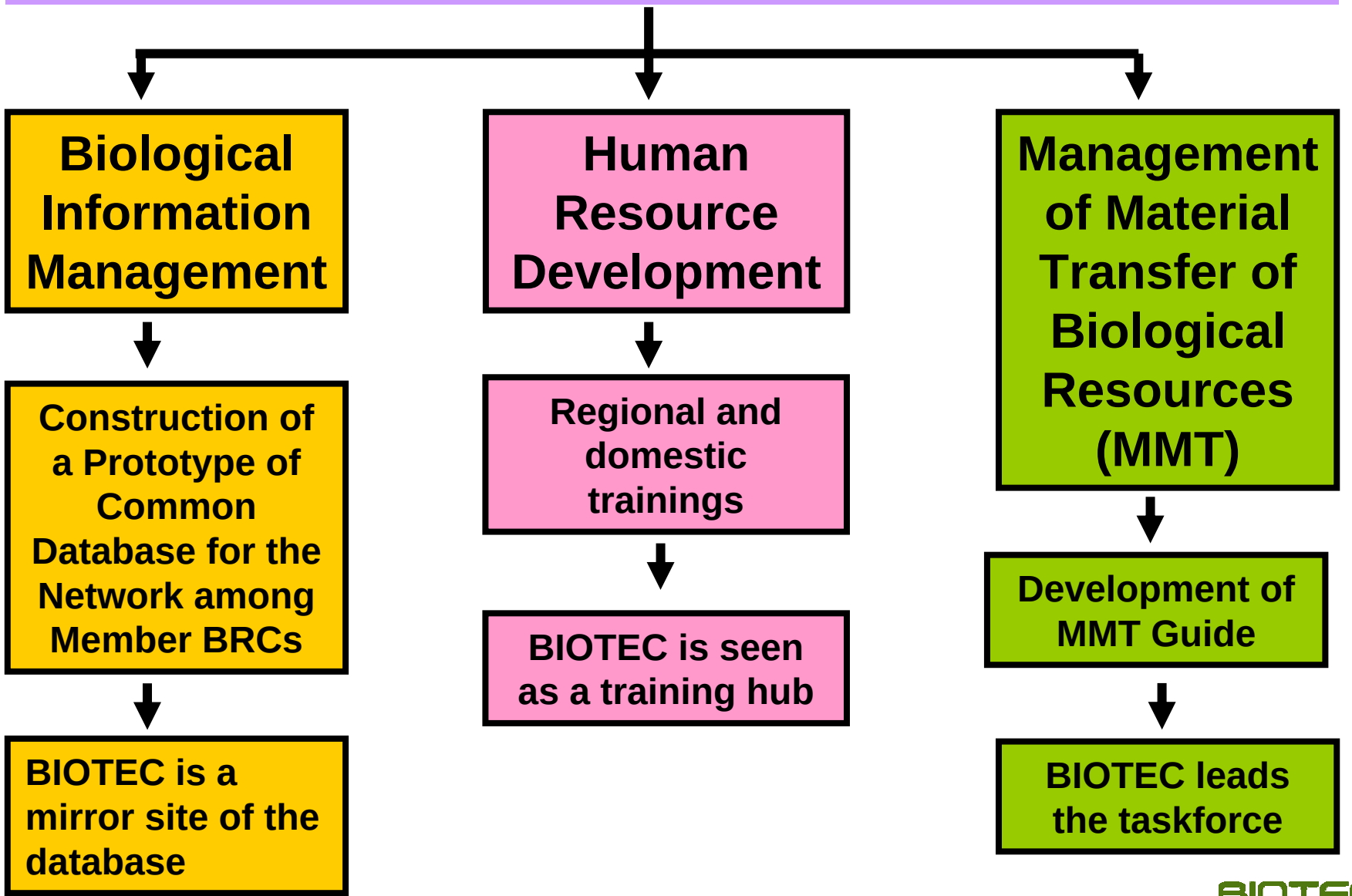
Biological Information Management
Chair: Dr. Ken-ichiro Suzuki (NBRC, Japan)

Human Resource Development
Chair: Prof. Indrawati Gandjar (University of Indonesia)

Management of Material Transfer (MMT)
Chair: Dr. Tanit Changthavorn (BIOTEC, Thailand)

BIOTEC

BIOTEC's roles in the Taskforces



CAPACITY BUILDING program for neighboring countries

Establishment of Regional Training Center in Biotechnology

- **Launched in 2004 as a result of the UNESCO Consultative Meeting on the Establishment of a Regional Training Center in Biotechnology**
- **Attract partners to support and co-organize training workshops, short courses, research training, scientific conferences, etc.**

