Nanotechnology: a new emergent technology - addressing uncertainties in risk assessment through structured expert opinion elicitation

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- **Start** on 12/2008
- CFSAN, FDA – USA: Villie's secondment from Fera
  - Initial point:
    - Interagency Risk Assessment Consortium (IRAC)
    - Led IRAC working group on "Nanotechnology and Risk Assessment"

- **Since** 11/2009
- Fera, Defra - UK
    - Cross programme collaboration
    - Partially funded by MoniQA European Union network of excellence

A joint effort that brings on board expertise from different fields

Mr **Rabin Neslo -** Applied Mathematician
Post-graduate student.

Prof **Roger Cooke -** Mathematician, Philosopher
Expert in uncertainty analysis & expert opinion elicitation.

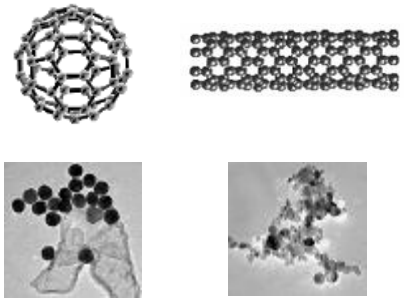
Dr **Qasim Chaudhry -** Chemist, Biochemical Toxicologist. Expert in nanotechnology field.

Dr **Villie Flari -** Risk Analyst, Biologist
Specialized in structured methodologies to elicit expert judgment and in communication of scientific uncertainties.

Interagency Risk Assessment Consortium
Lead of working group on "Nanotechnology and Risk Assessment"

Nanotechnologies – potential benefits

Nano-sized materials



- ✓ Less use of chemicals (e.g. catalysts, paints & coatings)
- ✓ Novel functional materials (e.g. packaging, construction)
- ✓ Healthy food products (e.g. less use of fat, salt, preservatives);
- ✓ Longer shelf-life of foodstuffs;
- ✓ Improved health and wellbeing (greater bioavailability of nutrients & supplements)
- ✓ Nano(bio)sensors for diagnostics and monitoring
- ✓ Cleanup of contaminated environments
- ✓ Water desalination and decontamination
- ✓ Nano-medicines (targeted drug delivery)

Sector Applications

- Cosmetics and personal care products
- Paints & coatings
- Catalysts & lubricants
- Security printing
- Textiles & sports
- Medical & healthcare
- Food and nutritional supplements
- Food packaging
- Agrochemicals
- Veterinary medicines
- Water decontamination
- Construction materials
- Electrical & electronics
- Fuel cells & batteries
- Paper manufacturing

Challenges

Risk assessment and decision making in the face of large gaps of knowledge

- Safety of nanomaterials to human health and the environment
- Technological challenges – detection/ characterisation, toxicological evaluation of nanomaterials
- Societal issues – ownership of benefits, responsibilities, liabilities
- Policy and regulatory issues
- **Major knowledge gaps** - will require a long time to address

