

# Commercialization of guayule latex

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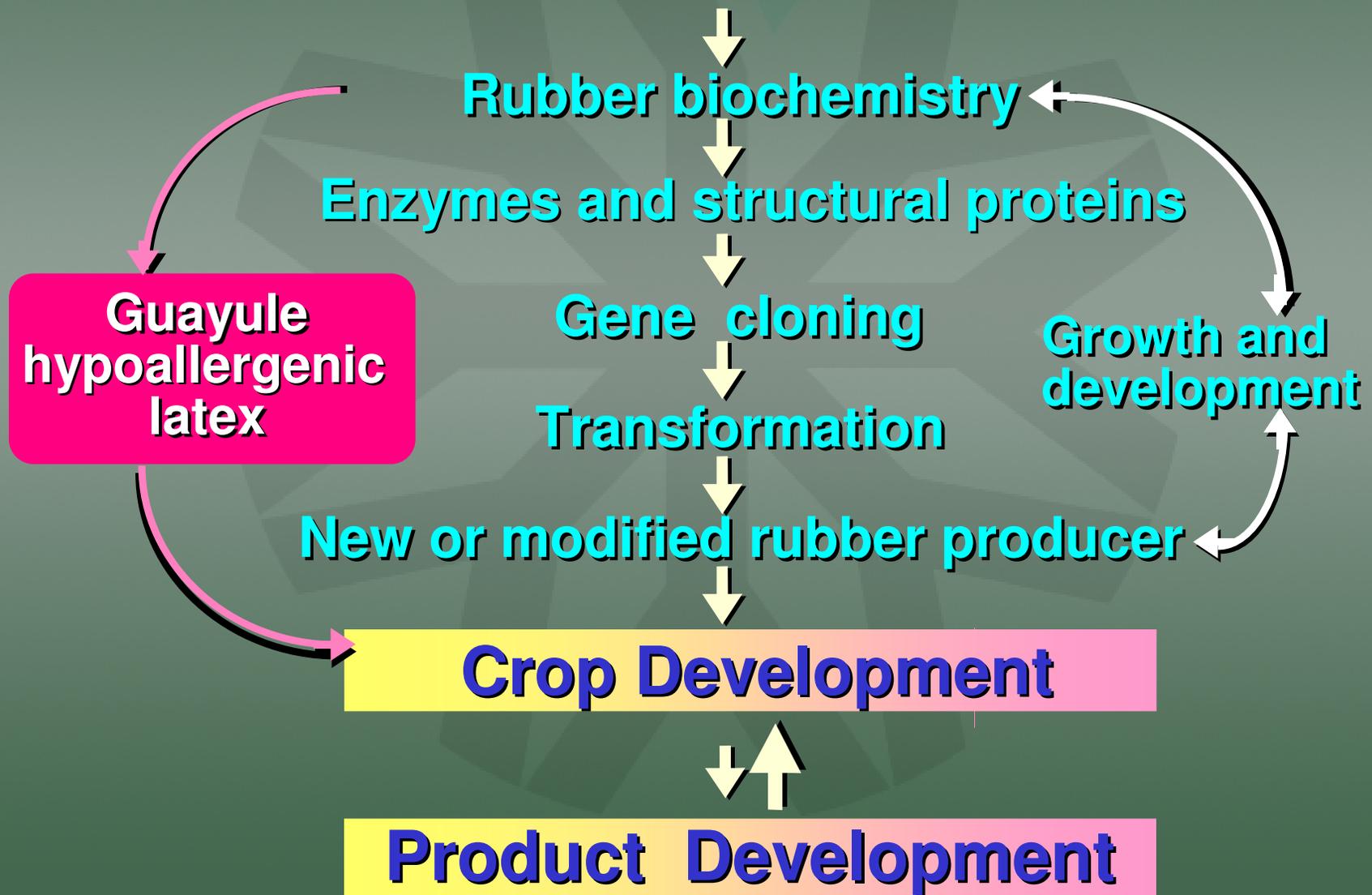
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# Why do we need Alternative Rubber Crops?

- Natural rubber (NR) is a strategic raw material vital to developed countries – **serious shortages are predicted by 2010, and 3 million tonnes per year by 2020** (International Rubber Study Group)
- The developed world is totally dependent upon NR imports from tropical countries – the U.S. consumes 14% of the world's supply (China surpassed US consumption in 2004 for the first time)
- Thailand, Malaysia and Indonesia (72% of global production) formed a cartel in 2002 to control rubber production and drive-up prices – more countries have since asked to join
- NR production is dependent upon one genetically-narrow plant species, *Hevea brasiliensis* (clones) – we need biodiversity
- A natural solution to Type I latex allergy – high performance, low protein, no cross-reaction

# The USDA Rubber Project – where it began (1989)

## Biotechnological Production of Natural Rubber



**Strategic need is only a market driver in crises...  
Emergency Rubber Project WWII**



**Tire made from guayule rubber**

**1991 - A commercial opportunity.....**



**Type I Tropical *Hevea* Latex Protein Allergy**

# Type I Tropical *Hevea* Latex Allergy Symptoms affecting up to 20 million Americans include:

IgE antibodies

Local urticaria

Systemic urticaria

Rhinitis

Conjunctivitis

**Asthma**

**Edema**

**Bronchospasm**

**Tachycardia**

**Anaphylaxis**

# Type I *Hevea* latex allergy arose because of:

Vastly increased usage of latex products in response to the AIDS epidemic (15-fold) – *Universal Precautions*

Processing shortcuts led to products high in soluble protein

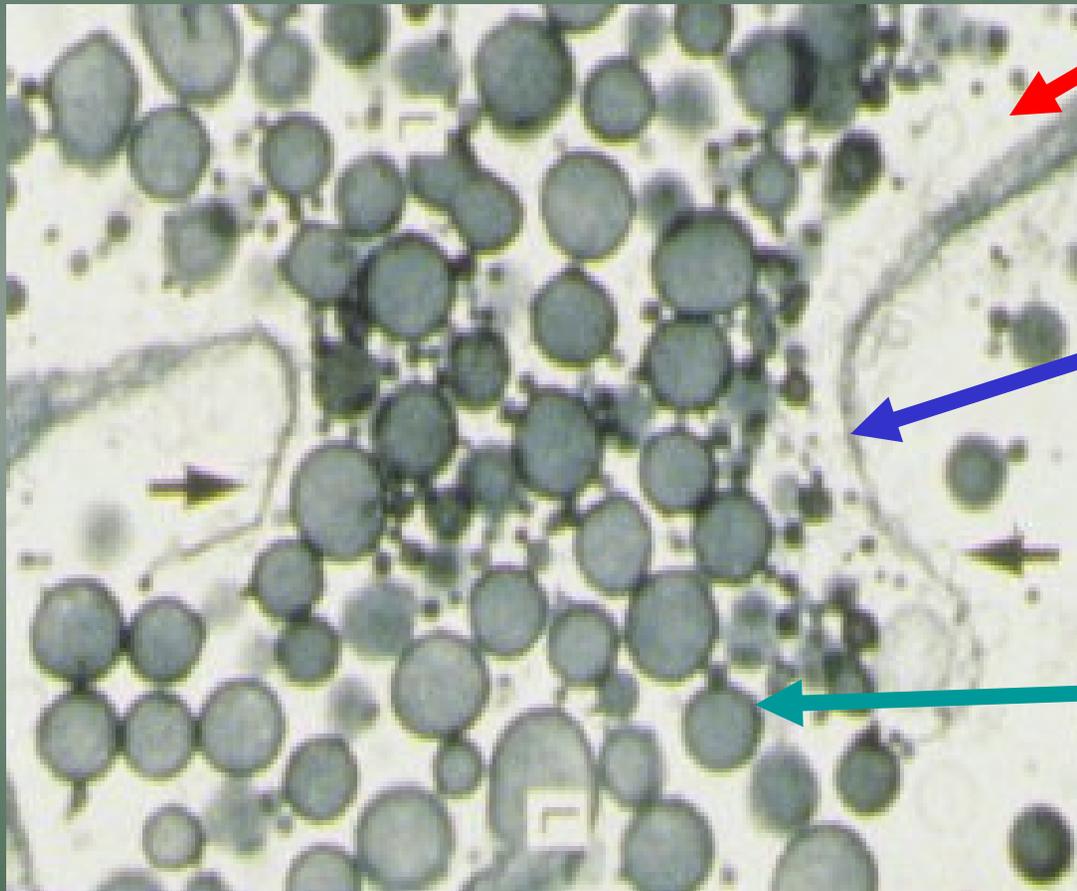
Use of “green” latex (partially-hydrolyzed) latex

