

REGULATION OF PLANT-BASED GENETICALLY MODIFIED PRODUCTS

ISSUES FOR DRUG DEVELOPMENT

2004 AAPS ANNUAL MEETING

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OUTLINE

- **INTRODUCTION**
- **REGULATORY FRAMEWORK FOR GM PLANTS**
- **STARLINK CASE**
 - **LESSONS LEARNED**
 - **REGULATORY IMPACT**
- **CONCLUSION**

INTRODUCTION

FRANKENFOOD

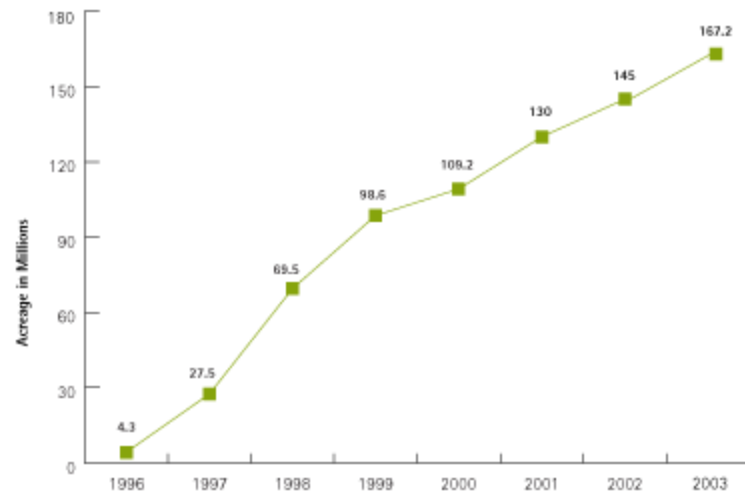


"No need to worry, trust us, you said. Unlabeled genetically engineered food is perfectly safe."

BIOTECHNOLOGY CROP GROWTH

40-FOLD  IN ACREAGE 1996-2003

INCREASE IN GLOBAL AREA OF BIOTECHNOLOGY CROPS – 1996 TO 2003



Source: ISAAA Global Review of Transgenic Crops 2003.

REGULATORY FRAMEWORK

COORDINATED FRAMEWORK FOR THE REGULATION OF PLANT BIOTECHNOLOGY

- **USDA: SAFE FOR PLANT LIFE**
- **FDA: SAFE FOR YOU**
- **EPA : SAFE FOR THE ENVIRONMENT**

Marketing GM Plants

- **Field Trials**

- **Notice**
- **Permit**

- **Non-Regulated Status**

- **Marketing**

The Starlink[®] Case

Detection of DNA fragments from Starlink[®] corn in grocery-store taco shells in September 2000

Starlink[®] corn approved for animal feed, not for human consumption

STARLINK[®] CORN

- **Bt: Bacillus thuringiensis**
- cry1A gene - pesticide production
 - » approved for use in humans and animal food
- cry9C gene - insecticidal resistance
 - » codes for allergic protein

The Starlink[®] Case (cont'd)

HOW DID THIS CONTAMINATION OCCUR?

- **NARROW INTERPRETATION OF REGULATORY AUTHORITY BY AGENCIES**
- **POLITICAL CLIMATE**
 - **PROMOTION OF GM FOODS**

USDA

**ANIMAL AND PLANT HEALTH INSPECTION SERVICE
(Plant Protection Act)**

GM CROPS

- IMPORTATION**
- INTERSTATE MOVEMENT**
- ENVIRONMENTAL
RELEASE**

USDA

PLANT- PEST TEST (7 CFR 340)

**A LIVING ORGANISM THAT INJURES
OR CAUSES DISEASES TO A PLANT**

**IF NOT A PLANT PEST, USDA GRANTS
“NON-REGULATED” STATUS**

**INSECT RESISTANCE – NOT A PLANT-
PEST RISK**

USDA APPROVAL OF STARLINK®

- **FIELD TRIALS (1996-1997)**
 - NOTIFICATION PROCEDURE
 - FONSI (finding of no significant impact)
- **AVENTIS PETITIONS FOR NON-REGULATED STATUS (MARCH 1998)**
 - STARLINK® NOT A PLANT-PEST
- **USDA GRANTS PETITION (MAY 1998)**

