WIPO IGC on IP and GR, TK & Folklore
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Regulatory Environment for Access to Genetic Resources and Benefit Sharing in Brazil: Role of a Local Company dealing in Research, Development and Innovation

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EXTRACTA
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BIODIVERSITY-RICH REGIONS IN BRAZIL

- Brazil holds 22% of the Global Plant Biodiversity
- >60.000 Species of Vascular Plants

Under 1500 plant species are documented by Brazilian Traditional Medicine (W.B.Mors et al, 2000). Could modern bioresearch and biotechnologies add significantly to potential pharmaceutical value?

CBD REGULATORY BACKGROUND IN BRAZIL

- CBD established National Control over Biodiversity (1992)
- 1999 EXTRACTA-GLAXOWELLCOME Contract preceded and influenced regulatory legislation
- Bonn Protocol (2001) proposed National Focal Points as Mediators for ABS
- Stern Regulatory Legislation in Year 2000-1 institutes the Management Council for Genetic Resources (CGEN) at the Ministry of the Environment (MMA), as the primary Government Regulatory Body for ABS and TK in Brazil
- 2001 Regulation states that:
  - Accreditation and GR Access Licenses are granted to National Entities only (Research Institutions and Companies duly registered in Brazil).
  - Landholder Informed Consent prior to GR Access: the Option for Private Possession of Biodiversity
  - ABS is Negotiated between Interested Parties with Contracts Registered by CGEN
  - IP applications dealing with GR and TK must declare legal origin
- EXTRACTA : first Private Company accredited by CGEN (2004-present)

EXTRACTA

AN ABS CONTRACTUAL STRUCTURE IN BRAZIL

Public Herbarium (Goeldi Museum)

Collectors

Landholder
Conserves and Grants Access to Biodiversity

Landholder – Extracta Access Contracts with Promise of Future Return of Benefits

EXTRACTA (Licensed by CGEN) And UFPA

R&D Contracts

Academia

Partnerships in R&D&I

Patents

INDUSTRY

CURB – Contract of Usage and Return of Benefits

- **EXTRACTA (represents Land & IP Holders)**
- **Industrial Client**

THE GLAXO-EXTRACTA MODEL CONTRACT (1999)

- GW pays the cost of HTS screening of EXTRACTA Bank of Chemical Biodiversity for Hits against selected targets.
- EXTRACTA is fully responsible for Access, Bioprospection, Invention and keeps 100% of IP over its products.
- GW has first refusal rights to license EXTRACTA candidate compounds with global marketing rights.
- GW carries on subsequent financial burden (IP, development, Licensing and Commercialization), against up to 3% of global sales in royalties (maximum when Natural Molecule reaches the market.
- EXTRACTA is fully responsible before Brazilian legislation, including ABS rights.

ASSEMBLING THE SCREENING COLLECTION

THE EXTRACTA BANK OF CHEMICAL BIODIVERSITY

- 215 Expeditions covered ~10,000 km^2 of Atlantic and Amazon Rainforests during 1999-2010.

- 4,905 Plants were collected under rigorous control (GPS, local Digital Photos, Herbarium Samples). Extraction samples from plant parts average 2.5kg, a small impact on Natural Resources.

- 11,586 TLC-controlled etanolic extracts yielded 31,492 chemical samples for HTS screening campaigns against targets of interest.

- A unified data base controls the Bank and screening results (proprietary software).

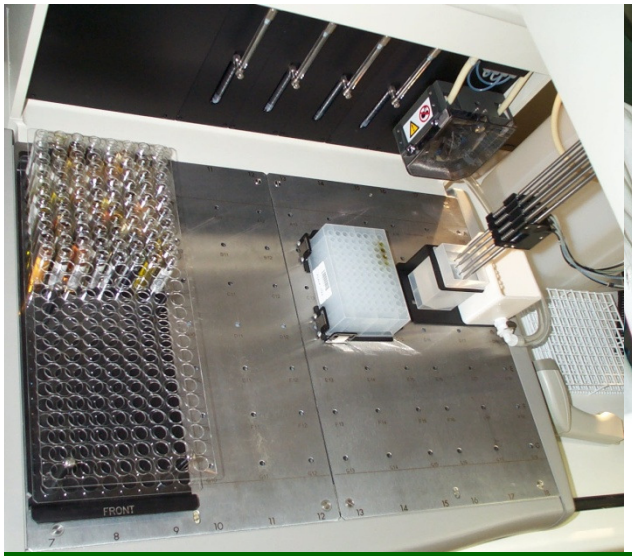
EXTRACTION CENTERS AT RIO DE JANEIRO & BELÉM

