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How can the diagnostic process be improved to enhance industry reactivity?

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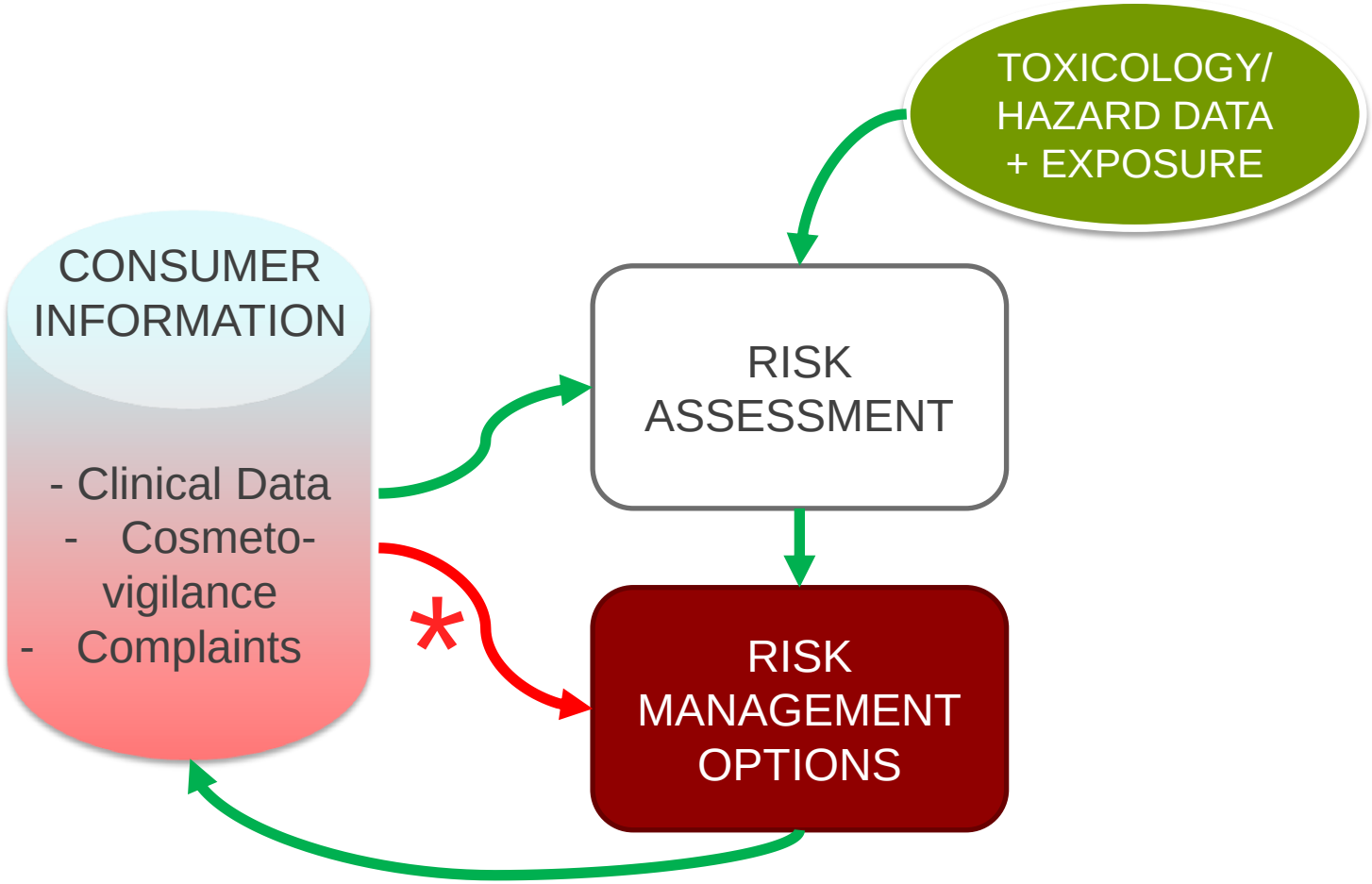
How can the diagnostic process be improved to enhance industry reactivity?

- Perspective
- Use of clinical data in risk assessment and management
- Industry intiatives
- Allergens of specific concern
- Conclude

The perspective of an industry risk assessor/manager



* Allergen of specific concern?

