Regulatory Coordination Relevant to GE Animals and Their Products: Domestic and International Challenges

Larisa Rudenko, Brinda Dass, and Harlan Howard
on behalf of the
Animal Biotechnology Interdisciplinary Group
FDA/CVM
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Brasilia
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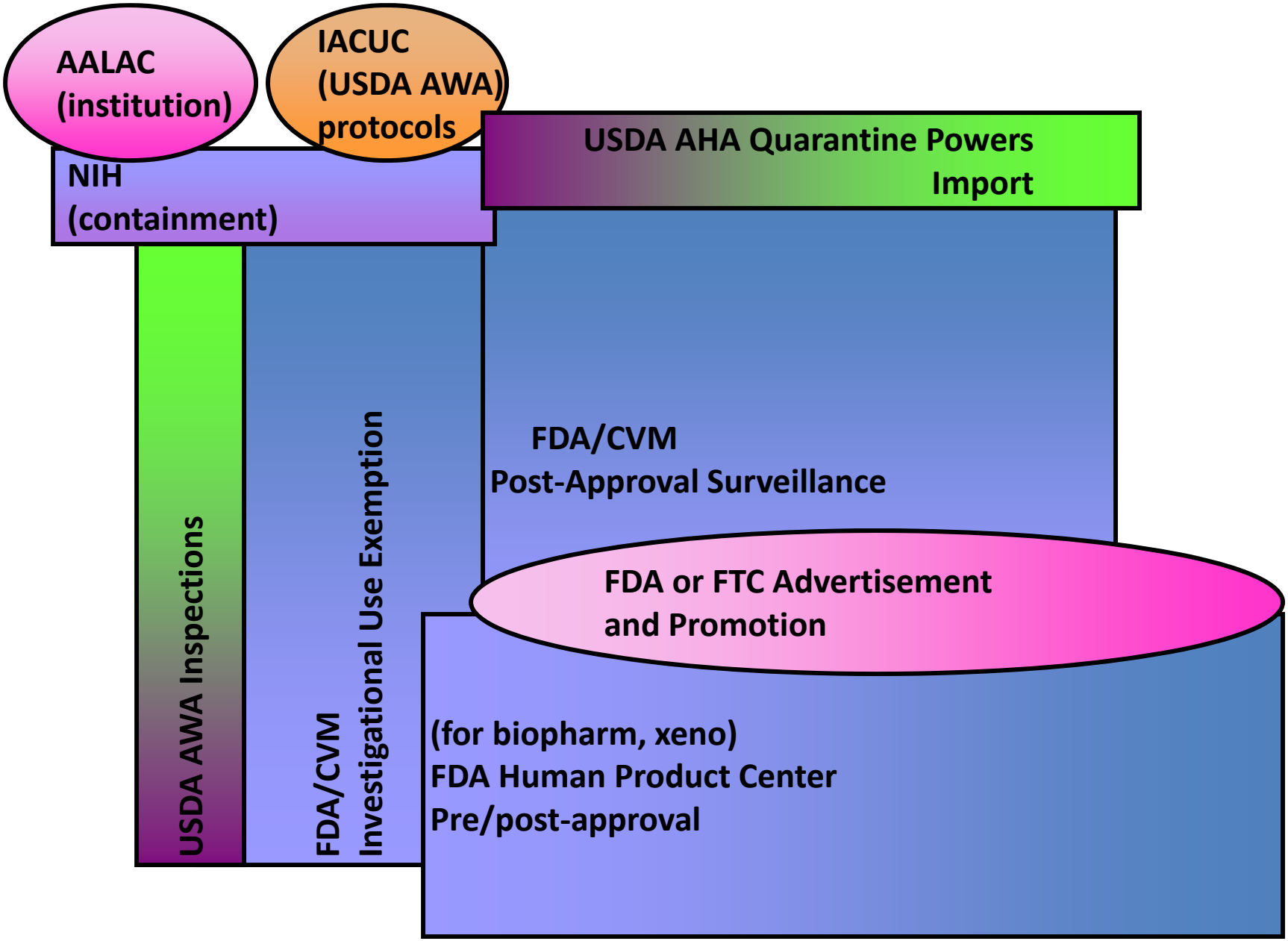
Goals

- Describe concept of coordination in the US
- International harmonization
- Challenges
- Some ideas

