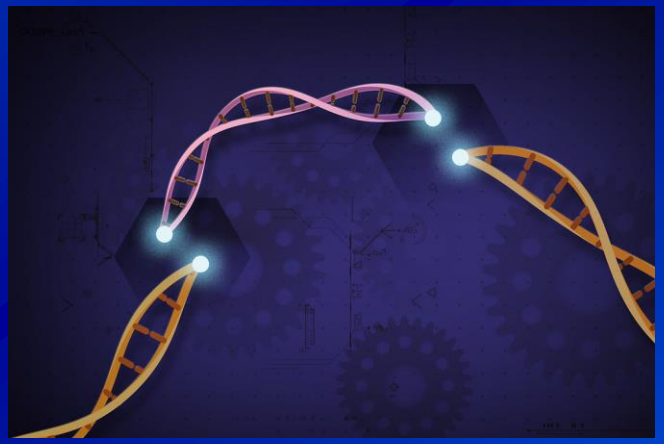
Environmental Assessment:
Unique issues and potential risks for biotechnology



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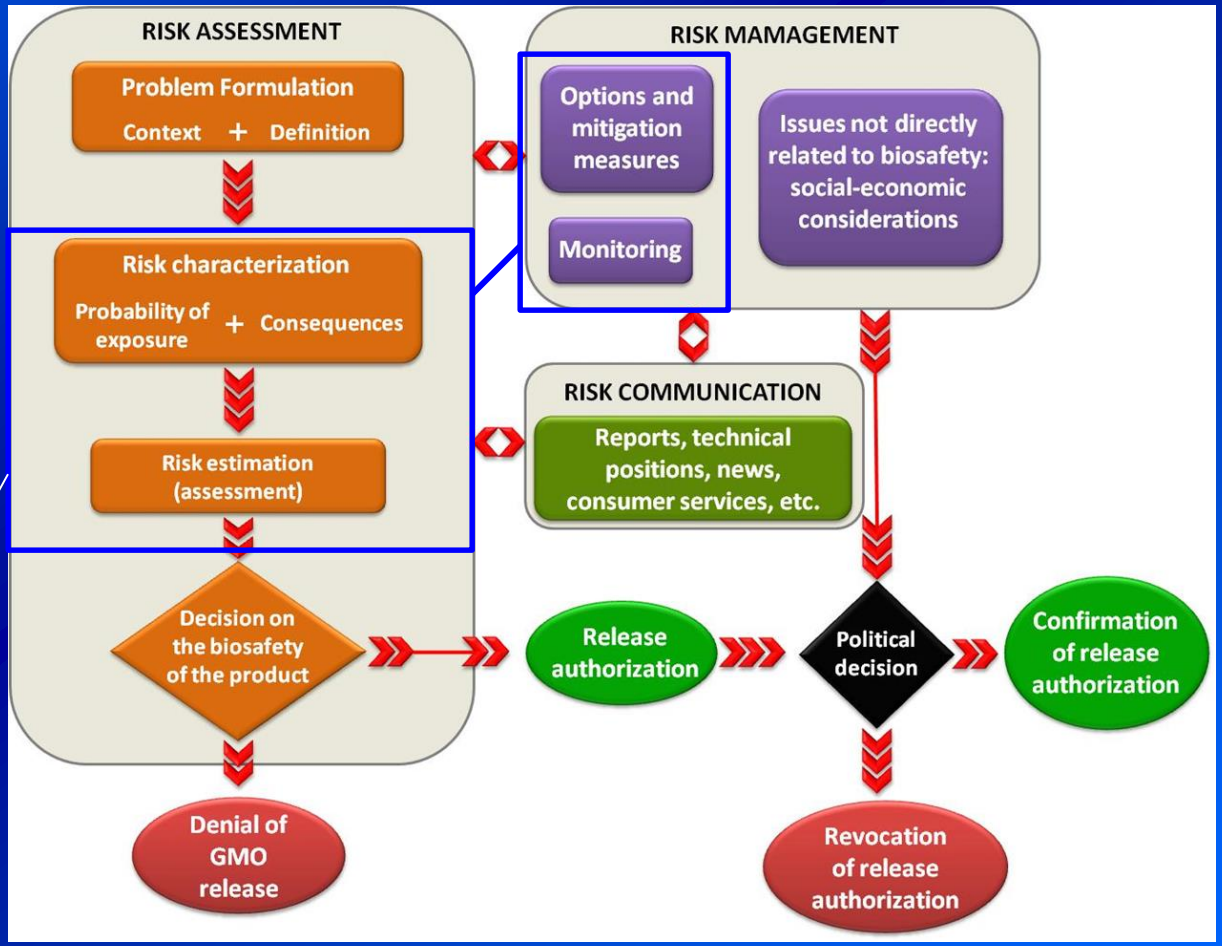
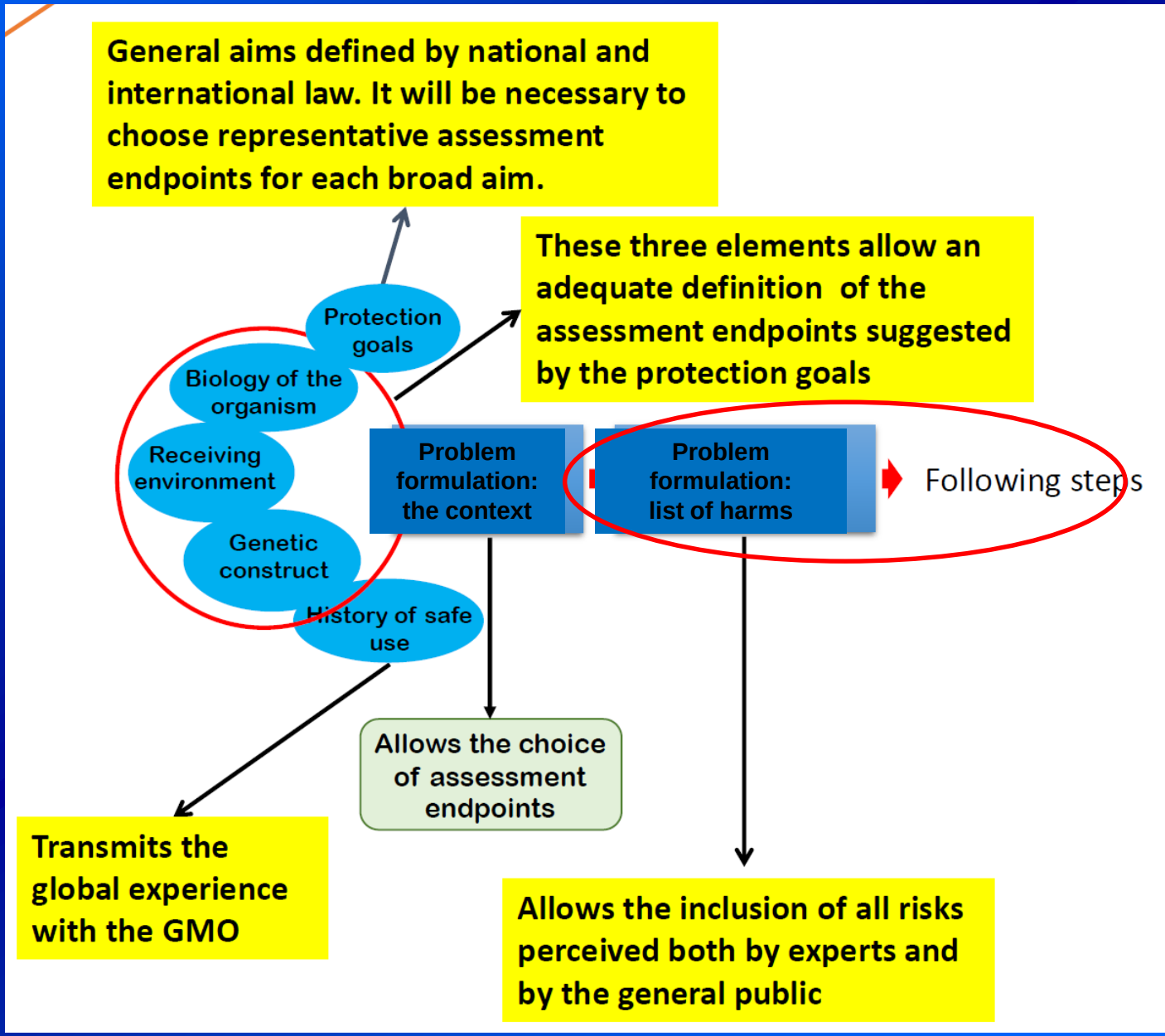
Environmental Risk Assessment (ERA) is embedded within a broader sociopolitical process termed Risk Analysis…