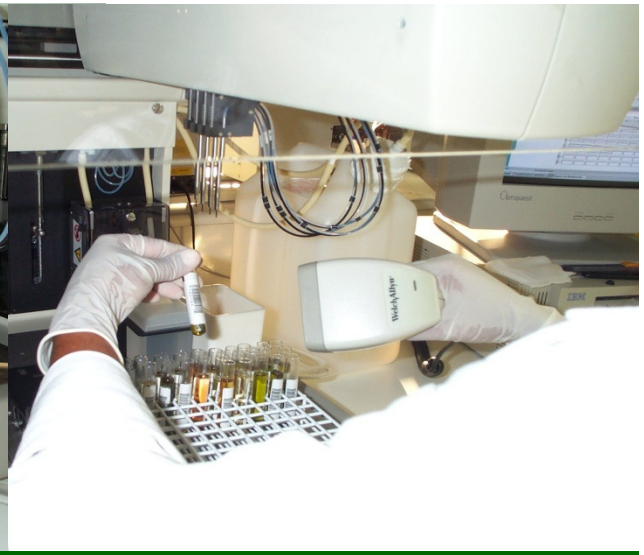
Extraction Facilities can process up to 15.000 extracts per year

Extracts are stored at – 30 °C until use in R&D

TARGETTING BIOACTIVITY WITH HTS SCREENING

Target Election, Bioassay Development and High Throughput Screening Strategies are Highly Inventive Steps in Drug Development





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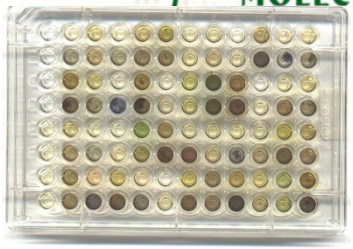
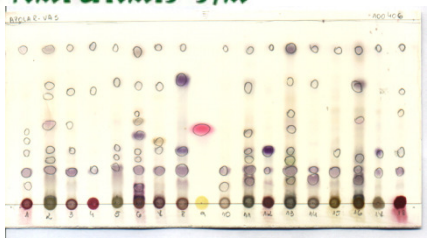
Glaxo Contract Caused EXTRACTA to Acquire Modern Technologies

Medium-High Throughput Screening at EXTRACTA: up to 24,000 operations daily

BIODIRECTED CHEMICAL FRACTIONATION OF EXTRACTS: TOWARDS THE PURE COMPOUND





1) Tannin score and removal
2) TLC quality control
3) Biodirected Extract fractionation in search of active compound

- UV-visible spectrometry and HPLC
- ***High definition LC-MS***
- ***NMR experiments***
- ***X-Ray Crystalography***

OUTSOURCED

GLAXO-EXTRACTA CONTRACT DISCONTINUED IN 2004

- ***Difficulties with ABS Regulation*** in biodiversity-rich countries and the ***Human Genome Drive*** led most Large PHARMA to revise their option for Natural Products as a source of innovation.
- GSK R&D Policy Changes after Merger led to discontinuation of EXTRACTA Contract in 2004. EXTRACTA remains with full rights to exploit results, but the absence of significant industrial partners forces company to shrink.
- EXTRACTA comes back progressively as Brazilian Governmental push for more research and innovation becomes sizeable.
- Substitute contracts with Brazilian Governmental Agencies (2007-present) provide EXTRACTA with funding to push Natural Products towards clinical trials (beginning 2011).