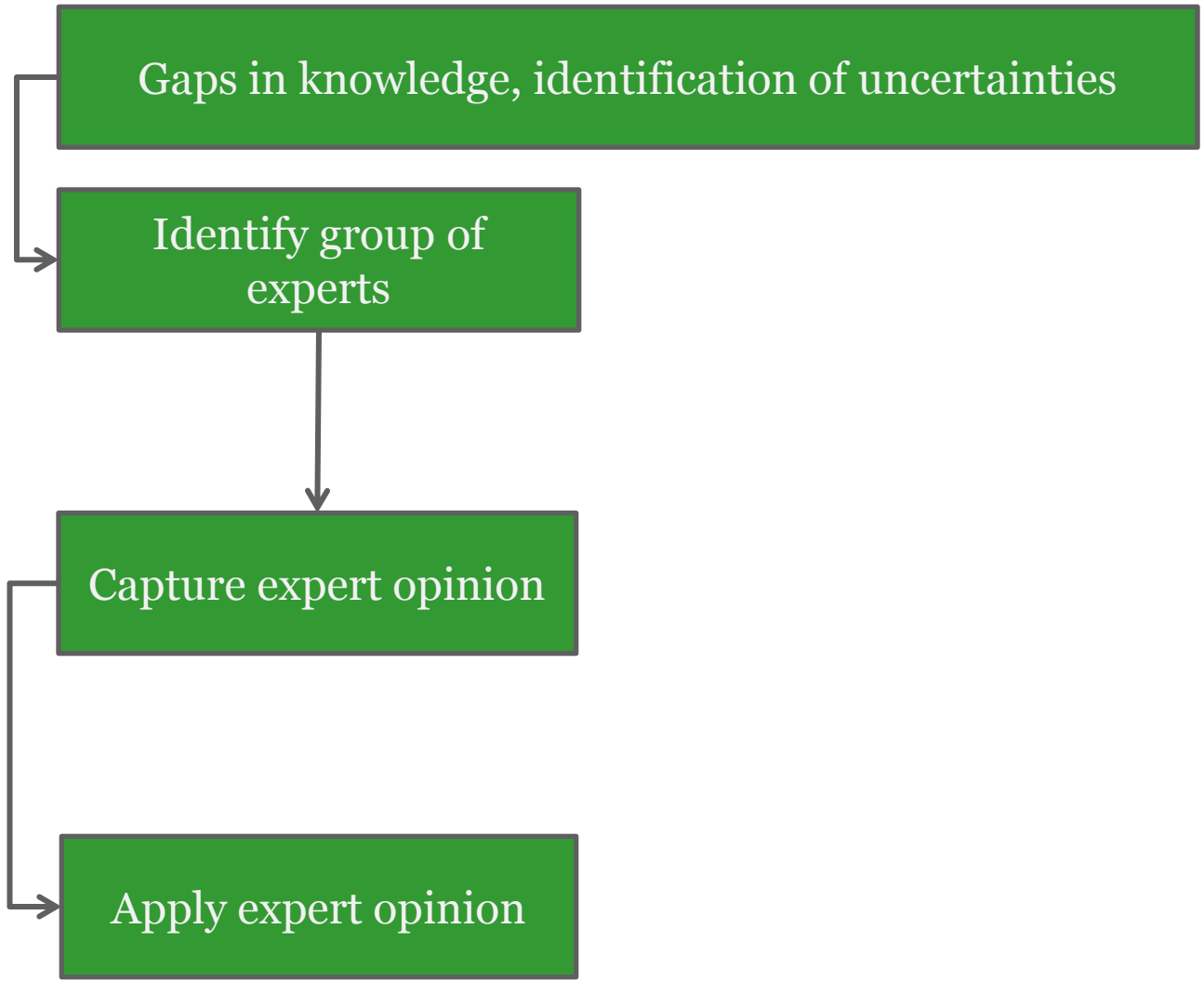
Challenges

Risk assessment and decision making in the face of large gaps of knowledge

- This level of uncertainty requires expert judgment
- Experts' judgment will vary: some will think from the exposure point of view, others from hazard point of view, etc.
- Coherent way to capture experts' knowledge on known and unknown?

EXPERT JUDGMENT – STATUS QUO

Risk assessment and decision making in the face of large gaps of knowledge



EXPERT JUDGMENT - QUESTIONS

Risk assessment and decision making in the face of large gaps of knowledge

Gaps in knowledge, identification of uncertainties

Identify group of experts

Why A expert instead of B expert?
Were the experts the most informative?
Were they under-confident, over-confident?

Capture expert opinion

Uncertainty of experts more often than not, not captured; if it is, it is captured via arbitrary scoring

Apply expert opinion

Expert opinion is not assessed; validity of expert opinion remains vulnerable to criticism

EXPERT JUDGMENT – ADDRESS QUESTIONS

Risk assessment and decision making in the face of large gaps of knowledge

Gaps in knowledge, identification of uncertainties

Identify group of experts

Why A expert instead of B expert?
Were the experts the most informative?
Were they under-confident, over-confident?

Calibrate experts

Capture expert opinion

Uncertainty of experts more often than not, not captured; if it is, it is captured via arbitrary scoring

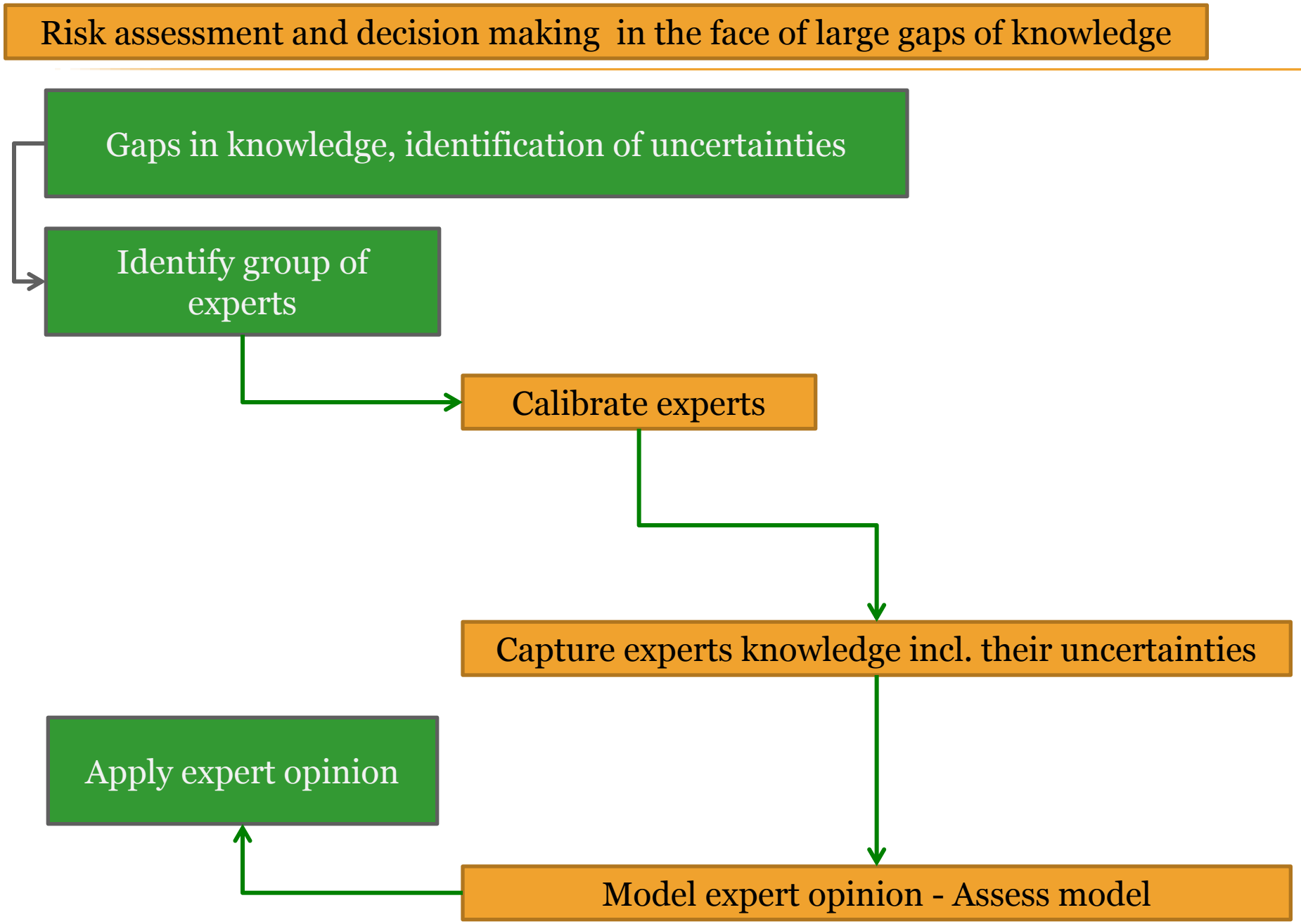
Capture experts knowledge incl. their uncertainties