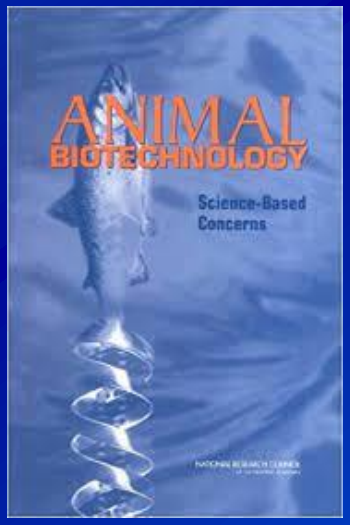
I'll be focusing on *two* parts – risk assessment and risk management – and on *environmental* endpoints…



Problem formulation is the foundation for risk assessment, identifying the harms whose ikelihood we will estimate…



Principles of environmental risk assessment



Sequence of steps:

- Identify potential *harms* – negative outcomes
- Identify the *hazard* that might lead to harms – the biotech animal
- Assess *probability of exposure* – likelihood of escape and persistence of that animal in receiving ecosystem
- Assess *probability of harm given exposure*
- $R = P(E) \times P(H|E)$

Note that these questions will be primarily answered by the applicant, but regulators should be trained to understand and oversee the risk assessment process.

Harms

Negative outcomes from exposure to the biotech animal:

- Decline or loss of a locally adapted population in the receiving ecosystem
- Decrease in ecosystem services – e.g., declines of a fishery, impact upon water quality or nutrient cycling

Jau catfish,
Zungaro jahu

Hazard

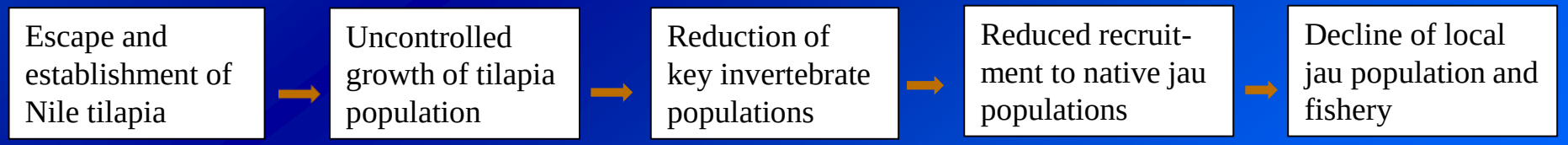
The biotech animal itself:

- Can the animal persist and establish itself in the receiving ecosystem?
- Is it native or *non*native?
- Are there sexually compatible species in the receiving ecosystem?
- Can escape and dispersal be prevented?
- Is the species invasive?
- Does the species pose ecological harm (e.g., from predation or competition)?
- Is there a history of safe use?

Pathways to harm

- How might exposure to the hazard lead to harm to your protection goal?
- Consider *all* pathways to harm – *note that some may be more relevant than others!*

- Pathway for harm for a transgenic Nile tilapia in Brazil:
  - Protection goal: Native jau catfish
  - Possible harm: Decline or loss of that fishery
- Risk pathway:



- → *What is the likelihood of this pathway to harm being realized?*

Probability of exposure

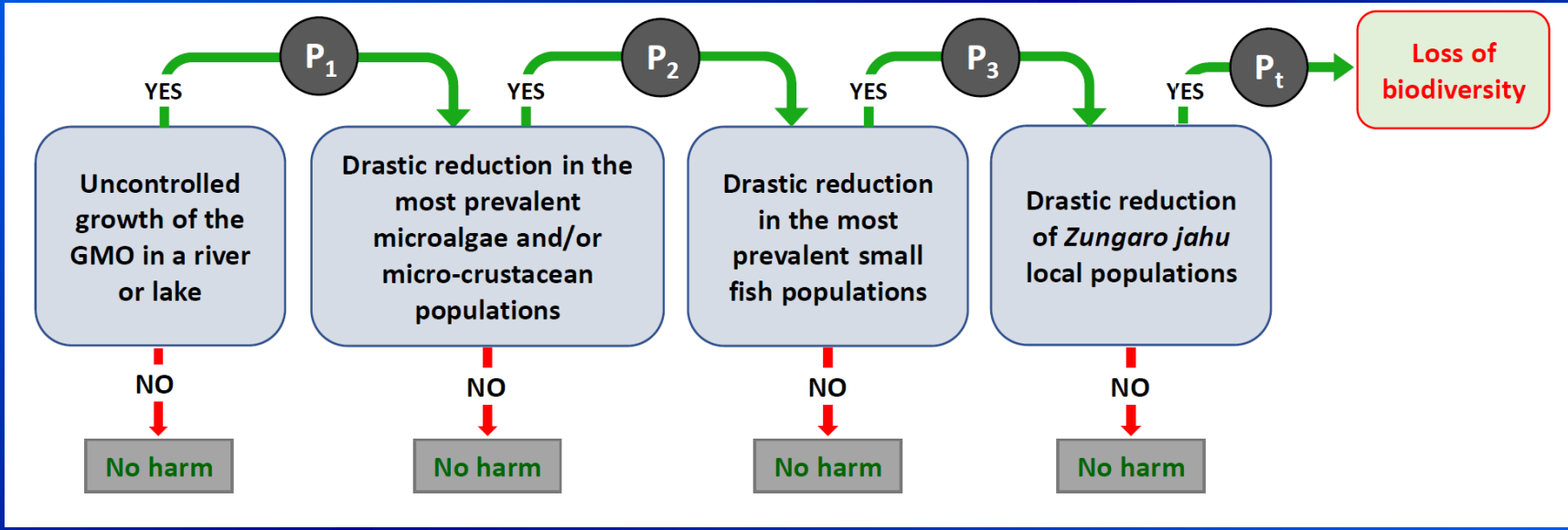
- What is the likelihood that the biotech animal will *escape* and *become established* in the receiving ecosystem?
- That likelihood follows from the production system used!

Poorly confined

Well confined

Probability of harm being realized upon exposure

- The chain of causality must be realized for harm to result, e.g.:



- $P(H|E)$ is the product of each of these causal stages being realized
- Note that we considered just one risk pathway; there may be additional ones

Note that risk assessment may be:

- Quantitative – produces continuous risk estimates
- Semi-quantitative – produces interval outputs (<10%, 10-50%, >50% risk)
- Qualitative – produces nominal outputs (low, medium, or high risk), based on expert or stakeholder opinion
- *Qualitative assessment is often sufficient to characterize and manage environmental risk*

Estimation of risk

- We then consider the likelihood of exposure and the risk of harm being realized given exposure that we just estimated to assess the risk associated with that pathway:

		LIKELIHOOD OF *H|E*			
LIKELIHOOD OF EXPOSURE	Very high	Low	Moderate	High	High
	High	Low	Low	Moderate	High
	Low	**Negligible**	Low	Moderate	Moderate
	Very low	**Negligible**	**Negligible**	Low	Moderate
		Marginal	Minor	Intermediate	Major
		OVERALL RISK			

- In most regulatory contexts, only marginal risk would prove acceptable

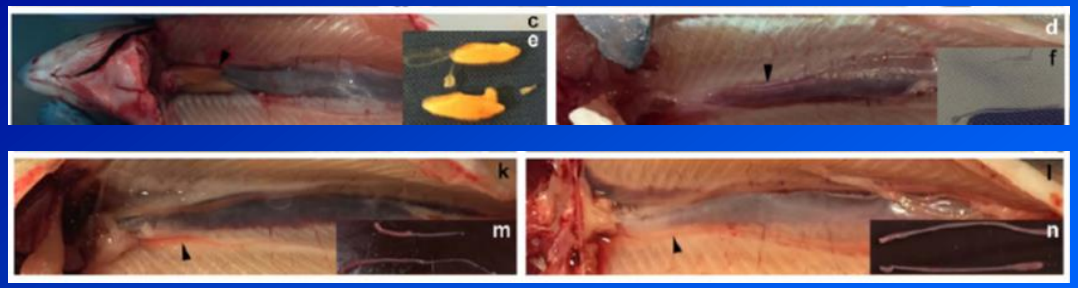
Environmental risk assessment

- Note that risk management is an *integral* part of the risk assessment process
- Recognize that $R = \boxed{P(E)} \times P(H|E)$;
- Hence, R may be minimized by minimizing $P(E)$

- Geographic confinement – produce the animal in a place where it will not persist outside of your facility – e.g., production of Nile tilapia in a temperate zone

Physical confinement

Reproductive confinement



Wild type

dnd knockout

Kleppe et al. (2017)

Perspectives on the process

- This constituted *one* pass through the risk assessment and management process
- At this point, any remaining stakeholder questions may remain relevant, or not
- Note that *some* questions may be answered by literature review, expert opinion, and laboratory experiments, as opposed to full-scale field experiments
- Only *relevant* questions should trigger new experiments
- Mandating studies disproportionate to risk increases cost and discourages development and use of innovations.