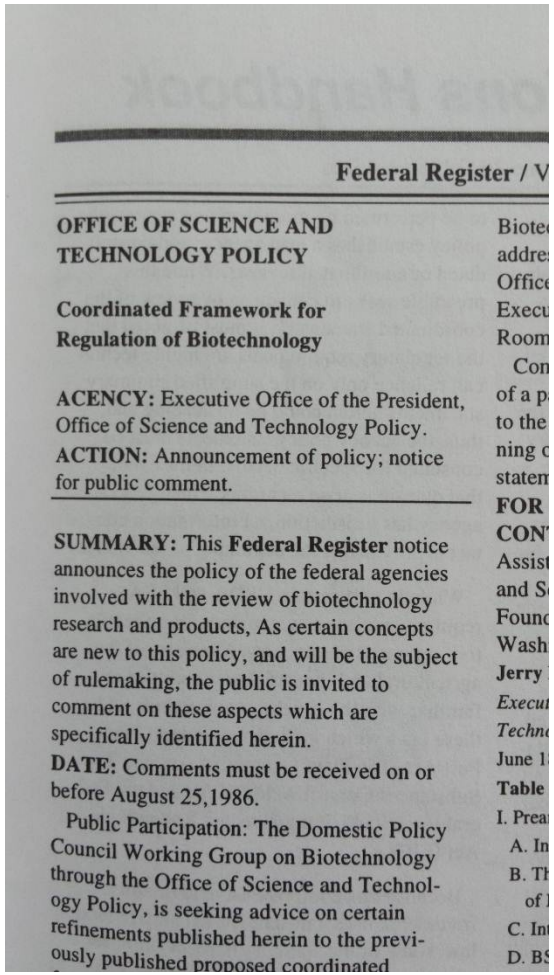
What Does Coordination Mean? (centered on regulations/regulators)

- Smooth interactions between and among parties involved in regulation in one country
  - Regulators and regulated entities (in US, sponsors)
  - Within a regulatory agency when $\geq$ 1 administrative unit is involved in
    - Review
    - Decision making
  - Among regulatory agencies within a government or geopolitical unit


AALAC
(institution)
IACUC
(USDA AWA)
protocols
NIH
(containment)
USDA AHA Quarantine Powers
Import
USDA AWA Inspections
FDA/CVM
Investigational Use Exemption
FDA/CVM
Post-Approval Surveillance
FDA or FTC Advertisement
and Promotion
(for biopharm, xeno)
FDA Human Product Center
Pre/post-approval

The Coordinated Framework (1986)-1

- Issued by the Office of Science and Technology Policy
- Establishes product-based regulation
  - Case by case
  - Primarily focused on plants and microorganisms
- Recommendations for which agency regulates what products
- Provides recommendations when authorities overlap or are ambiguous



Federal Register / V

OFFICE OF SCIENCE AND TECHNOLOGY POLICY

Coordinated Framework for Regulation of Biotechnology

ACENCY: Executive Office of the President, Office of Science and Technology Policy.
ACTION: Announcement of policy; notice for public comment.

SUMMARY: This **Federal Register** notice announces the policy of the federal agencies involved with the review of biotechnology research and products, As certain concepts are new to this policy, and will be the subject of rulemaking, the public is invited to comment on these aspects which are specifically identified herein.
DATE: Comments must be received on or before August 25,1986.

Public Participation: The Domestic Policy Council Working Group on Biotechnology through the Office of Science and Technology Policy, is seeking advice on certain refinements published herein to the previously published proposed coordinated

