Tools for Prioritizing Food Safety Concerns: An FDA Perspective

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Risk Management Challenges for FDA

Managing Food Safety Risk

- Each year CFSAN is called upon to deal with a series of new challenges in the areas of
  - Food Safety
  - Food Defense
  - Nutrition
  - Dietary Supplements
  - Cosmetics and Colors
- Additional have to maintain our ability to managed known foodborne hazards

Managing Food Safety Risk

Melamine

Spinach / EHEC

Clostridium botulinum / Carrot juice

FALCPA Implementation

Lettuce / EHEC

Raw milk cheeses / Listeria

Lead / Candy

Tomatoes / Salmonella

Perchlorate

Norovirus / Cruise ships

Raw milk / Salmonella

Nanotechnology / Cosmetics

Managing Food Safety Risk

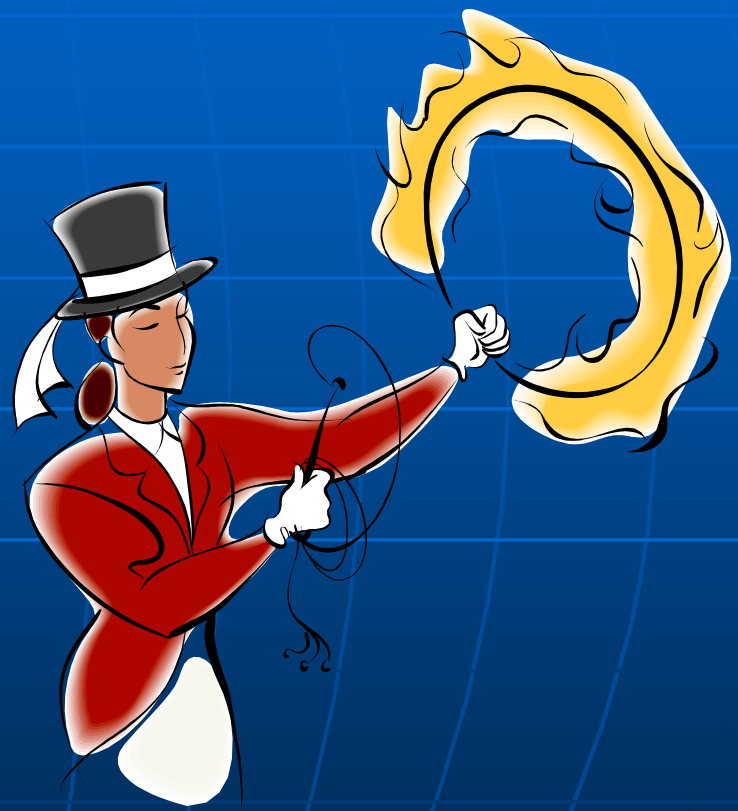
- Within each of those categories there are subsets of hazards areas that are be distinctly different in terms of adverse effects, relative risk, potential for mitigation
  - Chemical contaminants
  - Microbiological contaminants
  - Nutritional formulations
  - Food additives
  - Allergens
  - Many others

Managing Food Safety Risk

- We have a full table
- Trying to do everything means that nothing gets done well
- Have to make decisions on what hazards we will focus our efforts

Managing Food Safety Risk

- **Have various drivers that push us in different directions**
  - Public health threats
  - Administration goals
  - Congress
  - Press
  - Consumer groups
  - Industry
  - International trade



Managing Food Safety Risk

- While FDA will always have to respond to changing priorities and stakeholder concerns, it would benefit greatly from a more objective considerations of risks and our potential for mitigation
- Particularly important for 3 – 5 year budget planning