Risk analysis as an adaptive process

I have focused here

… but note that risk assessment serves a larger regulatory and societal process

These feedbacks make the regulatory regime "adaptive"

Ecological risk assessment

- Considered on a case-by-case basis:
- Host species
- Genomic change
- Receiving ecosystem

- *Let's consider some case studies…*

Case study – Slick cattle

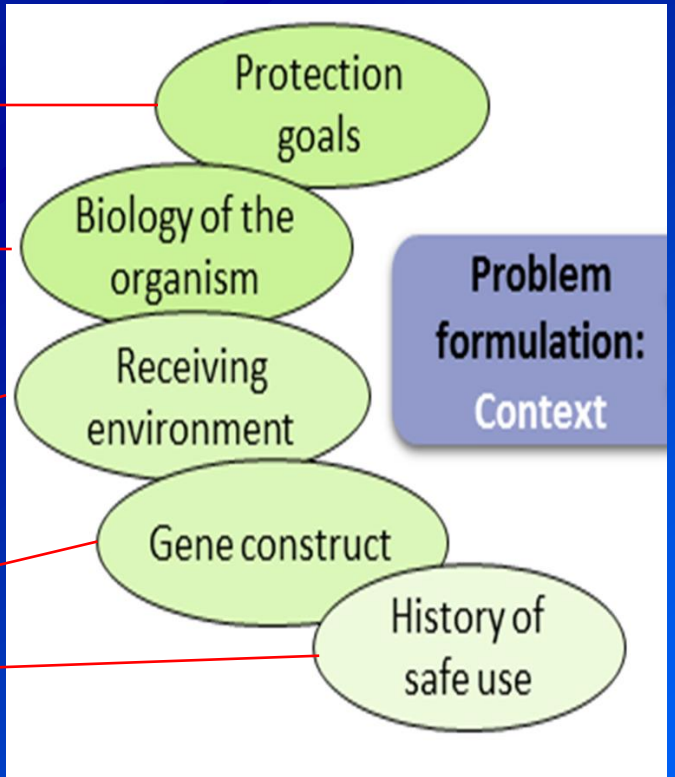
Biodiversity → no obvious goal

Non-native
No sexually compatible species
Dispersal easily controlled
Not invasive
Not relevant for wildlife food chain

Agricultural systems

CRISPR/Cas9 → gene silencing

Yes



Responses suggest no greater risk than conventional cattle production

Case study – *mstn* knockout tilapia

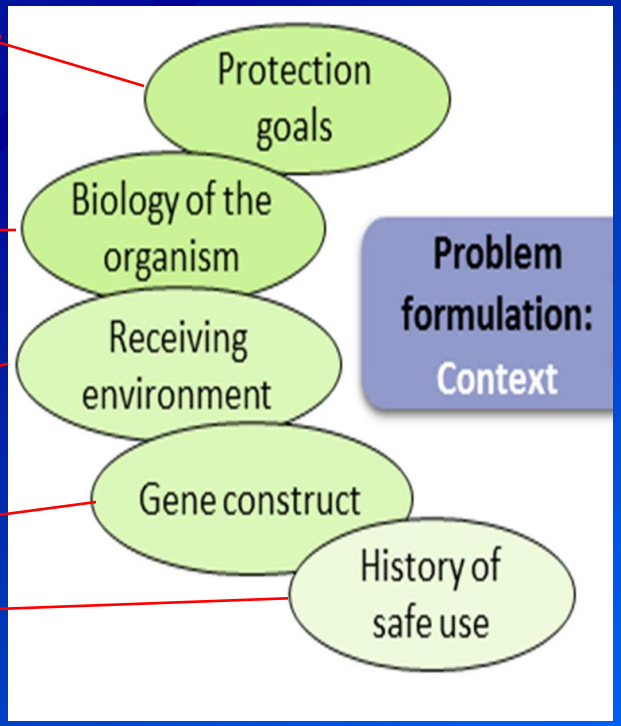
Biodiversity → competing native species

Non-native
No sexually compatible species
Dispersal hard to control
An *invasive* species
Relevant for aquatic food chain