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Toxicological and Exposure information

- Animal data – LLNA, GPMT, Buehler etc
- Human data – HRIPT
- Limited use currently of in vitro and in silico data
- Exposure data based on real use surveys

Risk assessment and management

- Use of Quantitative Risk Assessment (QRA)
- Aim to prevent Induction of sensitisation
- Specific to ingredient and product type
- Continual improvement of QRA through IDEA Programme (1st Workshop) and other intiatives (aggregate exposure)
- Risk management via IFRA standards, customer information, additional limitations

Use of clinical data in risk assessment

- Ideally clinical data will allow us to determine if the risk assessment is sufficiently protective
- Feedback into and revision of risk assessment could be made based on an emerging clinical picture
  - Early corrective actions
- However, clinical data is often not accompanied by sufficient information which can inform a risk assessment

Importance of clinical relevance (and more) for informing risk assessment/managment

Ideally a risk assessor/manager needs to know:

- Is there an issue with a specific ingredient?
- What is the source of the induction (occupational, cosmetic, other?)
- What level (dose) of ingredient is causing the issue?
- Is there an issue with a specific product type/body area?
- What is the scale of the issue?

Then, can risk assessment be reviewed and corrective risk managment measures be taken…?

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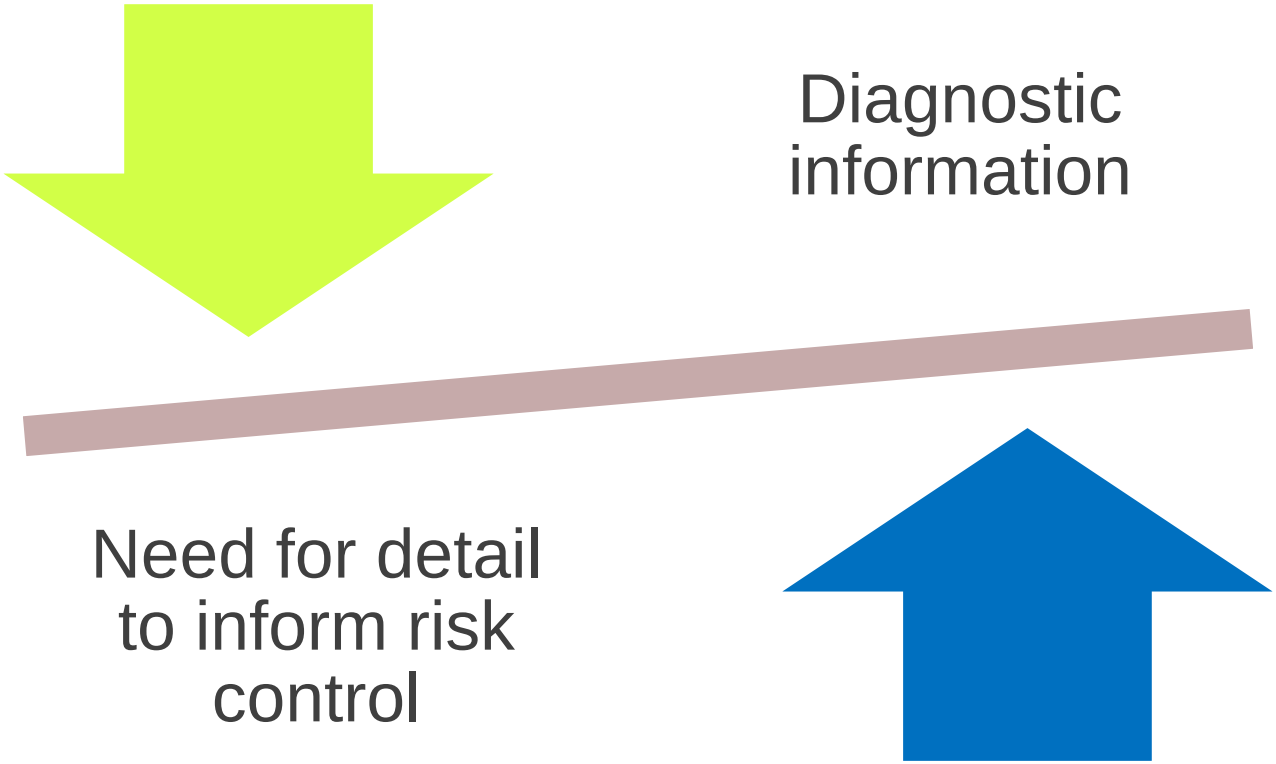
Clincal data	+ RA/RM	- RA/RM	Examples
Single cases	Potential for early warning Can provide specific data relevant to RA (product type, clinical relevance etc)	May be limited number of cases Relevance of reaction to RA/RM needs to be established	e.g. IVDK programme
Clinical-epidemiological studies	Provides evidence of an issue in targeted population Can inform additional risk management needs	Relevance to specific products rarely available Unspecific for RA/RM	e.g. FM1 → FM2. Targeted testing of a specific allergen
Epidemiological data	Provides information on general population Can inform addtional risk management needs	Unspecific for RA/RM	e.g. EDEN study


