GM Crops: Food safety issues

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Hector Quemada, Ph.D
Western Michigan University
Program for Biosafety Systems

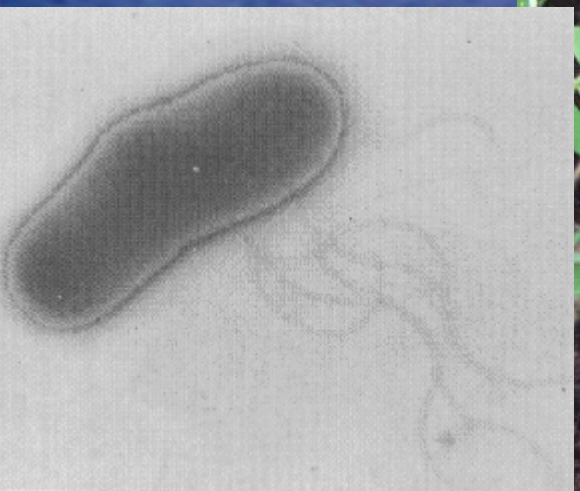
Topics to be covered

- Food safety issues associated with the genetic modification of crop plants.

- Food safety assessment, including Codex Alimentarius

Introducing DNA

Agrobacterium transformation



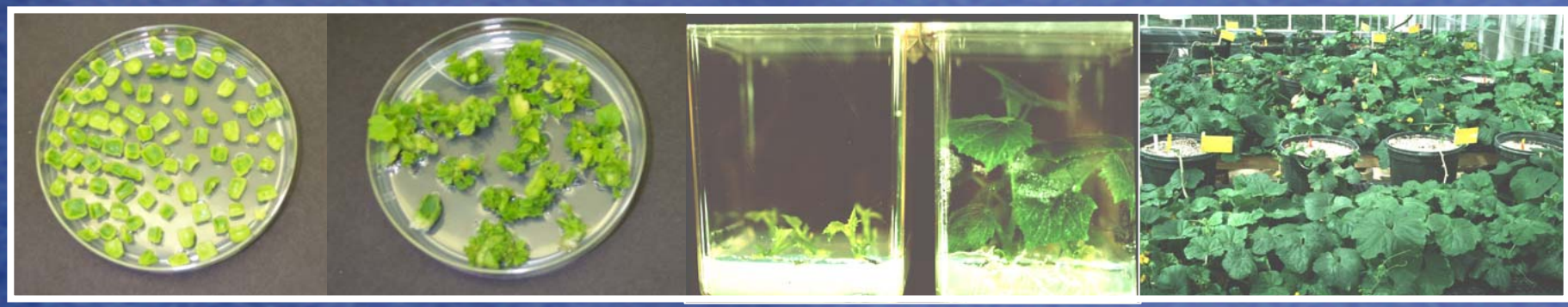
Particle bombardment

Regeneration

3. Regenerate cells with the new gene back into whole plants

selection

regeneration

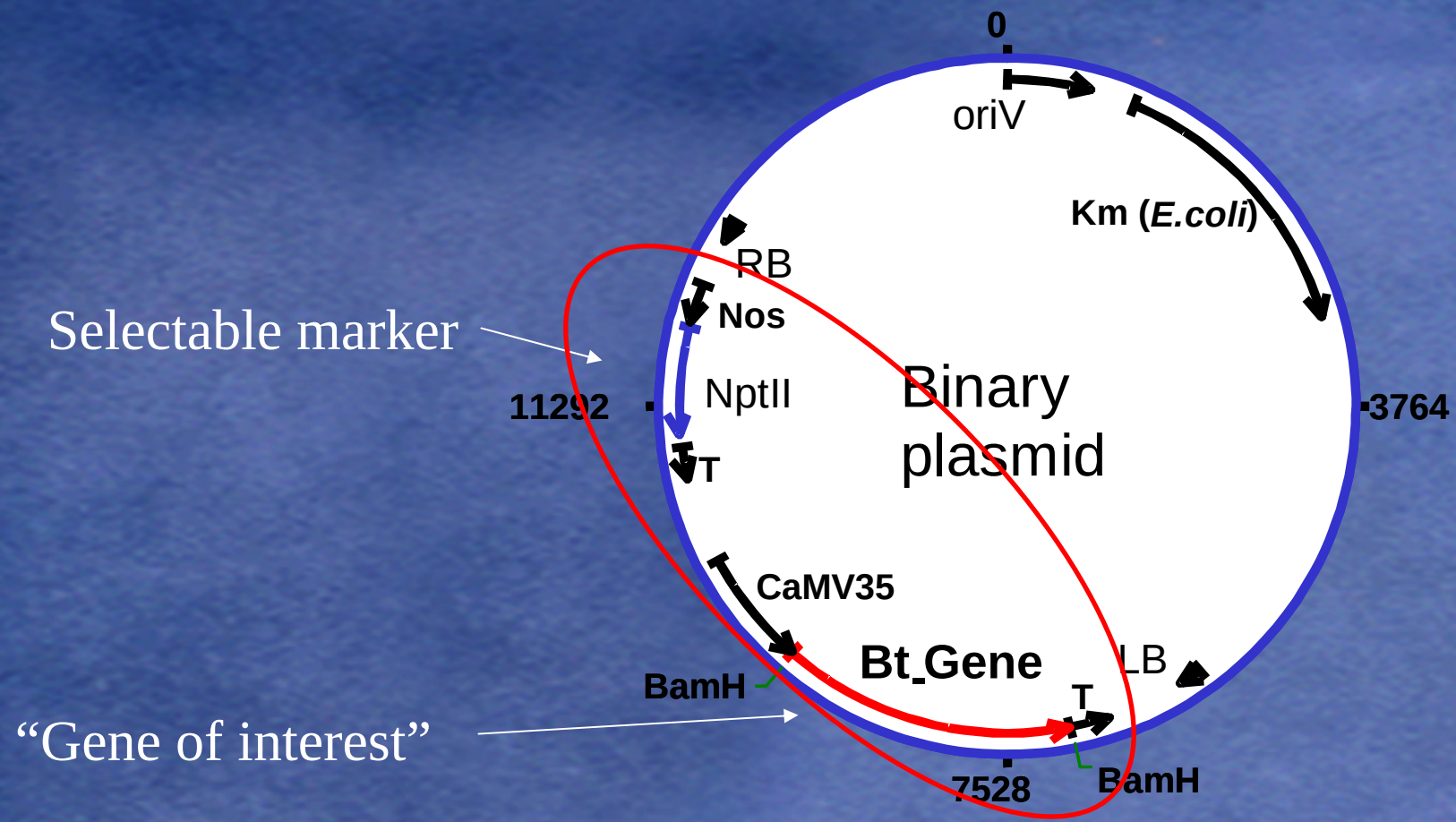


+ antibiotic

or

+ herbicide

Introduced DNA



Food Safety Issues—genetic engineering vs. traditional breeding

- Genetic engineering
  - Genes can come from non-related sources
    - Familiar, known food sources
    - Non-food sources
  - Transformation and regeneration process can cause unintended changes in the plant
    - Interaction with plant metabolism
    - Insertion process may disrupt open reading frames or create new ones
- Traditional breeding
  - Genes come mostly from related sources, but sometimes from unrelated sources
    - Familiar known food sources
    - Non-food sources (e.g. wild relatives)
  - Breeding process can cause unintended changes in the plant
    - Interactions with plant metabolism
    - Recombination process may produce non-functional genes or create new gene variants

How do we identify risks?

Risk identification

- Based on what we already know
- What do we know?
  - Plants or other organisms produce proteins that are toxic or allergenic.
    - ➔Transferred proteins from these sources might be toxic or allergenic
  - Results of other genetic modification methods: traditional breeding produces unintended effects.
    - ➔Genetic engineering might produce unintended effects

Safety evaluation: genetic engineering vs. traditional breeding

- Genetic engineering
  - Thorough characterization of gene and gene product
  - Extensive characterization of plant at molecular, biochemical level
  - Extensive characterization at field level
  - Extensive characterization of environmental effects (including effect on performance)
- Traditional breeding
  - Gene and gene products often uncharacterized (loci)
  - Minimal or no characterization of plant at molecular, biochemical level (exceptions)
  - Extensive characterization at field level
  - No characterization of environmental effects (aside from effect on performance)