Apply expert opinion

Expert opinion is not assessed; validity of expert opinion remains vulnerable to criticism

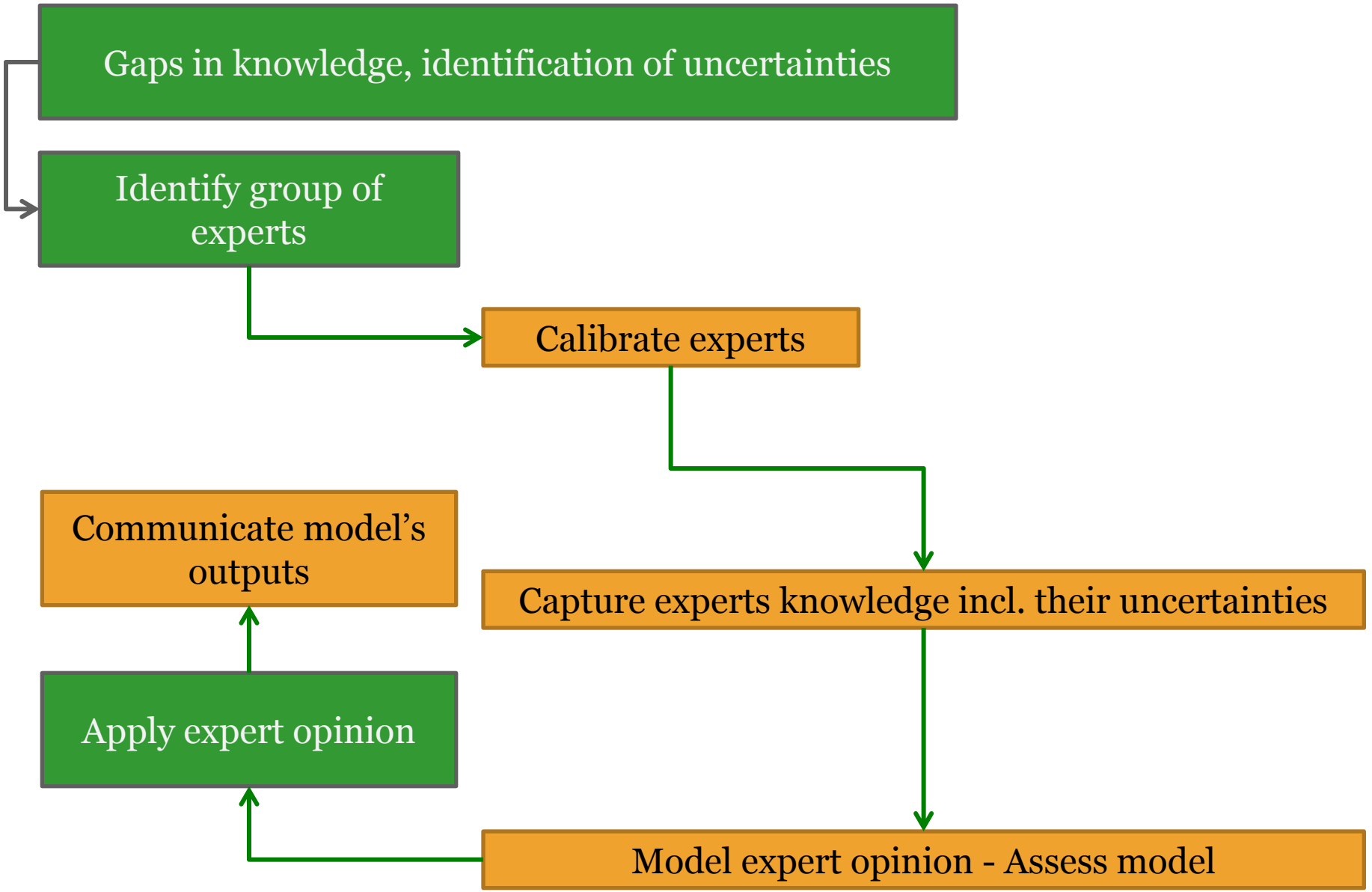
Model expert opinion - Assess model

EXPERT JUDGMENT – ADDRESS QUESTIONS



EXPERT JUDGMENT – ADDRESS QUESTIONS

Risk assessment and decision making in the face of large gaps of knowledge



EXPERT JUDGMENT PROTOCOL

The method models **expert knowledge (rankings)** by employing probabilistic inversion.