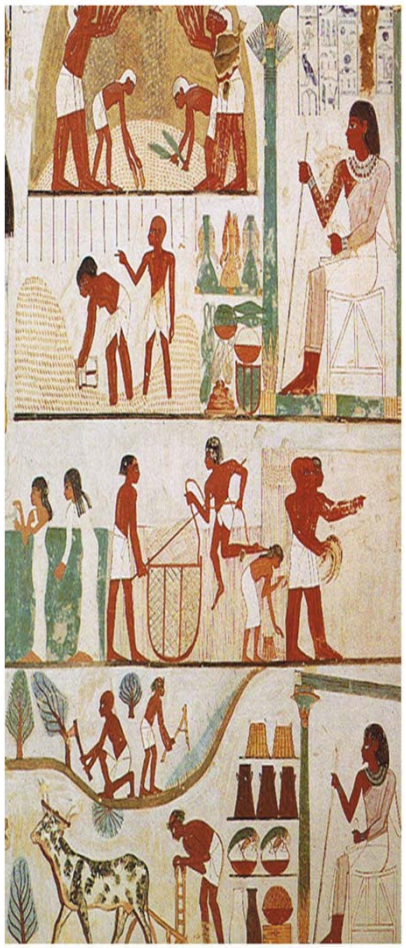
The Coordinated Framework (1986)-2

- Assumes that
  - All agencies regulate to same degree of rigor
  - Different agencies may have different regulatory “triggers”
  - When different components of a product’s life cycle trigger different statutory authorities, describes which agency performs which function
    - To date, mostly used for plants
      - Field trial
      - Food safety
      - Pesticides

Coordination Across the USG for Oversight of Regulation Relevant to GE Animals- Simple Case

I was lord and overseer of southern grain in this nome.

~The Nomarch Henku, Eqyptian 5th dynasty ~ 2830 BC or earlier.



- One administrative unit responsible for all regulatory decisions
  - Animal health/welfare
  - Food safety
  - Durability
  - Claim Validation
  - Post-Approval Oversight and Reporting
  - Environmental issues
- Often the case when FDA's CVM evaluates submissions

Coordination Across the USG for Oversight of Regulation Relevant to GE Animals- More Complex

- One primary agency to make “approval” decisions
- Additional agencies with jurisdiction (sole or overlapping) for other components (e.g., importation)
- Determination of “lead agency “
- Scientific expertise from other agencies may be integrated into review team to improve outcome
- Regulatory decision made by lead agency according to its authorities

GE Goat Producing ATryn: "Simple" Coordination within FDA

- Considerations
  - Two regulated articles/two approvals
    - CVM NADA approval
      - rDNA construct in GE goat to produce *rh* antithrombin in milk
    - Center for Biologics Evaluation and Research Biologics License Approval for ATryn
      - Anticlotting agent for individuals with hereditary clotting disorders in high risk situations

- Goals
  - Risk-based, non-duplicative reviews
  - Coordinated with "Final Product" Center
  - Harmonized data/review requirements

GE Mosquito: Interagency Coordination under the Coordinated Framework

- Initial jurisdiction unclear
  - Was *Aedes aegypti* a plant or animal pest (USDA)?
  - Did the rDNA construct in the mosquito meet the definition of a new animal drug?
- After interagency consultation, FDA determined to be "lead agency"
- Expertise enlisted for scientific advice from EPA, CDC, etc.
- Final decisions rest with FDA

Harmonization Goals (International)

- Discussion of vocabularies/key issues (e.g., triggers)
  - Hope for consensus; may agree to disagree
- Ensure equivalent safety standards, data/information
  - e.g., Codex, OECD
- Coordination within/among administrative and geopolitical units on key points
- Preserving each geopolitical unit's sovereignty
- Keeping guidelines, etc. as "living documents"
- Minimize science-based barriers to trade
  - SPS, TBT

Challenges-1
How Do You Harmonize When You Go First (and actual n is small)?

- Many countries/geopolitcal units have laws, regs, etc. on the books
- Few have been tested by full or partial implementation
- Going first has rewards and risks
  - For the sponsor
  - For the regulator

Challenges-2
Roles Assigned to Various Agencies: Distribution of Effort, Different Goals

- Regulation vs Promotion
  - Decision making does not promote a product or technology
- Avoiding conflict of interest
  - Scientific Expertise vs Communication
  - Regulation vs Trade Facilitation
    - Education of trade negotiators
    - Asynchronous approvals

Challenges- 3

- Can we harmonize when we have
  - Different regulatory triggers?
  - Product vs process regulation?
  - Nomenclature?
    - GMO, GE, genome editing, gene “tweaking”
- New technologies
  - Moving from considerations of “first generation” products to products from newer technologies

Challenges- 4

- Keeping regulatory implementation flexible and recursive
  - Accommodate changes in technologies that may require changes in terminology
  - Realize that harmonization documents also serve as capacity building/sharing instruments

- Keeping harmonization agreements as “living documents”