EXTRACTA INNOVATION PIPELINE

EXTRACTA PIPELINE: POSITIVE HITS NEED FINANCING TO RETURN BENEFITS LOCALLY

TARGET PATHOLOGY	PRIMARY BIOASSAY	Nº OF STRONGLY ACTIVE EXTRACTS	Nº OF PURIFIED ACTIVE FRACTIONS	PURE ISOLATED COMPOUNDS (95% pure)
Resistant Hospital & Community Infections	Meticillin - resistant S.Aureus (MRSA)	49	12	3
Chronic Obstructive Pulmonary Disease (COPD)	Elastase inhibition	32	18	7
Hepatitis C	Cell Protection against surrogate target	118	12	NA
Chagas Disease	Cruzipain inhibition	98	2	NA
Tuberculosis	InhA inhibition	38	13	NA
Diabetes Type II	PTP-1B inhibition	348	NA	NA
Development Candidate Extracts		*683*	*In yellow: Innovation Projects Financed by Brazilian Agencies FINEP and FAPERJ*	

FINEP

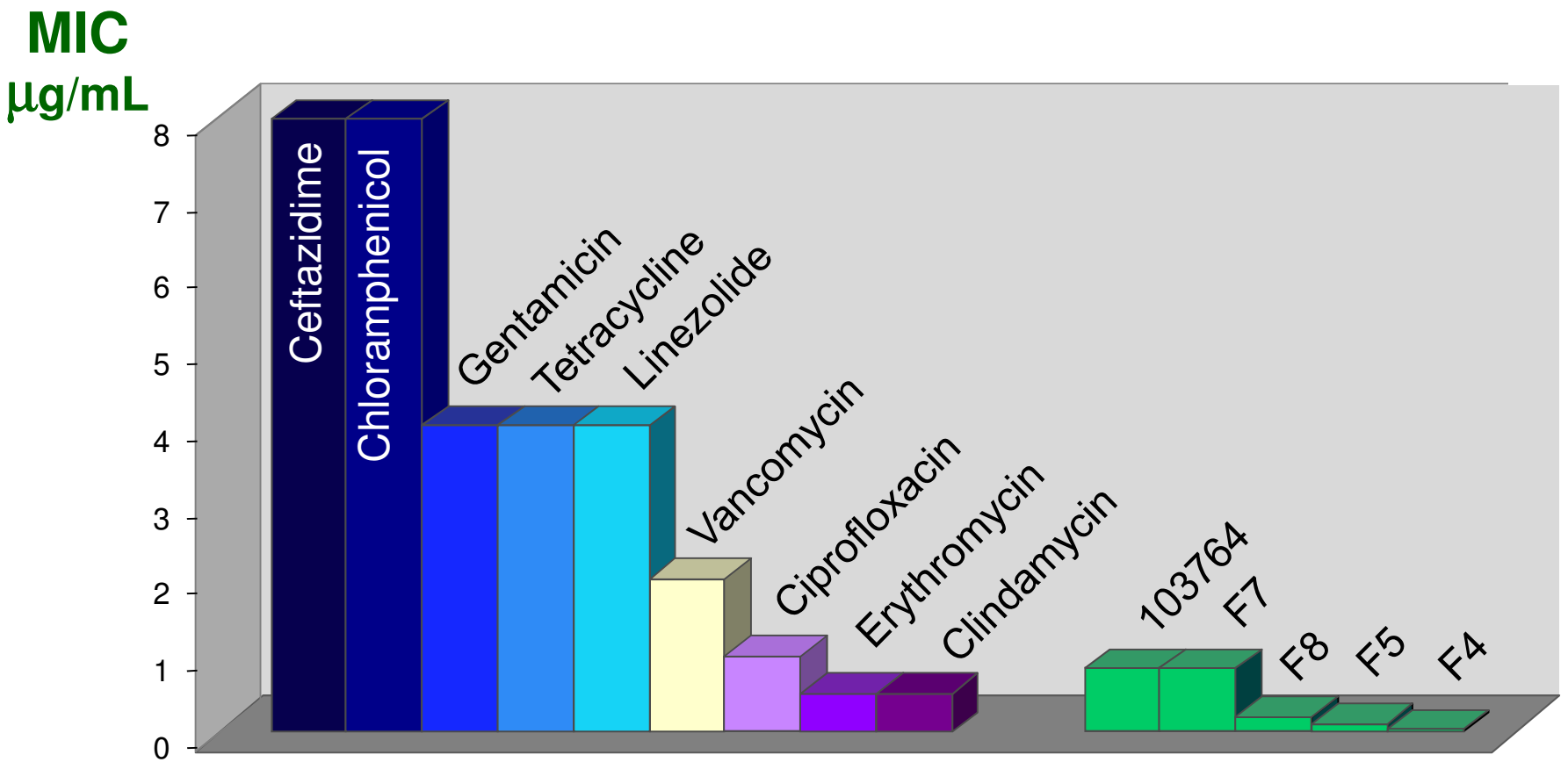
FAPERJ

ANTI-MRSA SELECTED CRUDE EXTRACTS

MIC Comparison between 3 selected Extracts and a Commercial Antibiotic against Meticillin-resistant *S. aureus*

ANTI-MRSA EXTRACTS, FRACTIONS AND PURE COMPOUNDS

MIC of Extract 103764 and its purified Fractions compared to Commercial Antibiotics



NATURAL PRODUCTS AND PHARMA: STILL OF FUNDAMENTAL INTEREST !