Risk Ranking

Risk Ranking

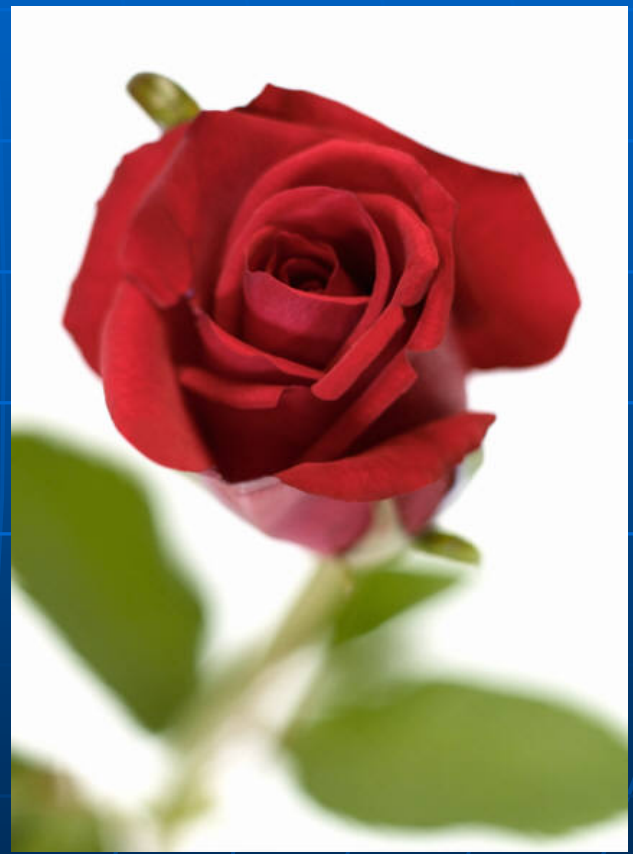
- Currently one of the most active areas of non-laboratory research is "risk ranking" risk assessment techniques as a means of finding more objective comparisons of risks to aid in the allocation of scarce food safety resources
  - Risk ranking risk assessment
  - IFT Contract for the Food and Drug Administration
  - Food Safety Research Consortium "Attribution and Risk Ranking" Project

Risk Ranking Terminology

Also known as

- Hazard Ranking
- Risk Attribution
- Risk-Based Priority-Setting
- Comparative Risk Assessment (CRA)
- Maintaining a “Risk Register”

Primary purpose is priority setting



Risk Ranking

- Technique that has been used for the past 20 years for priority setting
- Early work in U.S. focused on priority setting for environmental hazards
- Largely started as a qualitative or semi-quantitative approach
- Confused risk management and risk assessment - initially as a series of risk profiles – got a tarnished reputation as a result

Risk Ranking

- Can span the entire qualitative to quantitative spectrum with all the benefits and limitations of each
- Complexity increases with number of:
  - Class of agents (e.g., chemical, microbiological)
  - Agents within a class
  - Biological end points associated with an agent
  - Food classes
  - Diversity of foods within a class
  - Diversity in susceptibility of population

Risk Ranking Risk Assessments

- **Propose six levels based on increasing difficulty**
  - **Level 1: Single agent in multiple food classes**
  - **Level 2: Single class of agents in a single food class**
  - **Level 3: Single class of agents in multiple food classes**
  - **Level 4: Multiple classes of agents in a single food**
  - **Level 5 Multiple classes of agents in a single food class**
  - **Level 6: Multiple classes of agents in multiple classes of foods**

Risk Ranking

- When going beyond a single class of hazards, the greatest challenge is finding a single metric that can be used to compare risk with different characteristics
  - Chemical vs. Microbiological vs. Allergens vs. Nutrition vs. …….
  - Acute vs. Chronic
  - Threshold vs. Non-threshold
  - Intentional vs. Non-intentional
  - Potential for mitigation

Personal Thoughts on Framework for Risk Ranking that “Works” for Regulatory Agencies

Thoughts on Risk Ranking

f(Exposure) X f(Dose Response) = Adverse Events

- For each risk there is a relationship between exposure and adverse events
- Ideally solve for f(E) and f(DR) to predict AE and then validate against independent measure of AE
  - If know two of the factors, can determine the third
  - Differences in risk assessment modeling approaches reflect which two factors are known and to what degree
- Know how to do this fairly well for single agents

Thoughts on Risk Ranking

- Have not done as well in considering severity
- One potential approach is to consider multiple biological end points:

$$f(E_1) * f(DR_1) = AE_1$$
$$f(E_2) * f(DR_2) = AE_2$$
$$f(E_3) * f(DR_3) = AE_3$$
$$\downarrow$$
$$f(E_n) * f(DR_n) = AE_n$$

Thoughts on Risk Ranking

Would then have weight the impact of each biological end point so they can be summed:

$$\text{Severity } (S_o) = AE_1 * WF_1 + AE_2 * WF_2 + AE_3 * WF_3 + \ldots AE_n * WF_n$$