(in our case 21 **experts** on **nanotechnology research in the food sector**)

STEP 3: IDENTIFY & RECRUIT EXPERTS

(in our case **rankings** on 26 **hypothetical nanotechnology-enabled food products**)

STEP 4: ELICITATION

These **hypothetical nanotechnology-enabled food products** are **precisely defined** (by us) via a number of **criteria** or attributes.

STEP 2: SCENARIOS

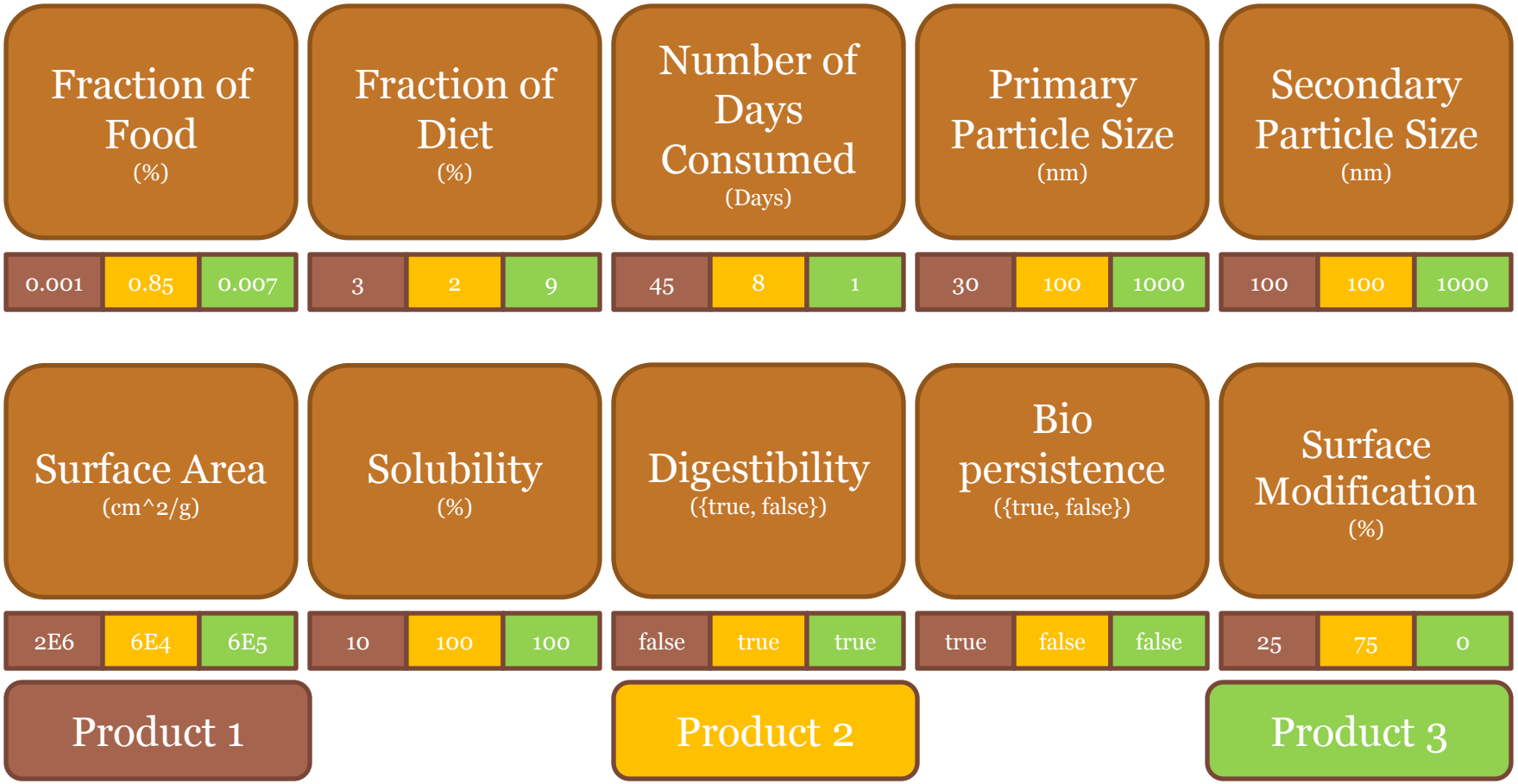
In our case these **criteria** are a number of **attributes** that are considered as **significant** in order to **assess/evaluate potential risk considerations** of **nanotechnology-enabled food products**.

STEP 1: CRITERIA

MOTIVATION

- What is the problem?
  - Large number of nanotechnology-enabled products, either in the market or being developed
  - Safe or not safe?
  - Classic paradigm of risk assessment possible, but…
  - ..lack of data – expert judgment unavoidable
- Possible solution
  - Identify most important criteria for assessing risk/safety
  - Create a screening tool

THE CRITERIA



MULTI CRITERIA DECISION MODEL (MCDM)