Single-use powdered gloves aerosolized latex proteins

***Hevea latex* is a living cytoplasm containing rubber particles and is protein rich.**



# *Hevea Latex*



**~50-75%  
hydrophilic protein  
in the cytosol**

**~10-25%  
hydrophobic  
membrane-bound  
protein**

**~10-25%  
hydrophobic  
protein bound to  
rubber particles**

People became allergic to all protein groups

## ***Hevea Allergy Summary:***

To protect the normal folks from getting the allergy just leach the latex products properly – expensive treatments do not appear necessary

**To protect the hypersensitive use something else (natural or synthetic)**

- both scientifically and litigiously trying to use *Hevea* latex for this subpopulation seems a “don’t even go there” proposition

# How to address Type I Latex Allergy

## Circumvention?

- Use something else *i.e. avoidance*
- Synthetics
- Alternative natural rubber latex source

# PROTECTIVE GLOVE MATERIALS

**Natural rubber** - best material, elasticity, tensile strength, fit, tactility and viral protection for surgical gloves (96%) and examination gloves.

## Synthetic surgical and examination glove materials

Generally poorly elastic, with high break rates and viral penetration rates, expensive, but nonallergenic with respect to protein-mediated latex allergies

Chloroprene (Neoprene)

Synthetic *cis*-polyisoprene

Nitrile rubber

Polyurethane

Styrene-butadiene (Elastyren)

Styrene-ethylene-butadiene (Tactylon)

EMA

**ASTM standards  
were lowered to  
permit use of  
synthetics**

## **Guayule Latex**

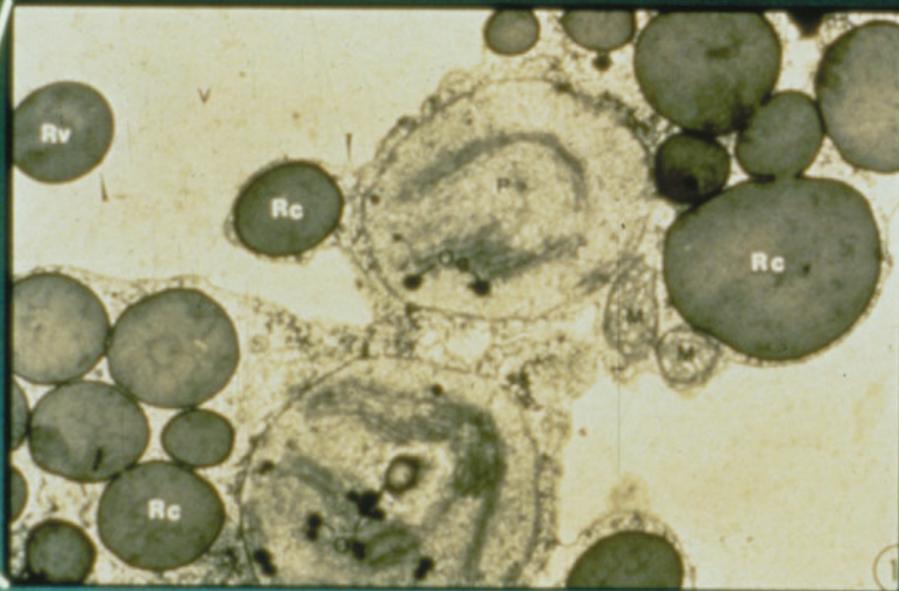
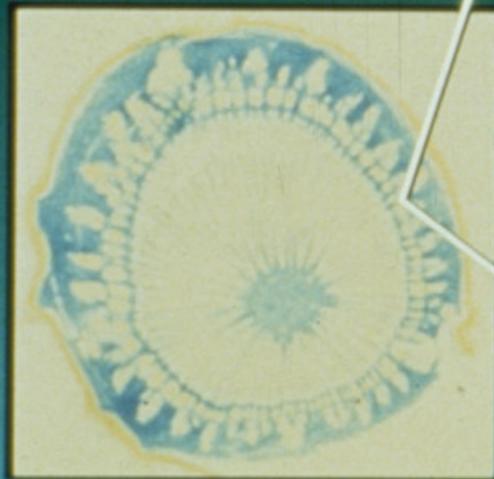
Guayule had not been considered as a source of latex because it does not make its rubber in the form of a tapable latex

However, guayule does still make its rubber in the form of rubber particles suspended in the aqueous cytosol

**Yulex® Natural Rubber Latex** is made by extracting these particles while maintaining the suspension.

# *Parthenium argentatum* Rubber Particles

Rubber particles are formed  
in parenchyma cells



*Parthenium argentatum*

# Rubber Particle Preparation



Latex Or  
Homogenate  
In Ice-Cold Buffer

Spin at 4000 xg  
10 min., 4°C



Rubber Particles  
Float into Layer

Scoop Off Layer  
and Resuspend

Spin at 3500 xg  
7 min., 4°C  
Repeat As Desired



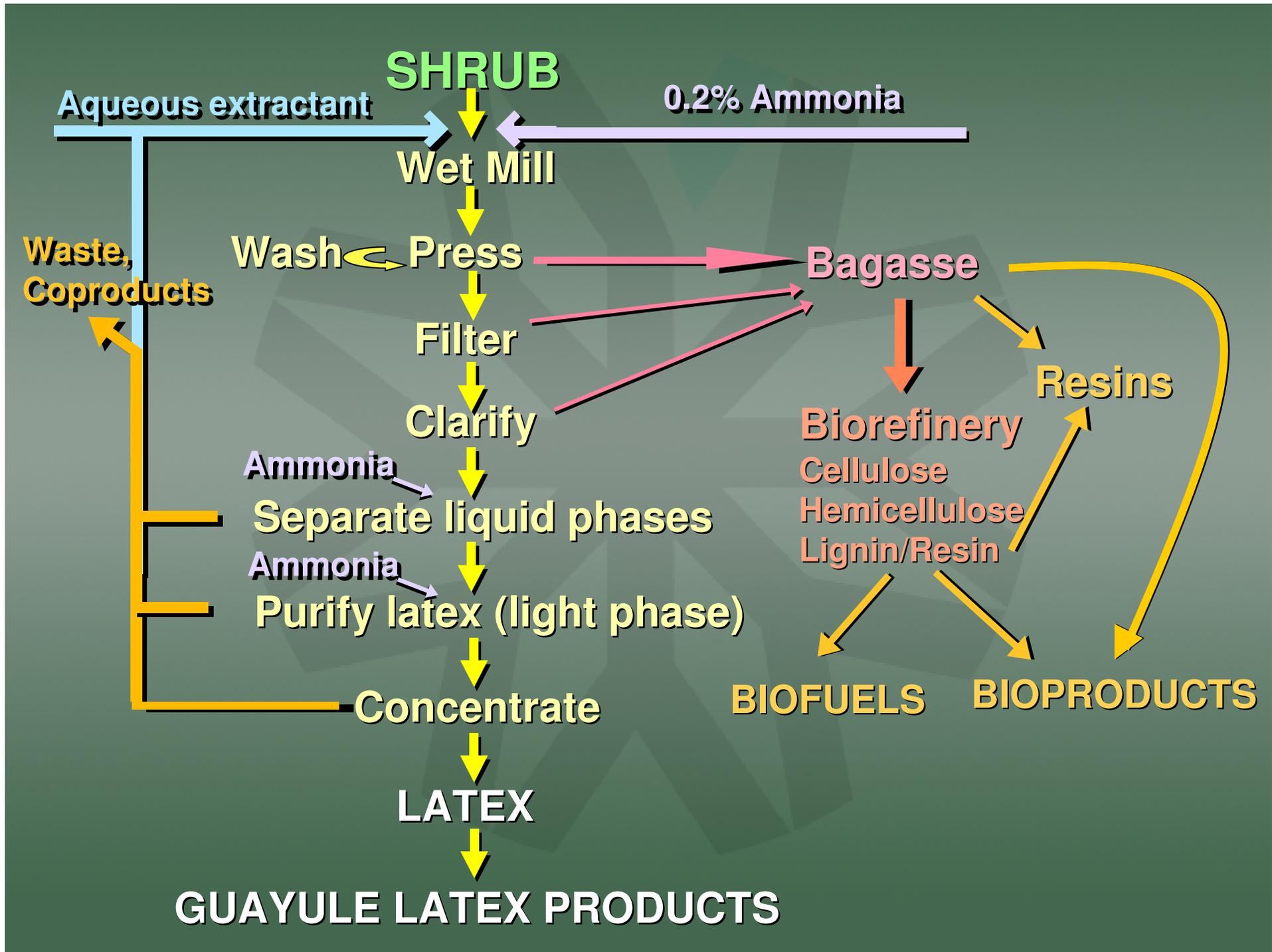
# **Six-year Search for Commercial Partner 1991-1997**