63% OF CONVENTIONAL SMALL MOLECULE DRUGS ARE BASED ON NATURAL PRODUCT MODELS
D.J. Newman & G.M. Cragg, *J. Nat. Prod., 2007, 70, 461-477*

ORIGIN OF 974 DRUGS IN MARKET OVER LAST 25 YEARS (1981-2006):

Natural Molecule:	6%
Natural Derivative Molecule (semisynthetic)	28%
Natural Mimics Synthetic	12%
Synthetic Using Natural Pharmacophore	5%
Synthetic Using Natural Mimics Pharmacophore	12%
Non-Biologically Originated Synthetics	37%
TOTAL	100%

WILL PHARMA BE STAGING A RETURN TO NATURE ?

PROPOSED RETURN OF BENEFITS TO THE LANDHOLDER

❑ EARLY BENEFITS

- ➢ Establishing bioactive plant identity and cloning the bioactive plant (tissue culture and other technologies)
- ➢ Engineering of Clonal Planting and Production
- ➢ Technology Transfer: Training of Extensionists and Farmhands
- ➢ Setting Production and Commercialization Goals
- ➢ Setting Fair Price Policies for Purchase of Raw Material by Industry

❑ LATE BENEFITS

- ➢ Participation in royalty sharing according to Initial Access Contract
- ➢ Participation in other returns ascertained in final CURB contract

OTHER EXTRACTA RESPONSIBILITIES

CGEN-REGISTERED CURB CONTRACT

- Business Deal with Licensee and its Registration at CGEN
- Statement of Landholders Rights
- Returning Benefits to Associated Institutions and Inventors
  - Financing Cost-Plus R&D and Advanced Personnel Training
  - IP Issues between Institutions and Inventor Employees
  - IP Issues between Public and Private IP Holders
- Other Responsibilities in the CGEN-registered CURB Contract
  - Handling of Brazilian Regulatory Issues by EXTRACTA
  - Handling of CBD-related Issues with Brazil´s Focal Point
  - Handling by EXTRACTA of Return-of-Benefits to Brazilian Parties

BRAZIL: IP PROTECTION OF GENETIC RESOURCES

BRAZIL IP PROBLEMS WITH BIOTECH AND GENETIC RESOURCES TODAY

- Patent Protection of Engineered Microorganisms only (no animal or plant cell protection, even if engineered)

- Express Prohibition of Patents for:
  - Plants and Animals, In Whole or In Part, Including Their Genome Or Germplasm (Entire or Part);
  - Any Chemical Expression of Their Genome or Germplasm, including derivatives and extracts.

BRAZIL: PROPOSED EVOLUTION OF IP FOR BIOTECH AND BIODIVESITY RESOURCES

- **Patent Protection For Any Engineered Organisms And Parts Thereof *(Important Progress).***

- **Express Prohibition Of Patents Limited To Naturally Occurring Plants And Animals, In Whole Or In Part, Including Their Genome Or Germplasm Considered as an Indivisible Entity *(Important Progress).***

- **Patent Protection For Plant And Animal Derivatives, Including Extracts, Derived Chemicals, Cell Lines And Gene Sequences, provided basic criteria for Patenting are met *(Congress Bill In Advanced Stage Of Approval).***

IN CONCLUSION…

1) Brazil and other Biodiversity-Rich countries had and still have problems with Regulatory Legislation. But almost all are successfully improving their regulatory environment to make full use of CBD mechanisms, in order to attract local and international investors to the joint sustainable exploitation of their Natural Resources.

2) Brazilian-style direct negotiation between foreign and local specialized entities (public and private) is a far more expeditious way to get business done. Local entities, within the framework of national legislation and with assistance of their Government are also the best means to internalize all types of benefit returns derived from responsible deals.