Conventional Methods

- Assign weights directly
- Computes scores
- No validation

Probabilistic Inversion

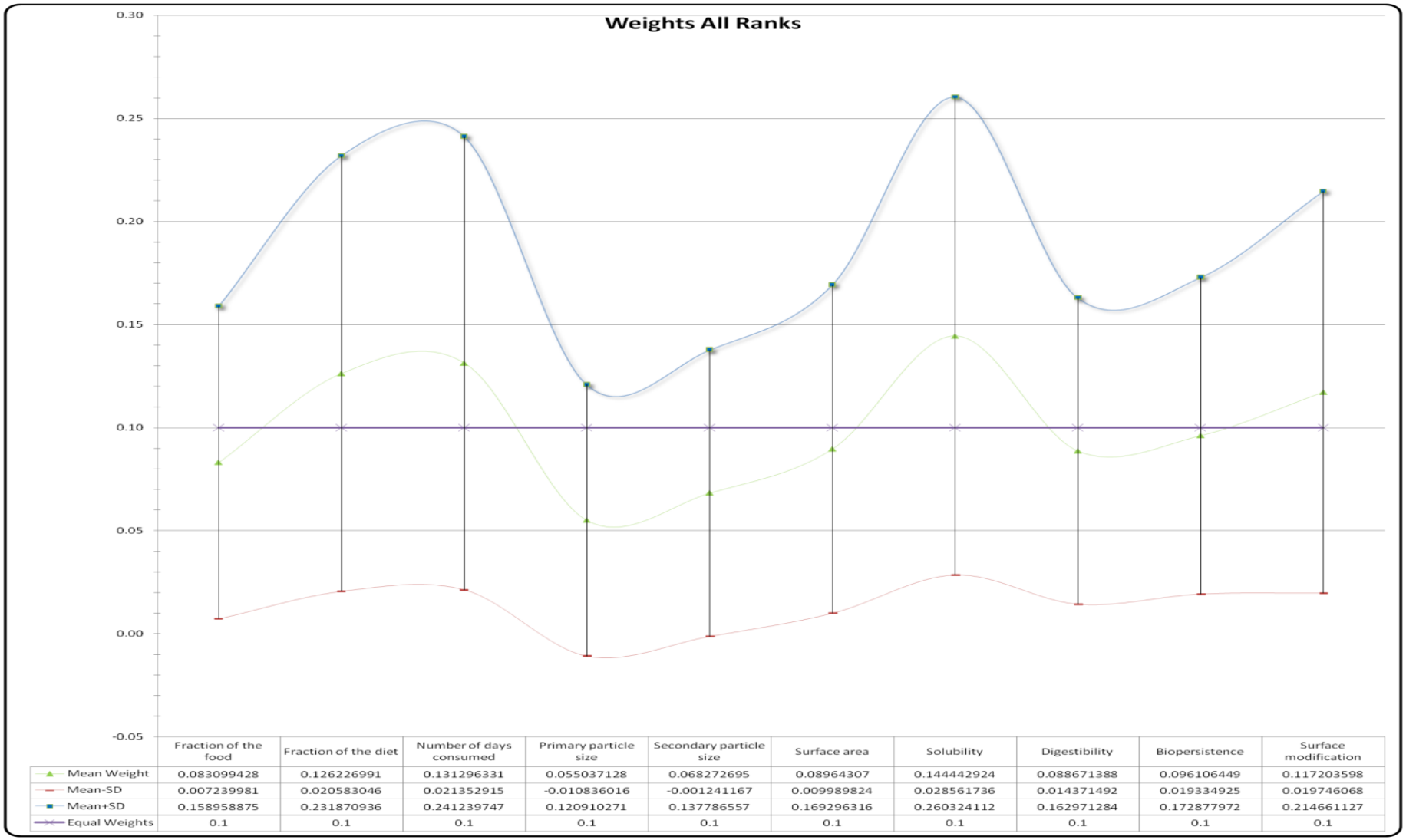
- Asks for ranks
- Finds a distribution over weights that recovers ranks
- Computes Scores
- Validation

$$\text{Score}(\text{product}(i)) = \sum_k \text{value}(\text{criterion}(k), i) \times \text{weight}(\text{criterion}(k))$$

VALIDATION

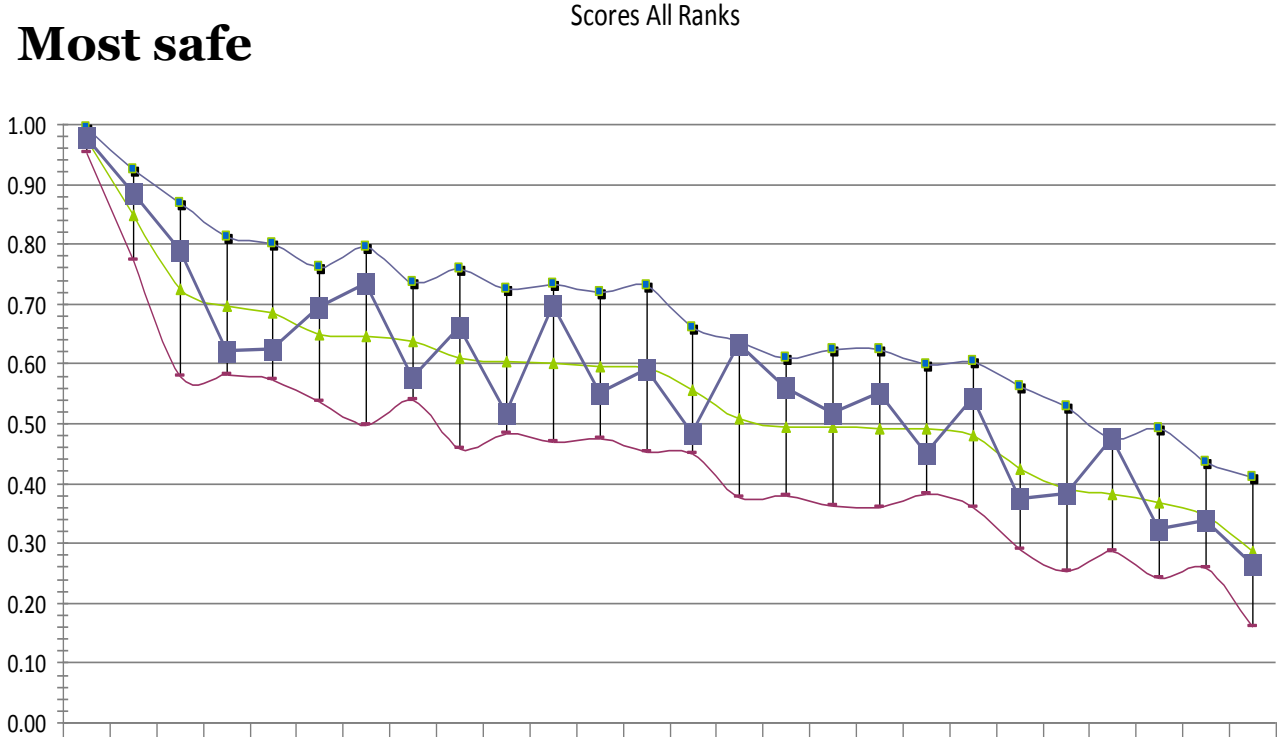
- Checks if experts' ranks are recovered from the distribution over weights
- Splits experts' ranks in a training set and a validation set
  - Solves model using training set
  - Tries to recover ranks in the validation set