BIOTEC

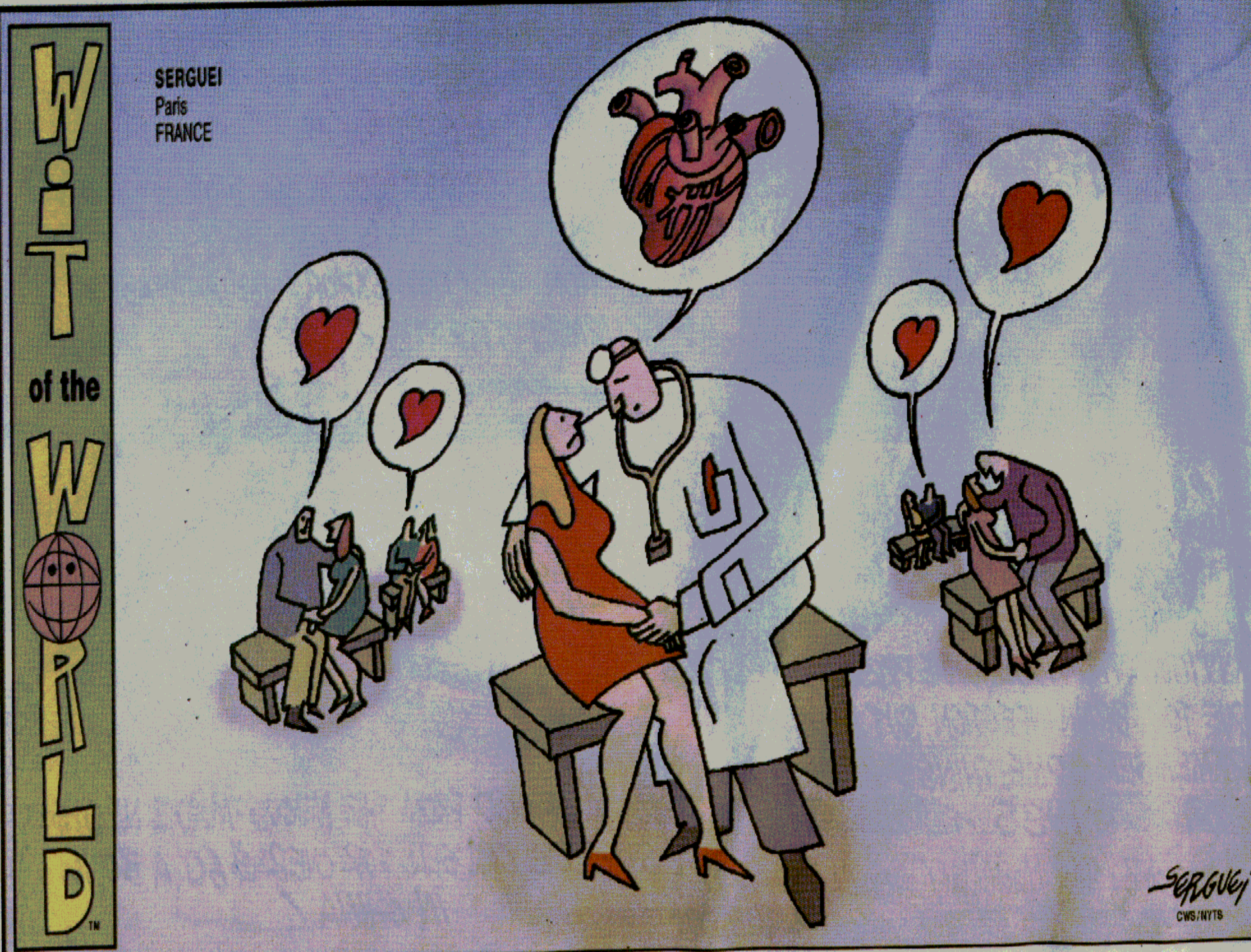
HRD Program for Neighboring Countries

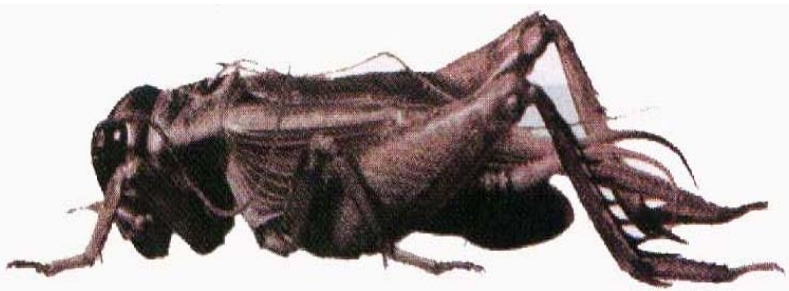
- Short and medium-term training at BIOTEC laboratories (3-12 months)

- Operating since 2001, targeting Cambodia, Laos, Myanmar and Vietnam. Pacific Islands were added in 2005 with special funding from the New Zealand Gov.