**This included overcoming commercialization  
barriers and identifying potential partners**

**Greatly assisted by the USDA-ARS, especially**

- (1) Office of Technology Transfer**
- (2) Information Service**
- (3) Other research locations**

**And by USDA-CSREES**

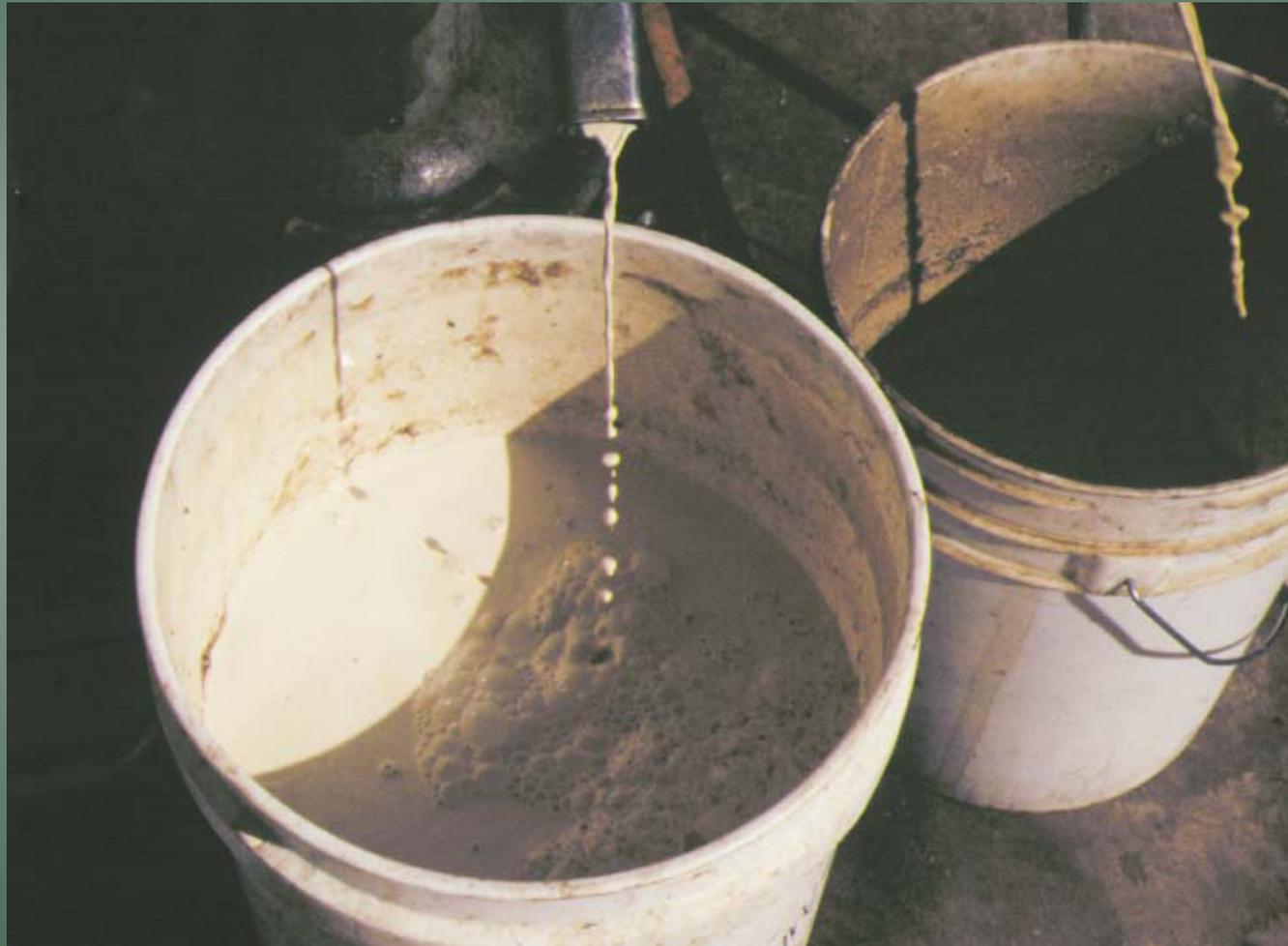


## Latex extraction from guayule – scale-up



With the help of CSREES, U of AZ, USWCL

# Guayule latex separation

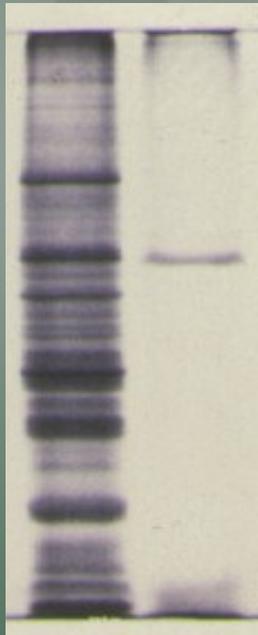


# Is guayule latex a safe alternative?

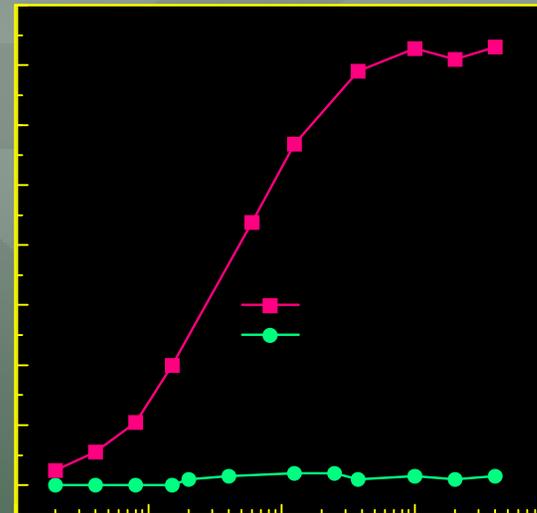
<2% of the protein

Purified  
Hevea

Guayul



Guayule latex proteins do not cross react to *Hevea* latex protein antibodies in mice, rabbits or people.