RESULTS – MODELLING EXPERT JUDGMENT



	Fraction of the food	Fraction of the diet	Number of days consumed	Primary particle size	Secondary particle size	Surface area	Solubility	Digestibility	Biopersistence	Surface modification
Mean Weight	0.083099428	0.126226991	0.131296331	0.055037128	0.068272695	0.08964307	0.144442924	0.088671388	0.096106449	0.117203598
Mean-SD	0.007239981	0.020583046	0.021352915	-0.010836016	-0.001241167	0.009989824	0.028561736	0.014371492	0.019334925	0.019746068
Mean+SD	0.158958875	0.231870936	0.241239747	0.120910271	0.137786557	0.169296316	0.260324112	0.162971284	0.172877972	0.214661127
Equal Weights	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1

RESULTS – MODELLING EXPERT JUDGMENT



	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
Score	0.97	0.85	0.72	0.7	0.69	0.65	0.65	0.64	0.61	0.6	0.6	0.6	0.59	0.55	0.51	0.49	0.49	0.49	0.49	0.48	0.43	0.39	0.38	0.37	0.35	0.29
Mean-SD	0.95	0.77	0.58	0.58	0.57	0.54	0.5	0.54	0.46	0.48	0.47	0.48	0.45	0.45	0.38	0.38	0.36	0.36	0.38	0.36	0.29	0.25	0.29	0.24	0.26	0.16
Mean+SD	1	0.93	0.87	0.81	0.8	0.76	0.8	0.74	0.76	0.72	0.73	0.72	0.73	0.66	0.64	0.61	0.62	0.62	0.6	0.6	0.56	0.53	0.48	0.49	0.44	0.41
Equal Weights	0.98	0.89	0.79	0.62	0.62	0.7	0.73	0.58	0.66	0.52	0.7	0.55	0.59	0.48	0.63	0.56	0.52	0.55	0.45	0.54	0.37	0.38	0.47	0.32	0.34	0.26

Experts' variability

→Scenarios

RESULTS – MODELLING EXPERT JUDGMENT

	Rank	Scenarios	Scores	Fraction of the food	Fraction of the diet	Number of days consumed	Primary particle size	Secondary particle size (Agglomeration)		Surface area	Solubility	Digestible	Bio persistent	Surface modification
Potentially safe	1	M	0.974	0.007	9	1	1000	Non agglomerated		6	100	Yes	No	0
	2	J	0.849	0.001	10	256	1000	Non agglomerated		6	80	Yes	No	0
	3	W	0.724	0.005	5	5	1000	Non agglomerated		6	0	Yes	No	100
	4	E	0.696	0.85	2	8	100	Non agglomerated		60	100	Yes	No	75
	5	L	0.686	0.9	5	50	30	100	30	200	100	Yes	No	0
Potentially unsafe	22	C	0.391	0.006	5	200	30	100	30	200	10	No	Yes	0
	23	O	0.381	0.001	15	277	100	250	100	60	10	No	Yes	25
	24	K	0.367	0.001	10	50	30	Non agglomerated		200	10	No	Yes	50
	25	G	0.347	0.001	8	243	100	Non agglomerated		60	10	No	Yes	75
	26	Z	0.286	0.001	9	360	30	Non agglomerated		200	10	No	Yes	25

RESULTS – PREDICTING EXPERT JUDGMENT

- International experts' workshop held on May 2010 at Fera, York, UK
- Experts were divided into three breakout groups
- Each breakout group devised hypothetical products that they considered either as safe or unsafe
- External validation of the model
  - We ranked these products with our model
  - Then compared the models' rankings with the expert rankings

RESULTS – PREDICTING EXPERT JUDGMENT

		Description of the product
Group 1	P1	Nano salt applied as a surface seasoning on crisps.
	P2	ZnO in low fat spreads as an antimicrobial agent.
	P3	Food colouring; Al_2O_3 to provide blue colour in children's shakes.
	P4	Nanopesticide as a residue on cereals.
Group 2	P1	Milk processed to cause a fraction of the protein content to encapsulate the lactose, forming non-digestible nano-encapsulates that render the lactose non-bioavailable and so makes the milk suitable for lactose-intolerant individuals. The milk is unchanged in all other aspects.
	P2	Skimmed (low-fat) milk processed in a way to change the fat droplets to become nano-sized and so make the milk have a more full-fat creamy mouth feel. The milk is unchanged in all other aspects.
	P3	Vitamin D encapsulated in protein that is extracted from milk, and dispersed into soft drinks. The encapsulation makes the vitamin compatible with the drink but it is readily digested to liberate the vitamin in vivo.
	P4	A nano form of iron that resists digestion but can be taken-up and then enter cells directly and then liberate iron, thus giving greater bioavailability. The application would aim to fortify breakfast cereals.
	P5	Nano gold used to coat an ice cream and so colour it.
Group 3	P1	Non digestible nanolipid in sausage to suppress appetite; the application is non water soluble, non digestible, and non bio-persistent.
	P2	Nano TiO2 in cake icing and sweets. The application is non water soluble, non digestible.
	P3	Nano carotene in margarine.