FDA (FDCA)

- **1992 POLICY STATEMENT (57 FR 22985)**
 - **CEDED AUTHORITY TO REGULATE PESTICIDES IN FOOD TO EPA**
 - **ADOPTED “SUBSTANTIAL EQUIVALENT” TEST**
 - **GM FOODS ARE NO DIFFERENT THAN FOODS DEVELOPED BY TRADITIONAL PLANT BREEDING**
 - **GM FOODS TREATED AS GRAS**
 - **INDUSTRY ALLOWED SELF EVALUATION**
 - **EXEMPTED FROM PRE-MARKET REVIEW**
- **Alliance for Bio-Integrity v. Shalala (116 F. Supp. 2d 166 (D.D.C. 2000))**

FDA APPROVAL OF STARLINK® -

- AVENTIS PETITIONS FOR SUBSTANTIAL EQUIVALENCE
 - NUTRITIONAL DATA
 - SAFETY DATA
 - ALLERGENICITY – TO EPA
 - PESTICIDE

FDA APPROVAL OF STARLINK®

- FDA
 - NO INDEPENDENT INVESTIGATION
 - GRANTS AVENTIS' PETITION
 - STARLINK IS “SUBSTANTIALLY EQUIVALENT” TO OTHER MARKETED CORN
 - CONCURRING WITH AVENTIS

EPA (FIFRA AND FDCA)

- **CRITERIA FOR PESTICIDE REGISTRATION**
 - **Registration is MANDATORY**
 - **DOES NOT CAUSE “UNREASONABLE ADVERSE EFFECTS ON THE ENVIRONMENT”**
 - **UNREASONABLE**
 - **EPA MUST CONSIDER THE “ECONOMIC, SOCIAL AND ENVIRONMENTAL COSTS AND BENEFITS” OF PESTICIDE**

EPA (FIFRA AND FDCA)

- **PESTICIDES USED IN PRODUCTION OF FOOD OR FOOD CROPS (Registration)**
 - **TOLERANCE**
 - **SAFE LEVEL (residue)**
 - **REASONABLE CERTAINTY THAT NO HARM WILL RESULT FROM AGGREGATE EXPOSURE TO THE PESTICIDE CHEMICAL RESIDUE, INCLUDING ALL ANTICIPATED RESIDUES**
 - **EXEMPTION**
- **ADULTERATED FOOD (FDA)**
 - **PESTICIDE RESIDUE EXCEEDS TOLERANCE**

EPA STARLINK[®] APPROVAL

- **AVENTIS PETITIONS**

- **PESTICIDE TOLERANCE EXEMPTION FOR STARLINK**

- **FOR AGRICULTURAL PRODUCTS**

- **SIMILAR TO cry1A CONTAINING GM CROPS**

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EPA APPROVAL OF STARLINK[®] (cont'd)

- AVENTIS DATA
 - FAILED “NO SIGNIFICANT RISK’ TEST
 - INCONCLUSIVE
 - cry9C PROTEIN: ALLERGENIC POTENTIAL
 - STABILITY
 - » THERMAL (90 °C, 2 HOURS)
 - » SIMULATED GASTRIC FLUIDS (4 HR)

EPA STARLINK APPROVAL (cont'd)

- **DATA FAILED TO SHOW STARLINK IS “SUBSTANTIALLY EQUIVALENT IN ALL ESSENTIAL RESPECTS” TO ITS UNMODIFIED PARENT**
- **CRITERIA: “REASONABLE CERTAINTY OF NO HARM”**

EPA STARLINK® APPROVAL (cont'd)