Siler DJ, Cornish, K, Hamilton. RG, (1996) *J. Allergy Clinnical Immunol.* 98:895-902;

Carey AB, Cornish K, Schrank p, Ward B, Simon R (1995) *Annals of Allergy, Asthma & Immunol* 74: 317-320;

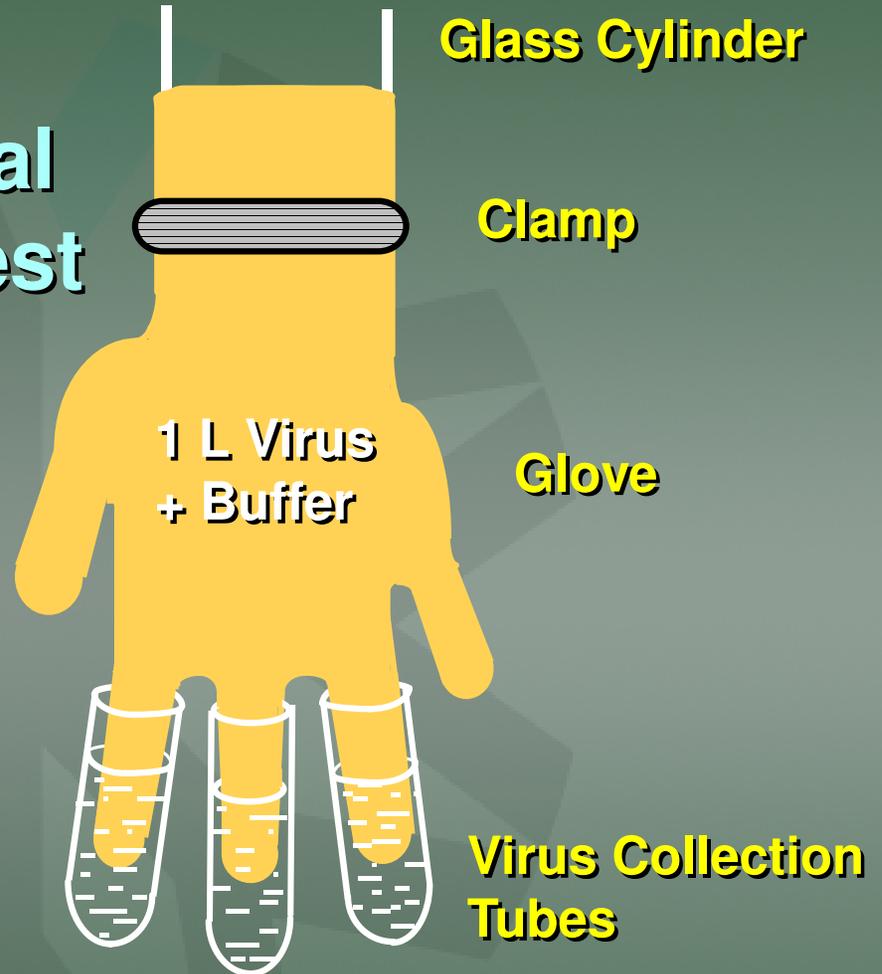
Siler DJ, Cornish K, (1994) *Industrial Crops and Products* 2: 307 – 313;

Ber DJ, Munemasa KH, Hamilton RG, Cornish K, Howard BA, Klein DE, Settupane GA (1993) *J. Allergy and Clinical Immunology* 91: 271



# Glove Viral Barrier Test

Guayule latex **glove** and **condom** films provide an effective barrier to the transmission of human viruses



Cornish, K., Lytle, C.D. Viral impermeability of hypoallergenic, low protein, guayule latex films. *Journal of Biomedical Materials Research* 47: 434-437. 1999.

# Many different people and sectors helped!

USDA-ARS, WRRRC, NCAUR, US WCL

USDA-ARS-NPS

USDA-ARS-OTT

USDA-ARS-IS

USDA-CSREES

DOE-NREL

Universities of Alberta, Arizona, California (Berkeley), Nevada (Reno), Utah, Colorado State, New Mexico State, Texas A & M

NIH, FDA, Cleveland Clinic, Scripps La Jolla, Johns Hopkins, Children's Hospital, Woodland Clinic

Rubber Research Institute of India

South African ARC

Greece – Crete and Gaia Research Institute, Athens

Goodyear Tire and Rubber Company, Plantations Division.

Hercules Corporation

Yulex Corporation

**Exclusive IP was essential to US business involvement and this was a solely ARS development – no CRADA umbrella**

## **Patents:**

**Hypoallergenic Natural Rubber Products from *Parthenium argentatum* (Gray) and other non-*Hevea brasiliensis* species, by Katrina Cornish**

**U.S. Patent No. 5580942. 1996 (the process)**

**U.S. Patent No. 5717050. 1998 (the product)**

**Both patents were exclusively licensed to Yulex Corporation in 1997**

**So how is Yulex doing?**



## VC-Funded - Current Investors

<u>Round</u>	<u>Amount</u>	<u>Date</u>	<u>Investor</u>
Seed	\$130K	8-99	Founders
Series A	\$435K	6-02	Angel Round
Series B	\$2.0M \$2.5M	2-03 4-04	Argonaut Holdings, LLC
Series C	\$8.0M	09-06	Argonaut Holdings, LLC
Series D		07-06	

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	<b>\$2.5M</b>		
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Series D		07-06	



**The guayule crop:** Guayule natural rubber can substitute for *Hevea* rubber in products from tires to catheters



# Guayule Cultivation Cycle

Perennial crop

Two years to first harvest, then annual harvests

No pesticides

Relatively little water

Far more rapid response time to market demands than possible with *Hevea*

Mechanized harvesting and processing

Full range of NR products possible

**Vice President of Agriculture (Mike Fraley)  
leading rapid acreage expansion**

# Mechanized harvesting using cotton equipment – a 21,540 lb module



# Transportation



# Delivery



# Yulex Bioprocessing Plant (2005)



# Processing

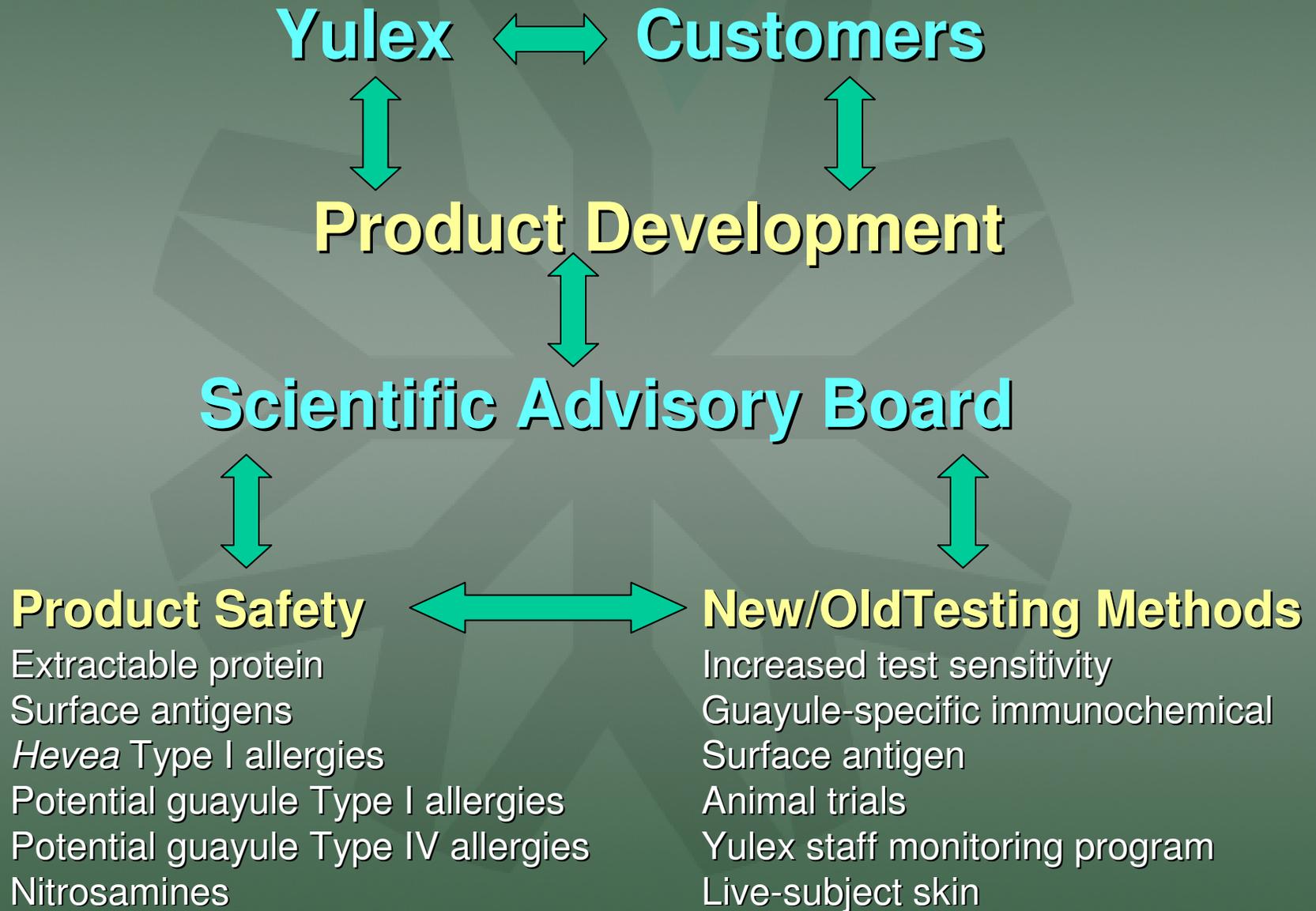
Semi-works plant has been optimized throughout and many steps upgraded