Safety evaluation: genetic engineering vs. traditional breeding

- Genetic engineering
  - Analytical procedures
  - History of safe use of gene products
  - Familiarity with the crop
- Traditional breeding
  - History of safe use
  - Familiarity with the crop

Safety evaluation process

- Intended effects (gene of interest and marker)
  - DNA is safe
  - Protein
  - Products of activity of new gene(s)
- Unintended effects

New protein or intended result of introduced gene activity

- Toxicity
  - Introduced protein may be toxic
  - New products of gene activity may be toxic
- Allergenicity
  - Transfer an existing allergen into a new crop
  - Transfer cross-reactive proteins into a new crop
  - Transfer other proteins that may sensitize, becoming an allergen
  - Increase endogenous allergens

New protein or intended result of introduced gene activity

- Toxicity
  - Avoid using genes encoding for known toxins
  - Tests
    - Sequence search
    - History of safe use
    - Digestibility
    - Heat stability
    - Toxicology
      - If not similar to proteins already consumed
      - High dose, acute study

New protein or intended result of introduced gene activity

- Allergenicity
  - Avoid using genes encoding known allergens, or genes from known allergenic sources.
  - Tests
    - Sequence search
    - Digestibility
    - Heat stability
    - *Experimental:* exploring animal or cell models—no validated animal models currently available

Unintended effects (Pleiotropic effects)

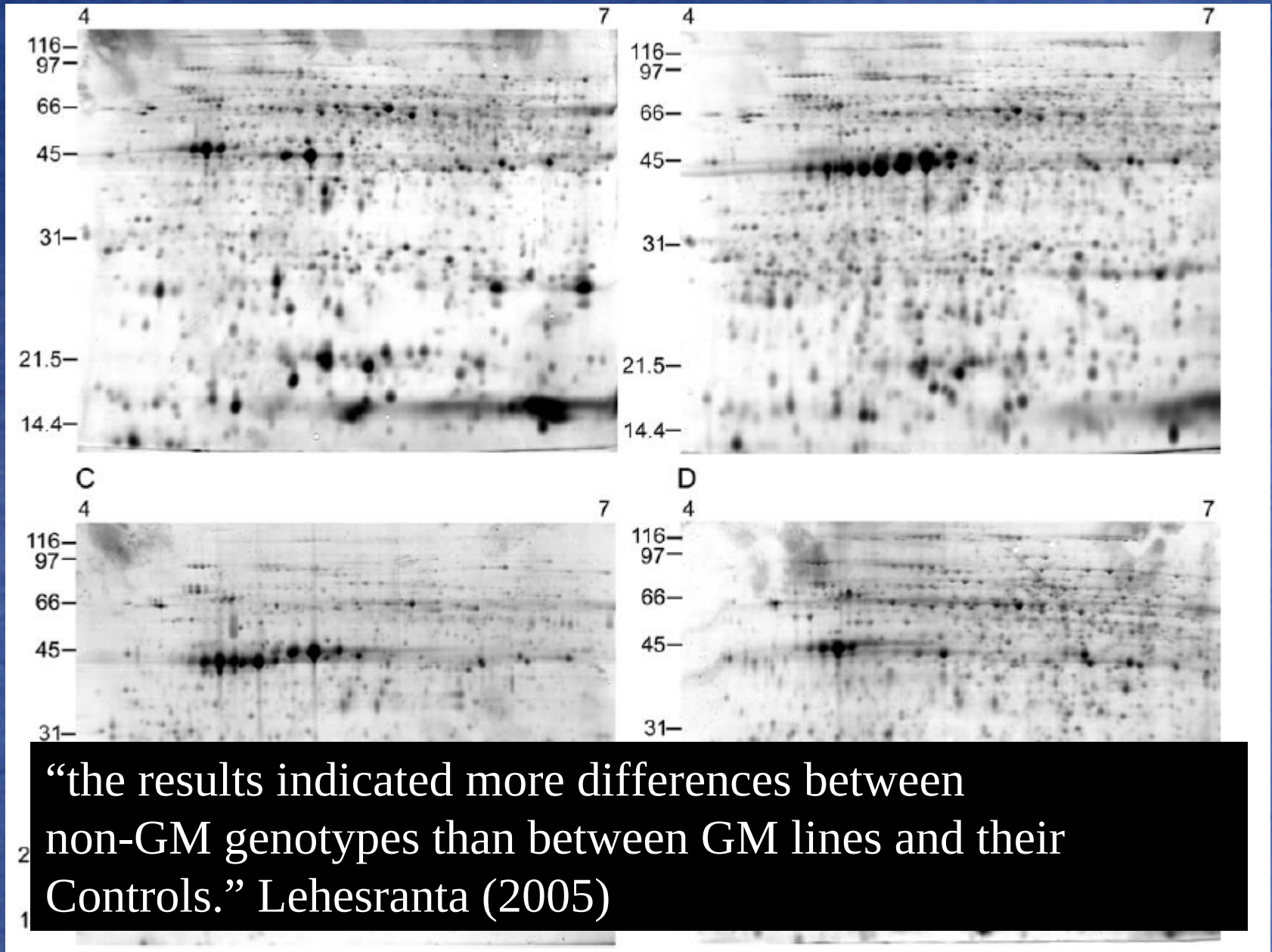
- Elevation of known endogenous toxins or allergens
- Change in nutritional composition
- Production of new toxins