- **AVENTIS AMENDS EXEMPTION PETITION**
 - ANIMAL FEED
 - INDUSTRIAL USES
- **GRANTED “SPLIT REGISTRATION”**
 - KEEP STARLINK FROM FOOD SUPPLY

GROWER GUIDE

**CORN CANNOT BE SOLD FOR
HUMAN CONSUMPTION (SIGNED
AGREEMENT)**

**TWO REMINDERS (PLANTING
AND HARVEST TIME)**

NEED FOR BUFFER STRIP

**POST HARVEST SURVEY TO ENSURE
AGREEMENT WAS FOLLOWED**

PRODIGENE CORN

- **Engineered to produce swine vaccine**
- **Found growing in soybean fields in Nebraska and Iowa; farmer ignored warning and harvested soybean and sent it to an elevator (2002)**
- **500000 bushels of soybean destroyed**
 - **“volunteers: from seeds left from a previous field trial**

POST STARLINK®

- FDA GUIDANCE DOCUMENT FOR DRUGS . . . DERIVED FROM GM PLANTS - FDA, SEPT. 2002
- FIELD –TRIALS (ENVIRONMENTAL INTRODUCTION) OF GM PLANTS ENGINEERED TO PRODUCE INDUSTRIAL COMPOUNDS ONLY BY PERMIT (INTERIM EFFECTIVE AUGUST 6, 2003 – DECEMBER 31, 2004)

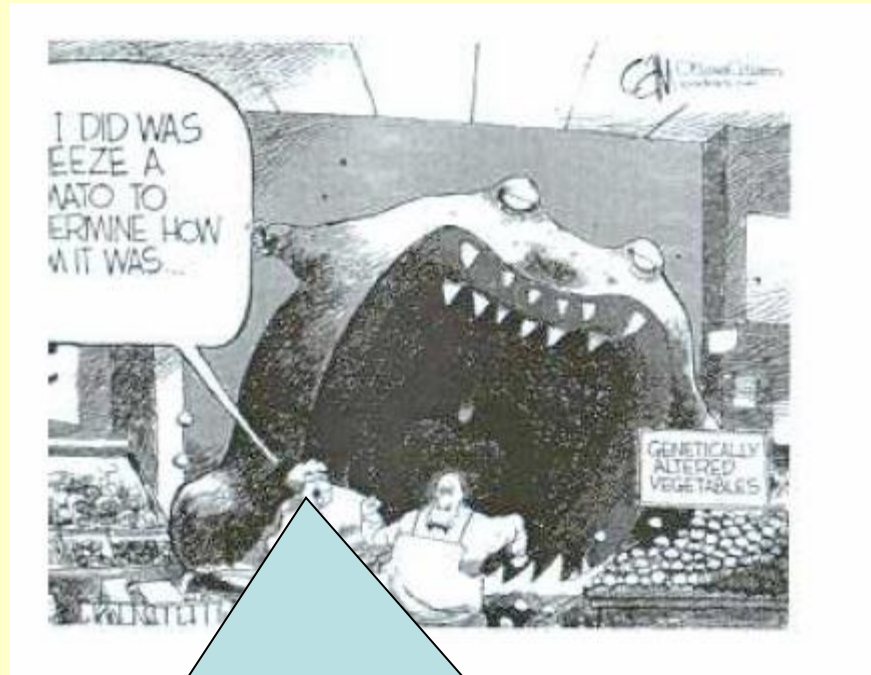
REGULATORY CHANGES

- ENHANCED PHYSICAL SEGREGATION
 - *mandatory filed site inspections*
 - *No biopharm corn be grown within 1 mile of open-pollinated corn*
 - *Restrictions on production of food and feed crops at the field test site and perimeter*
 - *Use of dedicated machinery*

CONCLUSION

- **REGULATORY CLIMATE CHANGING FROM :**
- **VOLUNTARY TO MANDATORY**

PHARMAGEDDON



ALL I DID WAS TO SQUEEZE A
TOMATO TO DETERMINE HOW
FIRM IT WAS