**Vice President of Manufacturing on board (Tony Nocera)**

First commercial plant on-line April 2006

Planning phase for large commercial-scale processing plant underway (on-line in 2007)

# Ongoing Product Programs



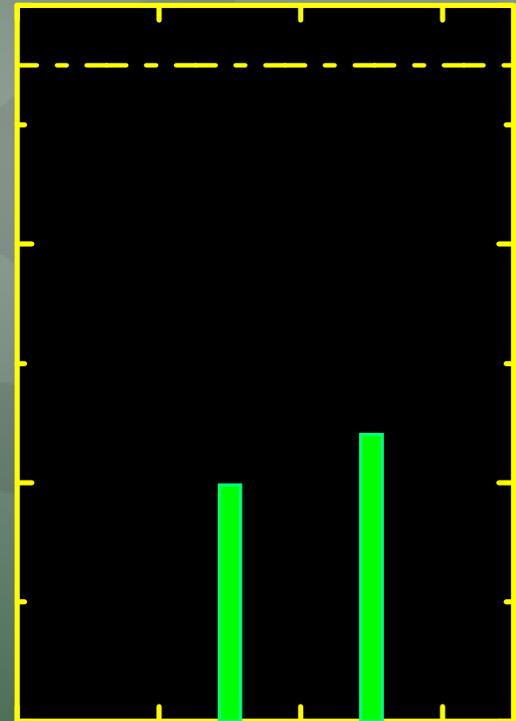
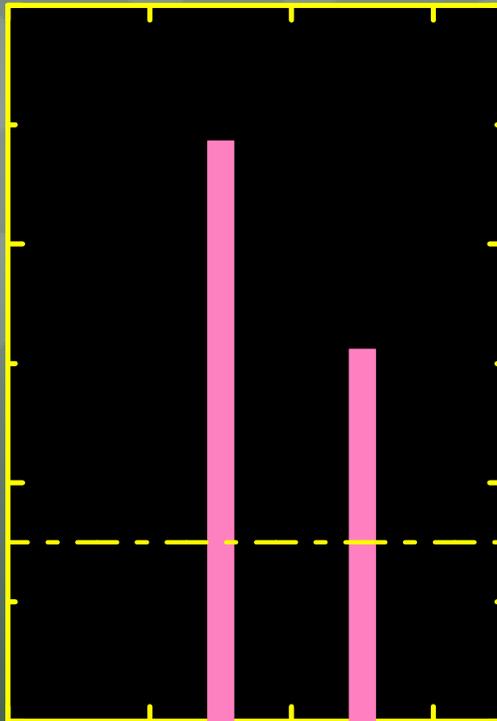
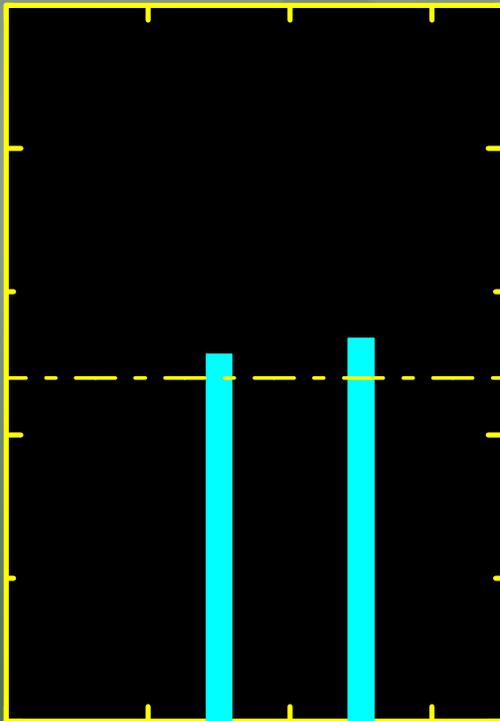
# Protein Content in Latex

(Modified Lowry, ASTM D5712-05)

<b>Sample</b>	<b>Protein</b> ( $\mu\text{g/g}$ dry rubber)
<i>Hevea</i> , sample 1	9,636
<i>Hevea</i> , sample 2	9,196
<i>Yulex</i> , sample 1	106

Protein assays by Wenshuang Xie and Colleen McMahan,  
USDA-ARS, Albany, CA

**Yulex® exceeds the surgical glove standard,  
ASTM D-3577  
- and beats NR for form, fit and feel**



Connect 2005 Most Innovative New Product  
Life Sciences – Medical Devices and Diagnostics

**Yulex Corporation**  
for  
**Yulex™**



# Yulex Distribution Agreement

2005 - 2010, \$150 million



**YULEX™**

"The Natural Solution to Latex Allergy"



***Centrotrade Rubber USA, Inc.***

# Yulex & Centrotech Partnership

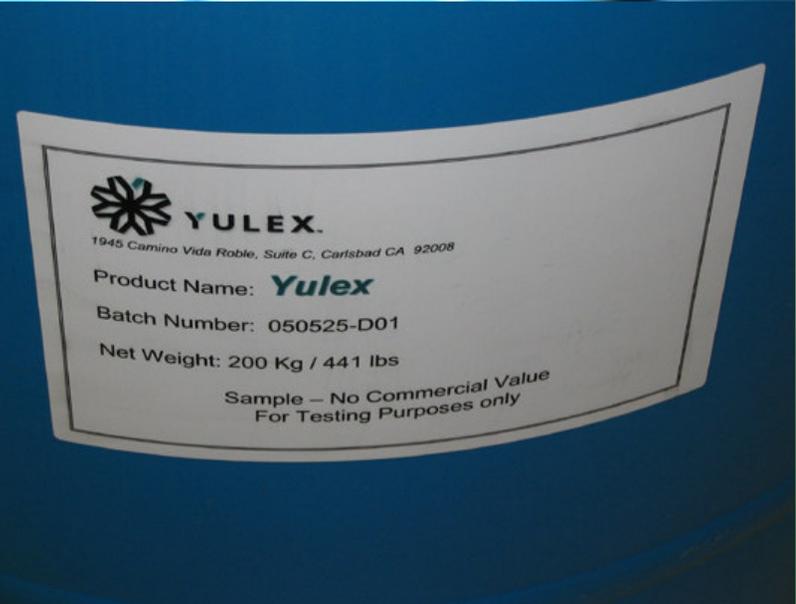
On May 10, 2005 Yulex signed an exclusive five-year distribution agreement with leading international natural rubber supplier and distributor Centrotech Rubber USA and Centrotech Deutschland GmbH.