Unintended effects (Pleiotropic effects)

- Assay levels of known endogenous toxins or allergens
  - Appropriate testing methods
- Change in nutritional composition
  - Proximate analysis
  - Other important components characteristic of the food crop
  - Wholesomeness studies (whole food feeding studies)

Unintended effects (Pleiotropic effects)

- Production of new toxins
  - Mode of action of introduced protein
  - Molecular characterization
  - Agronomic performance—indication of metabolic changes
  - *Experimental*: proteomic, metabolomic approaches—traditionally bred varieties vary more than transgenic vs. nontransgenic.



"the results indicated more differences between non-GM genotypes than between GM lines and their Controls." Lehesranta (2005)

International Food Safety Assessment Guidelines

Codex Alimentarius

Codex: Introduction

- Traditionally, usually no extensive evaluation of new varieties
- Use of animal models to measure toxicological endpoints is a major element of risk assessment
  - Well characterized
  - Known purity
  - No nutritional value
  - Exposure is low
  - Can test with many-fold factors of safety (no-effect)

Codex: Introduction*

- "*Animal studies cannot readily be applied* to testing the risks associated with whole foods, which are complex mixtures of compounds, often characterised by a wide variation in composition and nutritional value…*If the characterization of the food indicates that the available data are insufficient for a thorough safety assessment,* properly designed animal studies could be requested on the whole foods. Another consideration in deciding the need for animal studies is *whether it is appropriate to subject experimental animals to such a study if it is unlikely to give rise to meaningful information.*"

*italics added

Codex: Introduction

- Affirms substantial equivalence as the basis of safety assessment
- Substantial equivalence is not itself a safety assessment, but a means for identifying the differences between the new food and its traditional counterpart, which then become the focus of the safety assessment.
- Safety considered relative to conventional counterpart

Codex: Unintended effects

- Can also occur with traditional breeding
- Many are predictable, based on molecular characterization and existing information on likely metabolic effects of the introduced genes
- Assessment of unintended effects requires a multidisciplinary approach, including assessment of agronomic characteristics