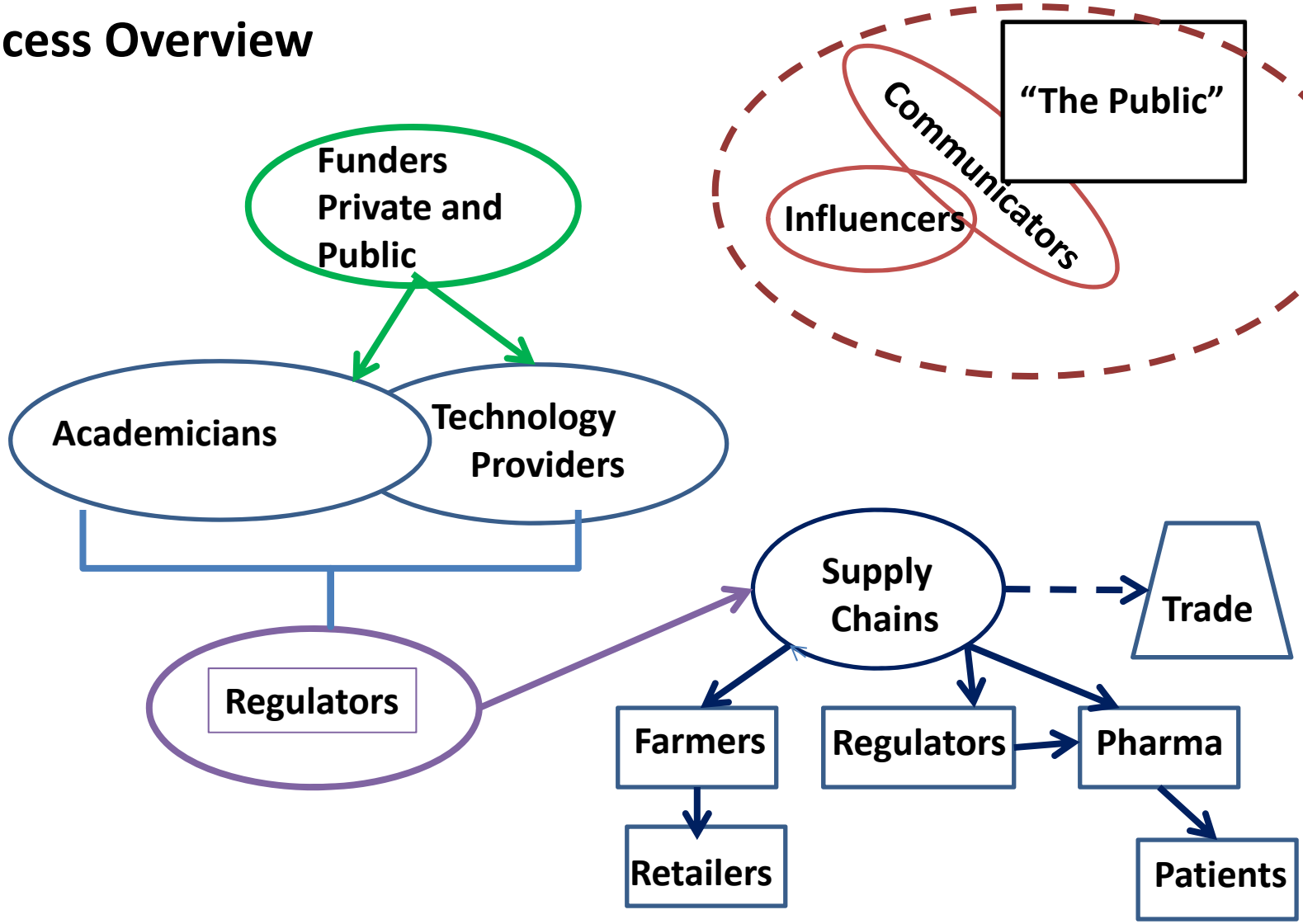
Challenges -5

- Keeping lines of communication open
  - Administrative considerations
    - Sharing data/information
    - CBI
- Communications with public/commentators
- Implications for trade

How Did This Workshop Address Coordination?

- How can all of the involved parties communicate and interact more productively?
  - Who are the parties?
  - What roles do they play?
    - What roles can't they play?

Process Overview



Grounds for Optimism

- Increased experience with the products of technologies can decrease regulators' concerns
- Workshops such as these open lines of communication, shared experiences
- Open communication can lead to increased trust
- Increased trust facilitates, but doesn't guarantee harmonization
- It's important to have realistic expectations....and hope.

When is the next conference?????