RESULTS – PREDICTING EXPERT JUDGMENT

		Score calculated by fitting the model on:							
		Potentially safe rankings		Potentially unsafe rankings		All rankings (potentially safe + potentially unsafe)		All ranks assuming equal weights for criteria	Ranking of products in terms of their safety by experts in breakout groups
		All	Most common (>0.1)	All	Most common (>0.1)	All	Most common (>0.1)		
Group 1	P1							1	1
	P2							2	2
	P3							4	3
	P4							3	4
Group 2	P1							2	3
	P2							1	1
	P3							5	2
	P4							3	4
	P5							4	5
Group 3	P1							2	2
	P2							3	3
	P3							1	1

RESULTS – PREDICTING EXPERT JUDGMENT

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Group 1	P1	1	1					1	1
	P2	2	2					2	2
	P3	3	3					4	3
	P4	4	4					3	4
Group 2	P1	2	2					2	3
	P2	1	1					1	1
	P3	4	5					5	2
	P4	3	3					3	4
	P5	5	4					4	5
Group 3	P1	2	2					2	2
	P2	3	3					3	3
	P3	1	1					1	1

RESULTS – PREDICTING EXPERT JUDGMENT

		Score calculated by fitting the model on:							
		Potentially safe rankings		Potentially unsafe rankings		All rankings (potentially safe + potentially unsafe)		All ranks assuming equal weights for criteria	Ranking of products in terms of their safety by experts in breakout groups
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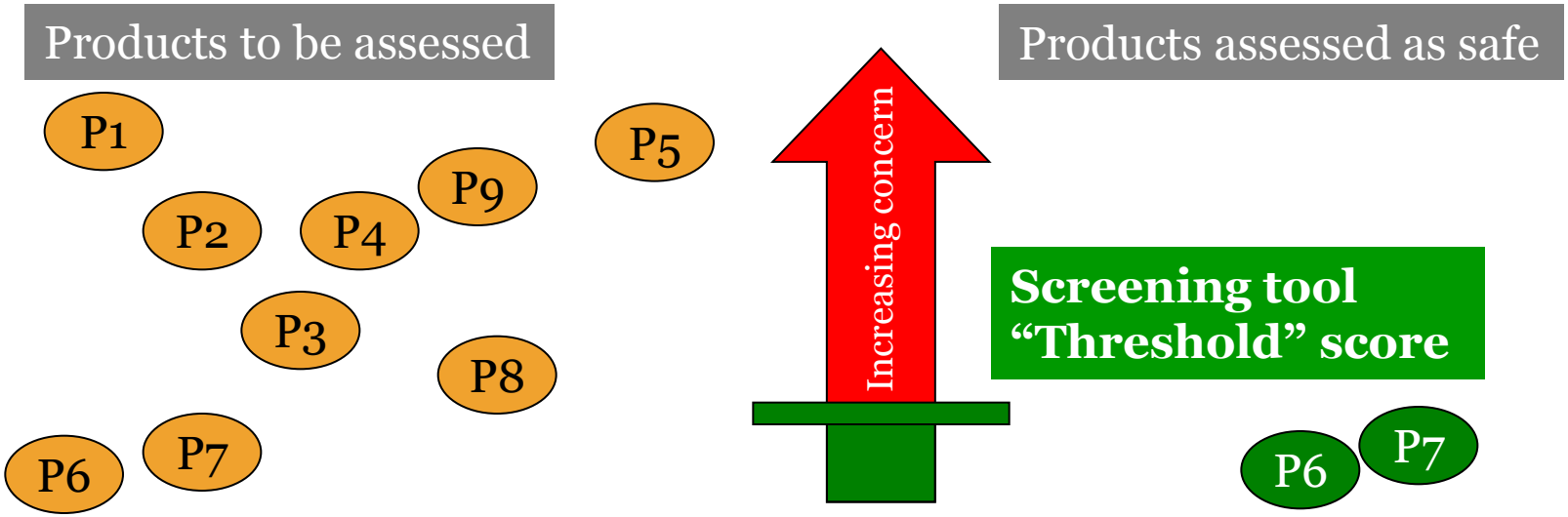
Group 1	P1	1	1	1	1			1	1
	P2	2	2	2	2			2	2
	P3	3	3	4	4			4	3
	P4	4	4	3	3			3	4
Group 2	P1	2	2	2	2			2	3
	P2	1	1	1	1			1	1
	P3	4	5	5	4			5	2
	P4	3	3	3	3			3	4
	P5	5	4	4	5			4	5
Group 3	P1	2	2	2	2			2	2
	P2	3	3	3	3			3	3
	P3	1	1	1	1			1	1