Centrotech's U.S. and European operations will distribute Yulex® Natural Rubber Latex worldwide to medical device manufacturers of surgical gloves, condoms, catheters and other latex-based medical products that are seeking an alternative to lower performing synthetic latex materials.

# yulex® (guayule latex) first sales in 2005



 **YULEX**  
1945 Camino Vida Roble, Suite C, Carlsbad CA 92008  
Product Name: **Yulex**  
Batch Number: 050525-D01  
Net Weight: 200 Kg / 441 lbs  
Sample – No Commercial Value  
For Testing Purposes only



# **Yulex has entered Revenue Phase**

**First Royalty Payment**

**(credited against licensing fees)**

# Regulatory Affairs

ASTM

FDA

ISO



**Designation: D 1076–02**

# **Yulex® - Guayule latex**

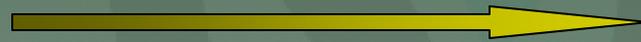
Modifications were made to the standard to accommodate the commercial introduction of guayule latex  
- Introduction of a new Category 4.

## The New Latex Category (not “Type”)

- **Category 4** — Centrifuged, or centrifuged and creamed, guayule latex, or other natural rubber latex, containing less than 200 micrograms total protein per gram dry weight of latex, with ammonia or other hydroxide, with other necessary preservatives and stabilizers.
- No detectable protein by D-6499, antigenic *Hevea* protein.
- Other changes to text in the body of the standard are included.
- Also, relevant changes to D1418 (nomenclature) and D 1566 (standard terminology).
  - NR to remain term for Natural Rubber from *Hevea brasiliensis* NRG to be added to mean Natural Rubber from guayule (*Parthenium argentatum*)

# Dipped Medical Products

COMMODITY



DIFFERENTIATED

Exam glove

Surgical glove

Condom

Catheter

6 g

12 g

1-2 g

< 0.5 g

\$0.035

\$0.50

\$1-2

\$8-10

\$2.65/lb

\$19/lb

\$450/lb

>\$8,000/lb

100-150,000

15,000

7,000

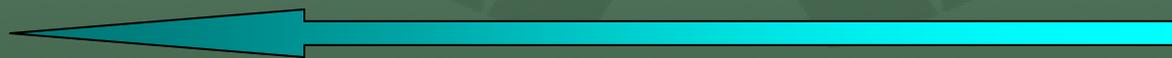
< 500

tons/yr US

tons/yr US

tons/yr US

tons/yr US



**YULEX**

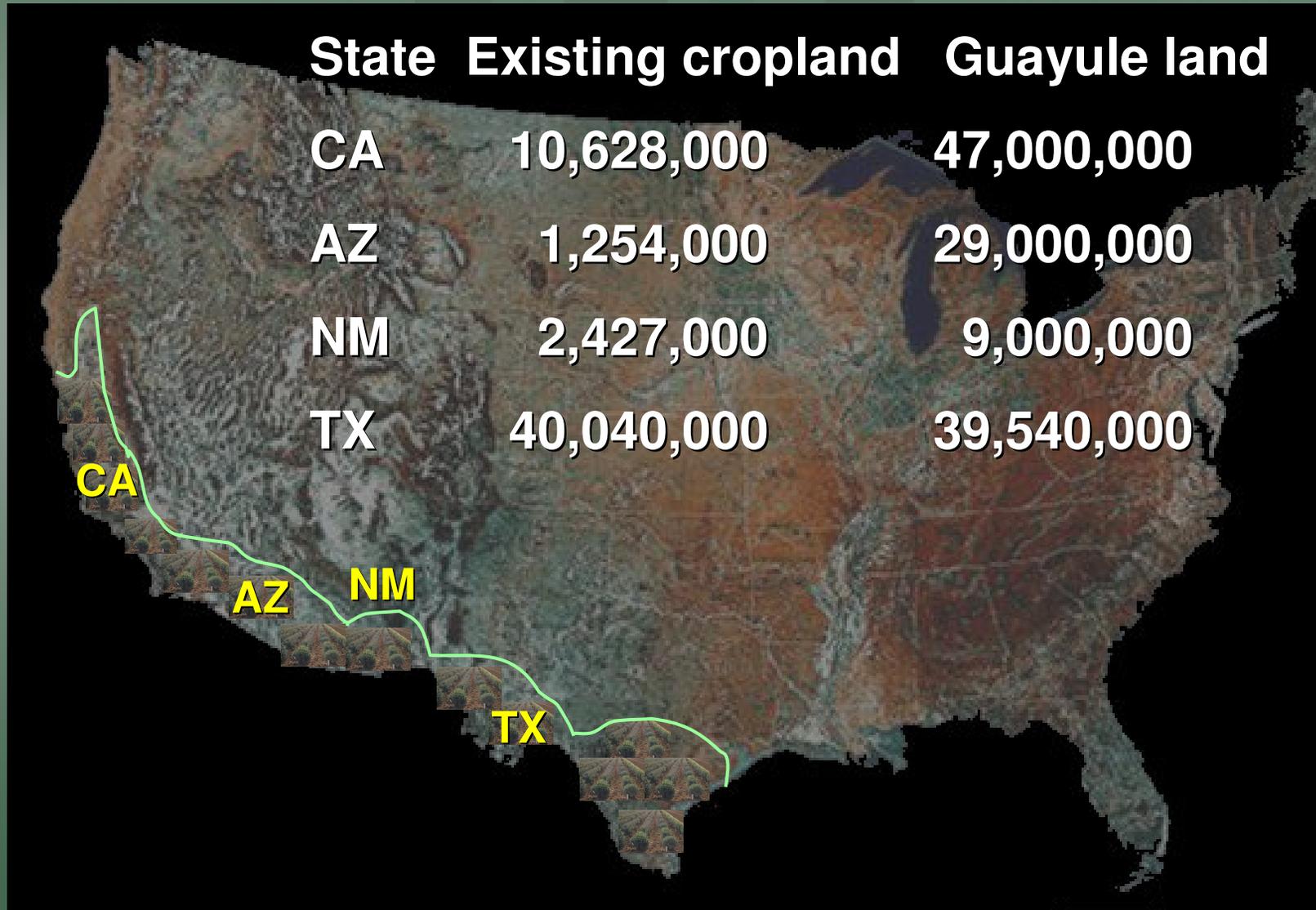
## Annual guayule acreage needed for different markets (at one ton latex per acre per year)

	2005	2020
Medical and high-end consumer products	350,000	2,000,000
All NR latex	1,000,000	6,000,000
All NR products	8,000,000	12,000,000
All rubber	20,000,000	30,000,000

Demand is rapidly increasing as China and India industrialize – especially automotive and medical demands