Ponds, rivers, and lakes

CRISPR/Cas9 → gene silencing

No



Responses suggest need for effective confinement

Case study – PRRSV-resistant pig

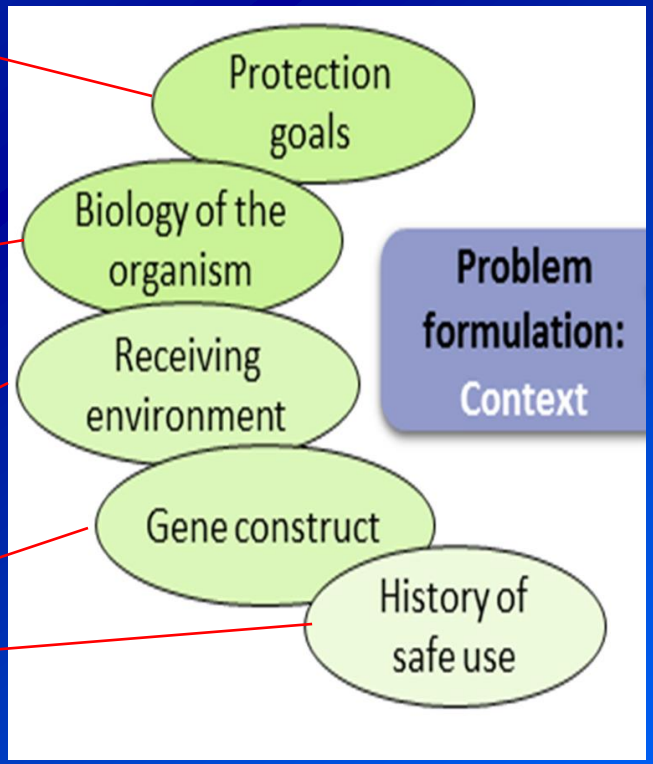
Biodiversity → no obvious goal

Non-native
No sexually compatible species
Dispersal likelihood a function of confinement
An *invasive* species
Poses risk of harm to native ecosystems

Agricultural systems

CRISPR/Cas9 → gene silencing

To some extent



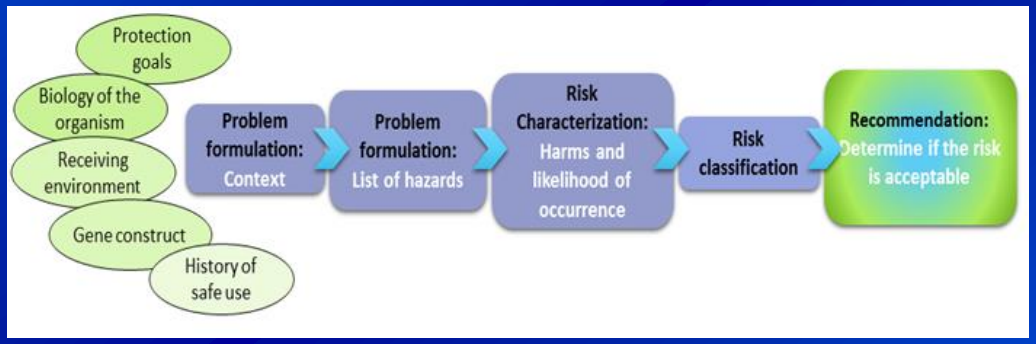
Responses suggest need for effective confinement