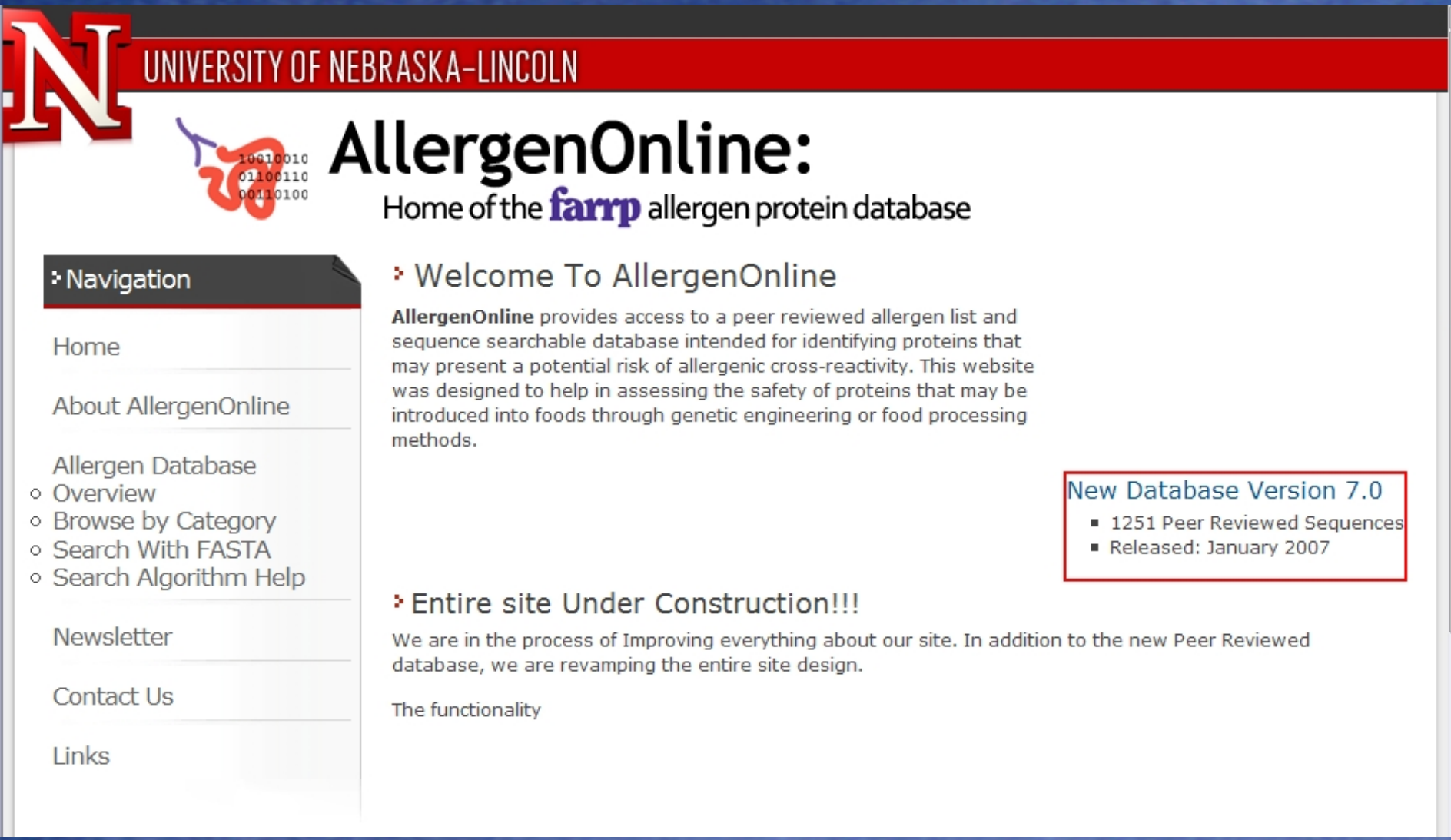
Codex: Framework

- Description of the recombinant-DNA plant;
- Description of the host plant and its use as food;
- Description of the donor organism(s);
- Description of the genetic modification(s);
- Characterization of the genetic modification(s);
- Safety assessment:
  - expressed substances (non-nucleic acid substances);
  - compositional analyses of key components;
  - evaluation of metabolites ;
  - food processing;
  - nutritional modification; and
- Other considerations.

Codex: allergenicity assessment

- Source
- Sequence similarity to known allergens
- Structural properties
  - Enzyme resistance
  - Heat stability
  - Acid degradation
- Other tests if above shown a concern.

Allergenicity databases



www.allergenonline.com

Codex: Antibiotic resistance markers

- Alternate markers should be used in future
  - Should be demonstrated to be safe
- Gene transfer to gut microorganisms or human cells is rare
- For food safety assessment
  - Clinical and veterinary use and importance
  - Presence in food compromises therapeutic use of antibiotic?
  - If poses a risk to human health, should not be used

EFSA (2004):

Furthermore, resistance to antibiotics in group I is widespread in naturally occurring prokaryotic gene pools. This, together with the other reasons provided in this document, indicates that there is no rationale for restricting or prohibiting the use of this group of ARMGs.

ENTRANSFOOD (Kuiper et al., 2004):

The presence of category I genes, like neomycin phosphotransferase (npt II) and hygromycin phosphotransferase (hpt), would not contribute to the spread of resistance in the environment and therefore not pose an additional environmental or human health risk.