*(International Rubber Study Group, 2005)*

# Guayule growing region (ERP) - 124,540,000 acres (probably more as climatic requirements may have shifted)



# Total Utilization of

# Guayule

Product ..... latex and rubber

+

Coproduct ..... resin

+

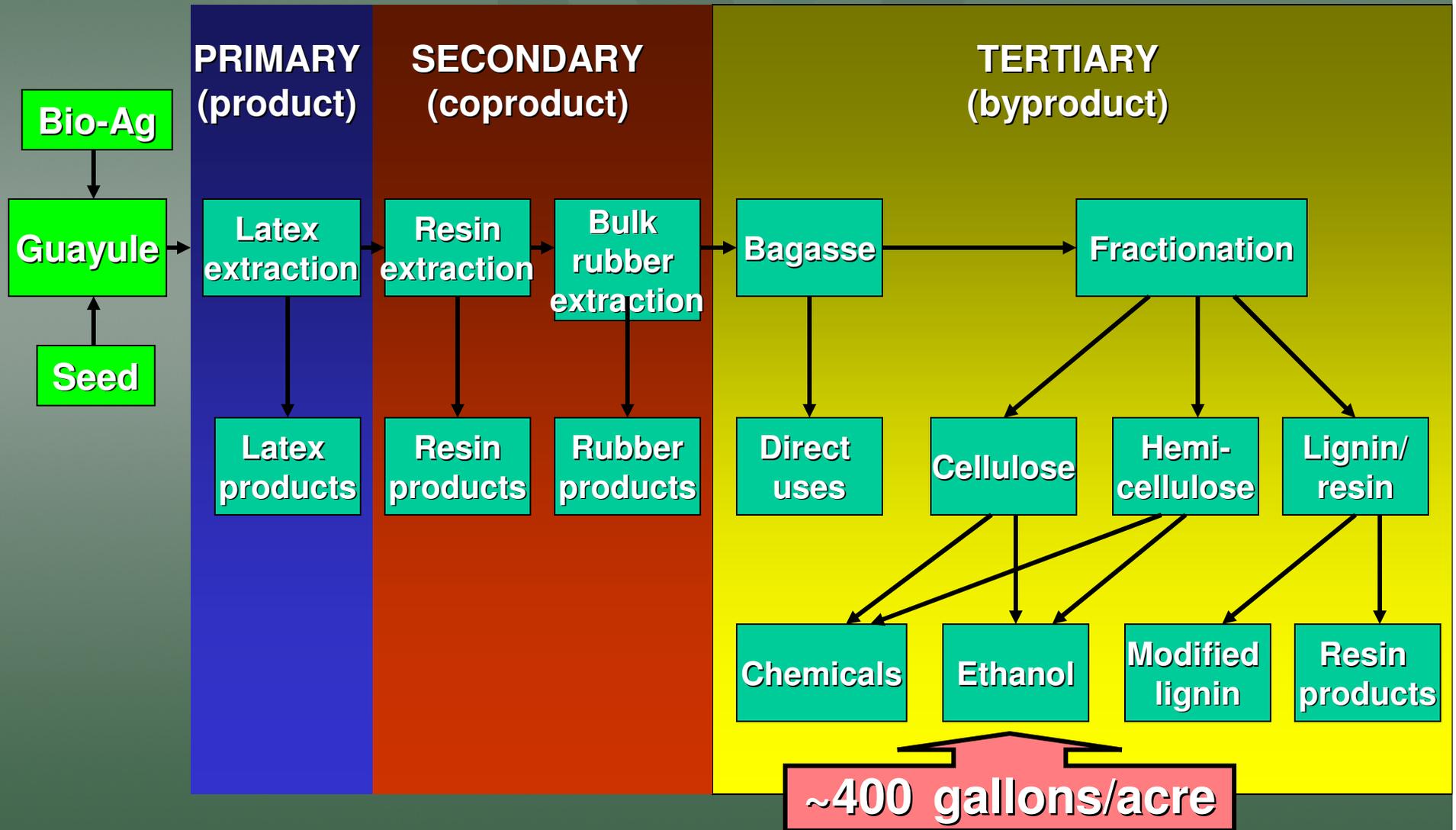
Byproduct ..... bagasse



**Latex extraction by wet-milling guayule shrub also generates bagasse – a high energy “zero-cost” feed-stock of 9,720 Btu/lb and 15 lb/cu ft**