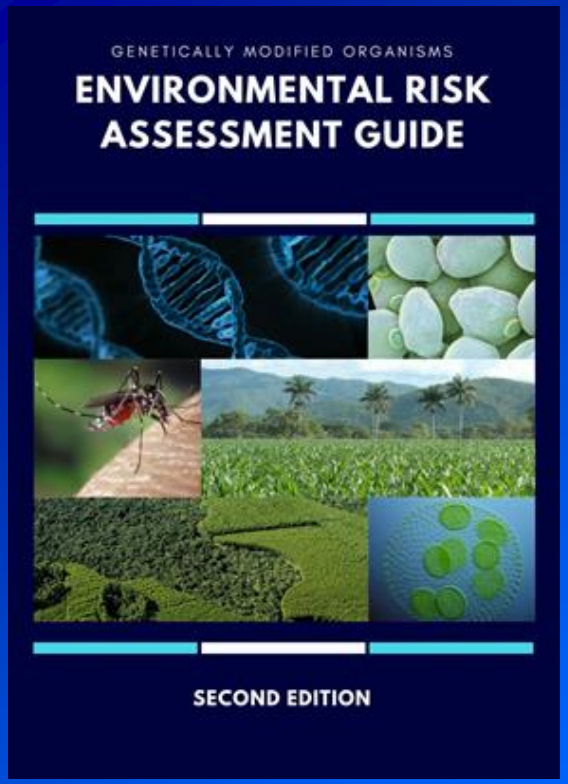
Take-home messages

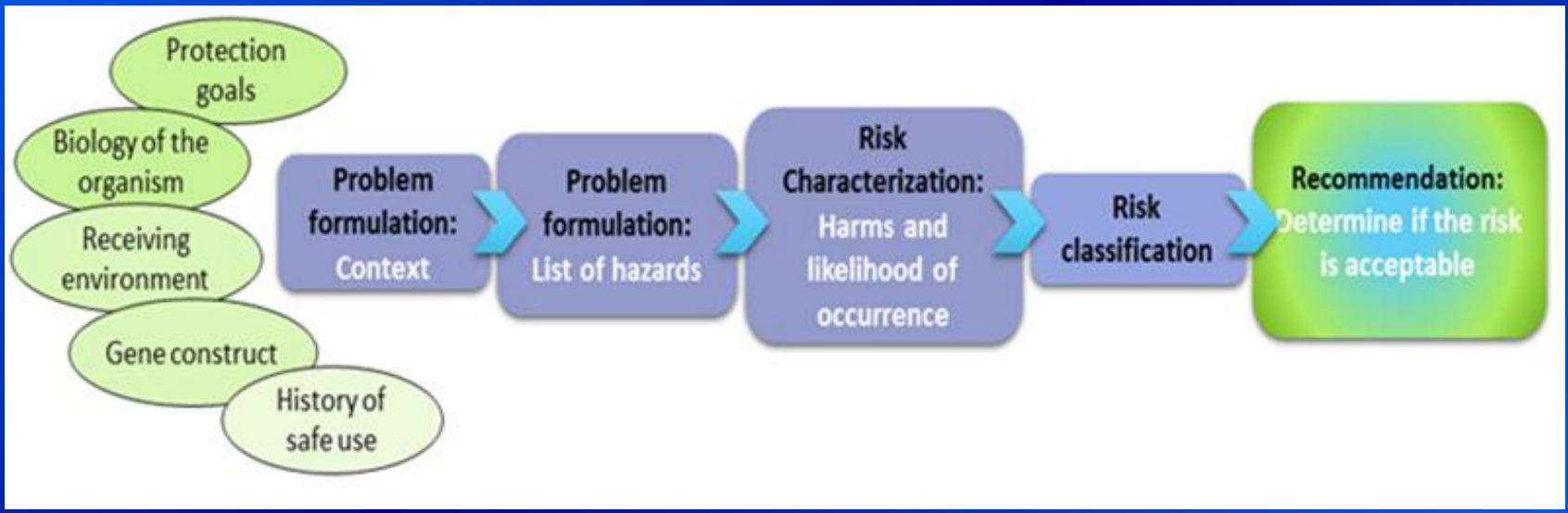
- Environmental risk assessment *is* relevant for regulatory oversight of many GE animals
- Frame the relevant questions thoughtfully in the context of the product and its production in *your* regulatory context
- Qualitative risk assessment will prove sufficient in many cases to identify, estimate, and manage any risks

Continue your learning…

- There are useful, user-friendly resources…
- http://2015.igem.org/wiki/images/9/98/Tec_Guadalajara_ERA_Guide.pdf






Protection goals
Biology of the organism
Receiving environment
Gene construct
History of safe use
Problem formulation: Context
Problem formulation: List of hazards
Risk Characterization: Harms and likelihood of occurrence
Risk classification
Recommendation: Determine if the risk is acceptable