- *WF = weighting factor for each biological end point
- Could be relative public health consequences, economic impact, etc – find common metric

Thoughts on Risk Ranking

- To be fully useful to risk managers for priority setting, need consideration of potential for control
  - Inherent risk vs. loss of control (compliance)
  - Potential for risk reduction – finding the low hanging fruit vs. this is as good as it gets

Example: Role of Compliance

% Defectives (10^6 cfu/g)	Criteria: 0.04 CFU/g	Criteria: 100 CFU/g
0.00000	0.5*	5.7
0.00001	1.7	6.9
0.00010	12.3	17.4
0.00100	119	124
0.01000	1,185	1,191
0.01800	2,133	2,133
0.10000	11,837	11,848
1.00000	117,300	117,363

FAO/WHO *Listeria monocytogenes* risk assessment

Thoughts on Risk Ranking

- Consideration of risk management options
  - Need to consider multiple options within each hazard
  - WTO SPS agreements requires consideration of equivalent options
    - Developed nations vs. Developing nations
  - May have to do sufficient “what-if scenarios” to characterize impact of risk management options for each hazard
- Avoid making risk management decisions within the risk assessment - focus on a uncertainty neutral risk assessment

Thoughts on Risk Ranking

$$S_R = S_o * MP$$

- In order to make informed decision about program priorities, need to assess "mitigation potential" (MP) on the extent of the severity reduction (S_R) achieved through an intervention
- Need to compare the MPs for each hazard
- Within a hazard, ranking of MPs could be the best basis for
  - Short term goals
  - Investments in research for intermediate term goals
  - Identifying what areas require entirely different approaches (long term goals)
  - Differentiating need for enhanced compliance vs. development of new risk reduction strategies

Thoughts on Risk Ranking

- For hazards where there are multiple risk management options, may have to consider multiple control measures

$$S_R = S_o [MP_1 * Opt_1 + MP_2 * Opt_2 \ldots + MP_n * Opt_n]$$

$Opt_{1 \rightarrow n}$ = % of food serving produced using control measure 1→n

Thoughts on Risk Ranking

$$S_F = S_o - S_R = S_o(1- MP)$$

- Could base longer term food safety activities on final (residual) severity (S_F) magnitude based on differential between S_o and S_R

Risk Ranking: Hypothetical Example

Hazard	Diarrheal Cases	Septicemia Cases	Death
Salmonellosis	1,000,000	1000	10
Listeriosis	200	2000	400
Campylo-bacteriosis	2,000,000	1000	5
Mycobacterium bovis tuberculosis	0	100	2

Risk Ranking Example

Diarrhea: 1X, Septicemia: 10X, Death: 1000X

Hazard	Diarrheal Cases	Septicemia Cases	Death	S_o
Sal.	10^6	10,000	10,000	1.020×10^6
List.	200	20,000	4×10^5	4.20×10^5
Camp.	2×10^6	10,000	5,000	2.015×10^6
TB	0	1000	2000	3.00×10^3

Risk Ranking Example

Hazard	S_o	MP	S_R	S_F
Sal.	1.020×10^6	0.30	3.06×10^5	7.14×10^5
List.	4.20×10^5	0.50	2.10×10^5	2.10×10^5
Camp.	2.015×10^6	0.10	2.015×10^5	1.80×10^6
TB	3.0×10^3	0.90	2.7×10^3	3.0×10^2

Thoughts on Risk Ranking

- At some point “ability to pay” and “return on investment” will be have to be factored into the analysis
- Costs are not just $$$

Thoughts on Risk Ranking

- **Do we worry too much about dose-response relations?**
  - **In most cases risk mitigation involves changing exposure and does not involve changing host susceptibility**
  - **Still conceptual challenges with**
    - **Modeling subpopulations that are more susceptible**
    - **Dealing with agents where a portion of the population is not susceptible**
- **Potential area for simplification**

Thoughts on Risk Ranking

- **Challenges**
  - Increasing the ability to quantify risk rankings
  - Finding a common metric (Daly? Qaly? PseduoQaly?)
  - Comparing long and short term risks
  - Comparing hazards with different risk perceptions
  - Conducting “uncertainty neutral” risk rankings

Thoughts on Risk Ranking

- Our future success in advancing risk ranking techniques beyond level 2 is going to be highly dependent on finding a common metrics that is reasonable, understandable to the public, and easy to use