Lessons learned through collaboration

- Start building-up research capability before entering into negotiations
- Set-up realistic and clear expectations from the beginning
- Set-up both short and long-term benefit returns in various forms
- Aim for capacity building *via* training and technology transfer, which are more valuable than monetary compensation
- Honor the agreements and collaborate in good faith
- Build-up trusting relationships among parties



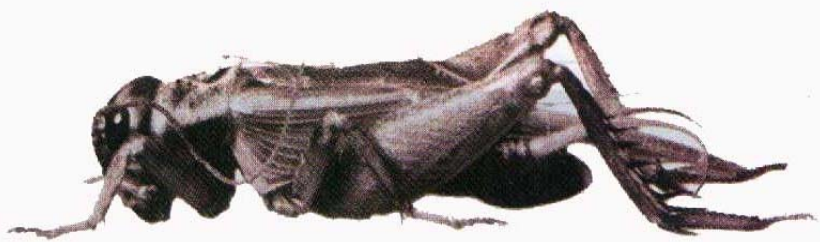


USA

Pest

CHINA

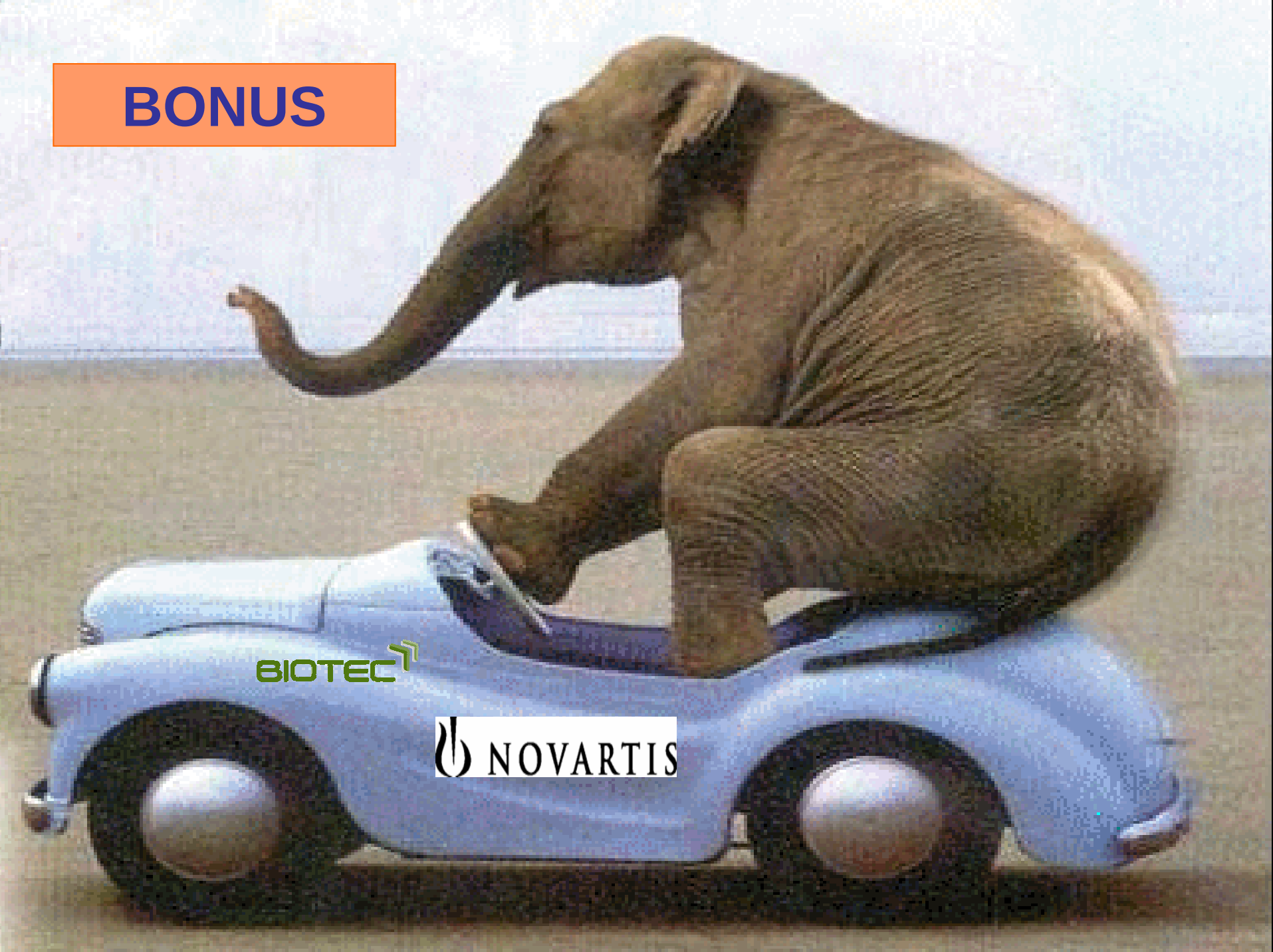
Pet



NORTHERN THAILAND

Appetiser

BONUS



Thank You

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