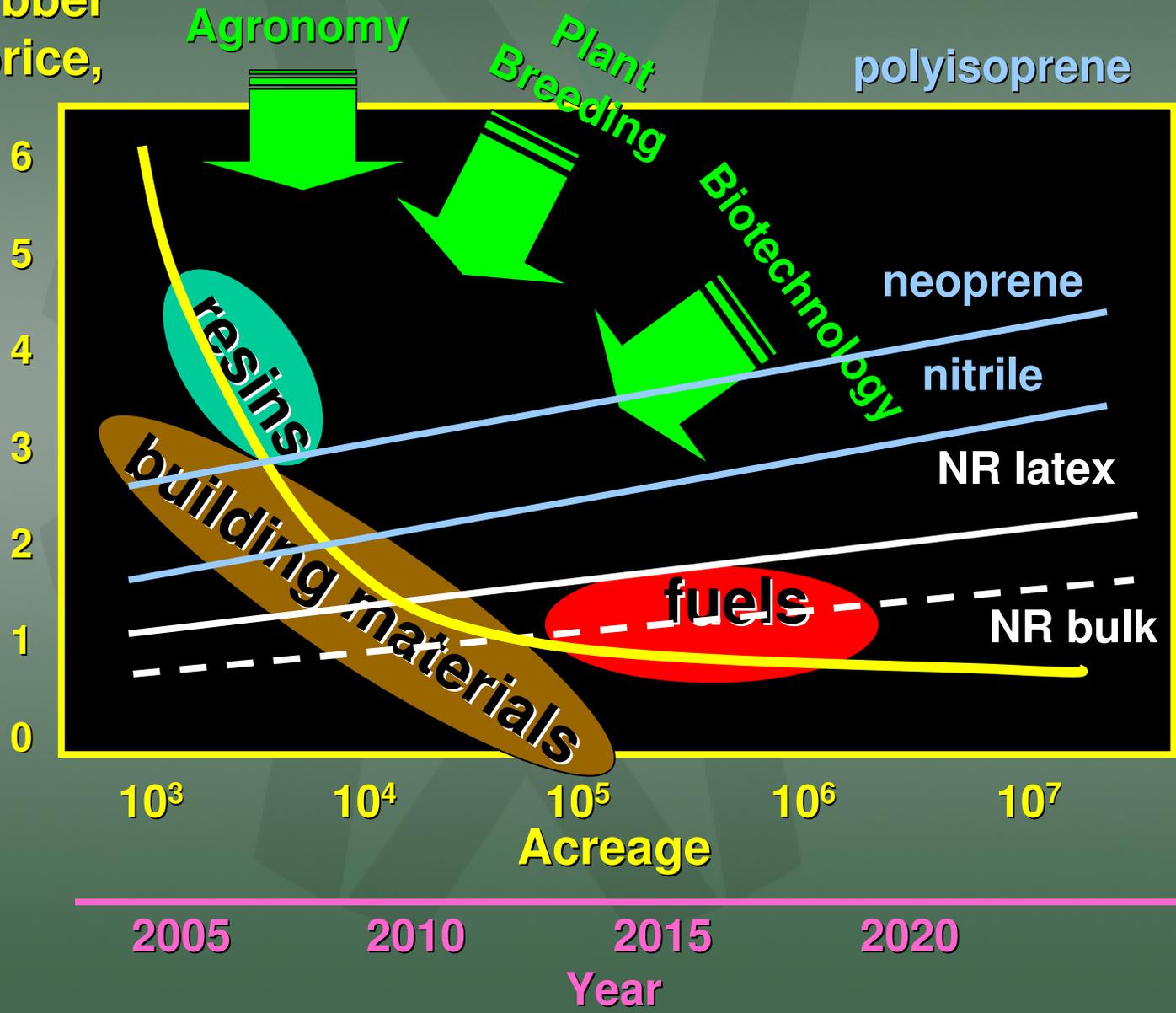


# Yulex Biorefinery

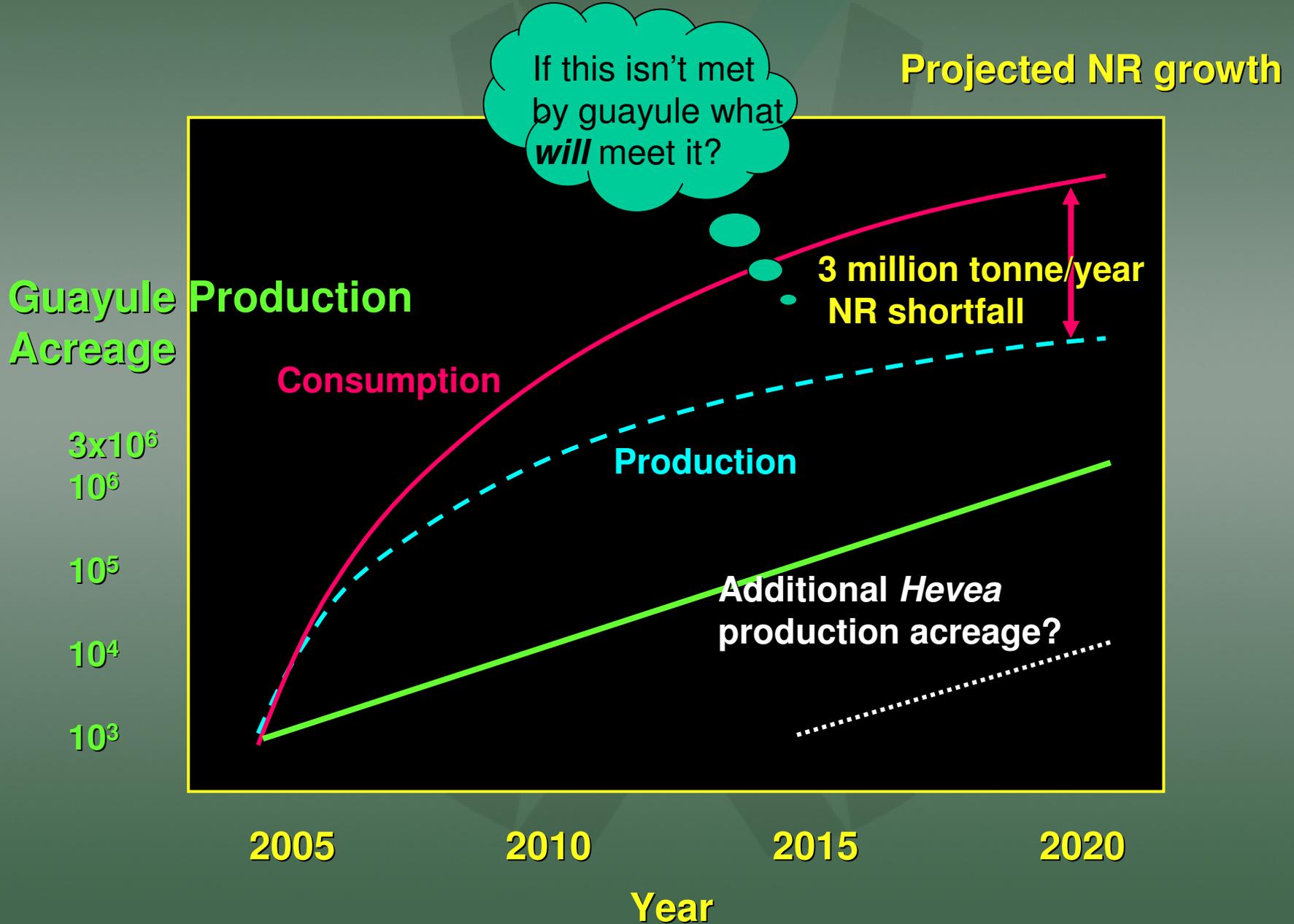


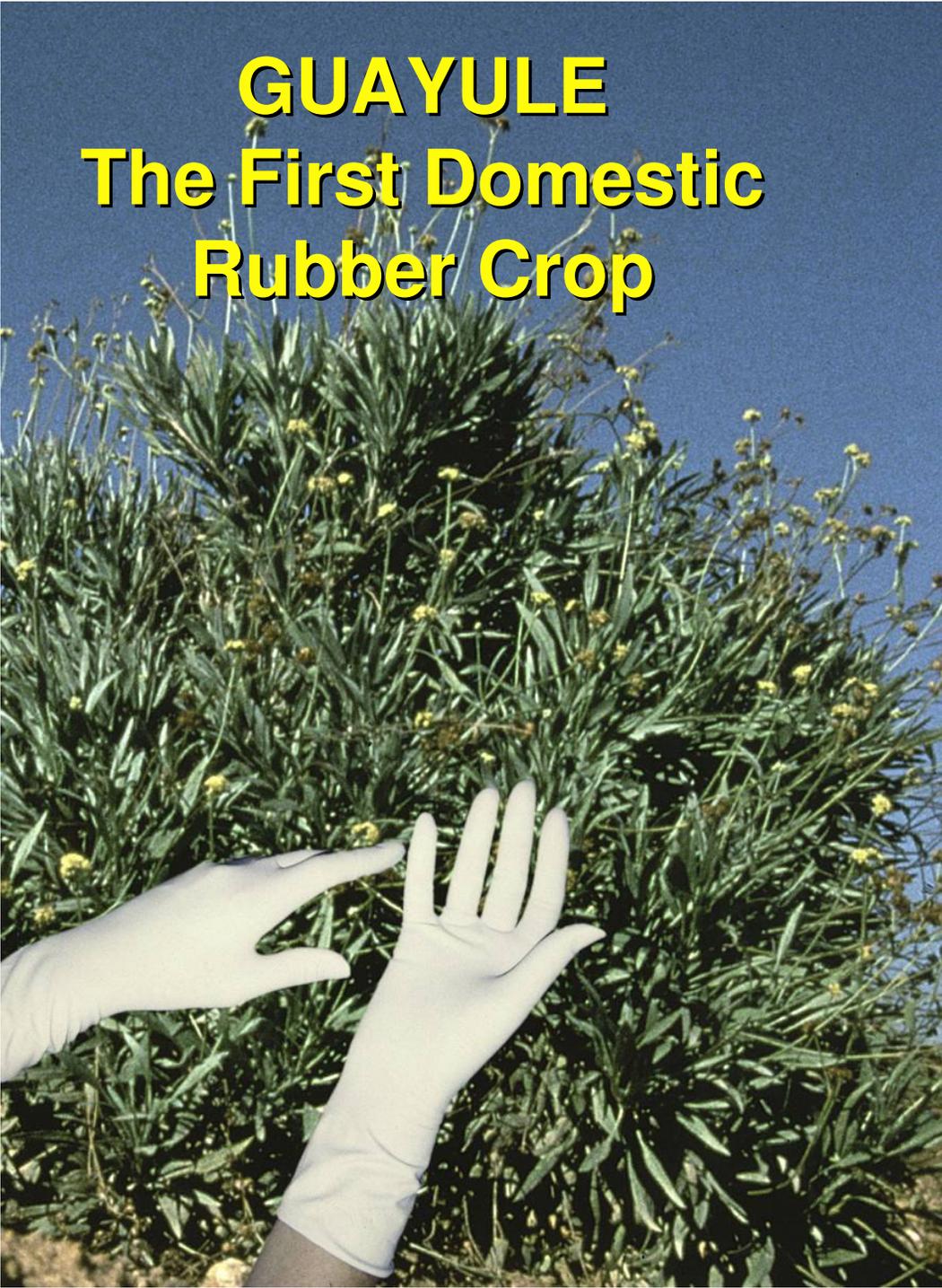
# YULEX Economic Drivers

Yulex  
Latex/Rubber  
Selling price,  
\$/lb



# Guayule can respond to market demands much more quickly than *Hevea*





# **GUAYULE**

## **The First Domestic Rubber Crop**

**Tropical *Hevea* protein-free**, high quality Yulex® latex medical products can be manufactured, safe for use by people with Type I latex allergy.

Many other products, including tires, can also be made from guayule rubber.

Domestic rubber production provides non-subsidized agriculture, rural development, and raw materials security.