RESULTS – PREDICTING EXPERT JUDGMENT

		Score calculated by fitting the model on:							Ranking of products in terms of their safety by experts in breakout groups
		Potentially safe rankings		Potentially unsafe rankings		All rankings (potentially safe + potentially unsafe)		All ranks assuming equal weights for criteria	
		All	Most common (>0.1)	All	Most common (>0.1)	All	Most common (>0.1)		
Group 1	P1	1	1	1	1	1	1	1	1
	P2	2	2	2	2	2	2	2	2
	P3	3	3	4	4	4	3	4	3
	P4	4	4	3	3	3	4	3	4
Group 2	P1	2	2	2	2	2	2	2	3
	P2	1	1	1	1	1	1	1	1
	P3	4	5	5	4	5	5	5	2
	P4	3	3	3	3	3	3	3	4
	P5	5	4	4	5	4	4	4	5
Group 3	P1	2	2	2	2	2	2	2	2
	P2	3	3	3	3	3	3	3	3
	P3	1	1	1	1	1	1	1	1

APPLICATION AS A SCREENING TOOL

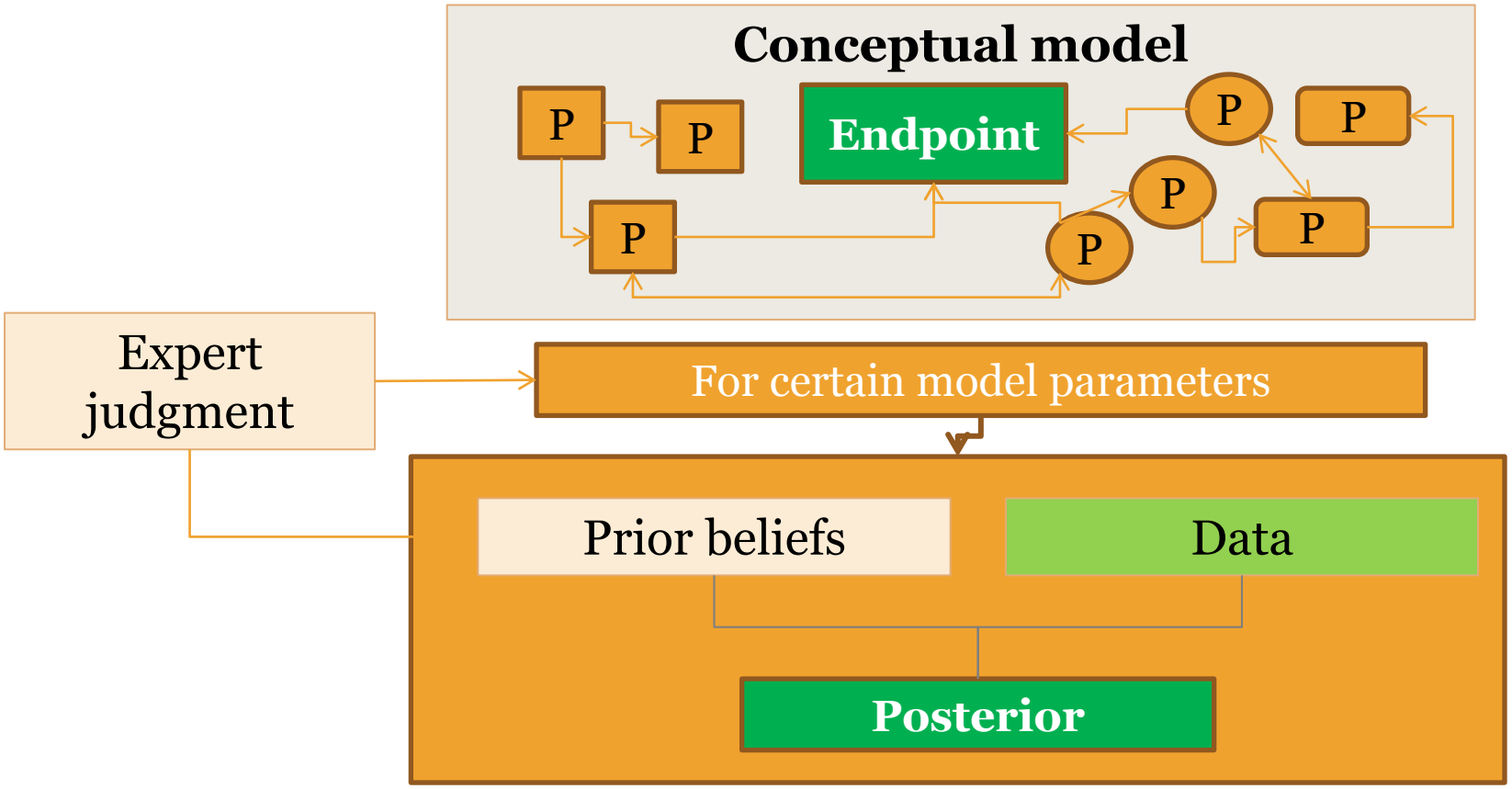
How could such results feed in the challenge of risk assessment of nanotechnology-enabled food products?



• a tiered approach of ranking/sieving nanotechnology-enabled food products could be applied.

PRODUCTS CONSIDERED UNSAFE

- More customised screening decision making tools possible
- Possible that risk assessment should be done case by case



WAYS FORWARD

- Model appears promising
  - Method was applied to other problems
  - It is dynamic process; “shelf life” of the model
  - The most important part is defining the right criteria for each model
- More research, funding, needed
  - Continuation of MoniQA funding 2011
  - Possible international collaboration with end users (e.g. policy makers, regulators, risk assessors, industry)

CONTACT US!

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