Diagnostic information
Need for detail to inform risk control

Some fragrance industry initiatives

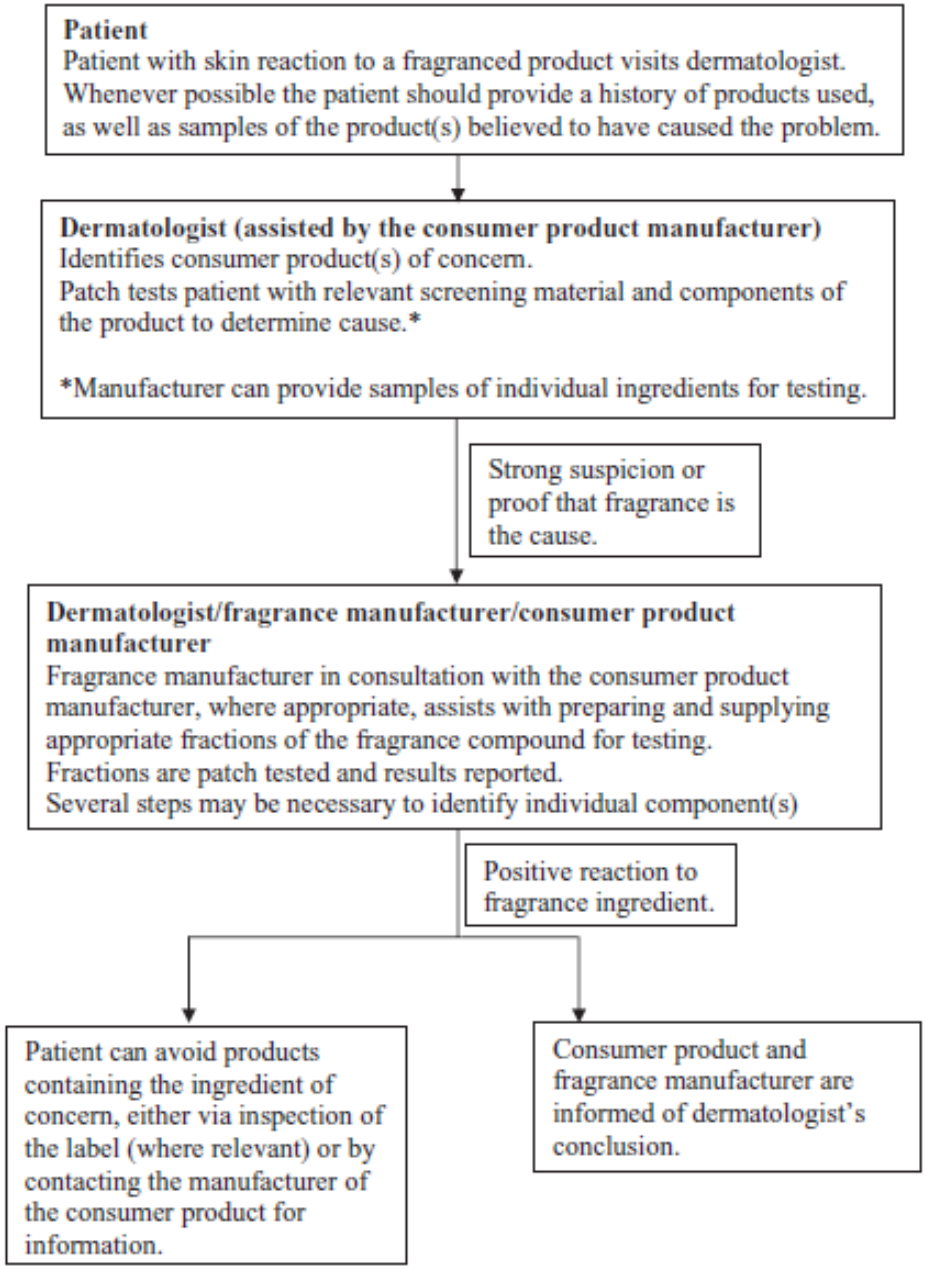
- Early detection of fragrance allergens
  - e.g. RIFM discussions with ESCD, IVDK, Clinicians
- IFRA procedures on providing information to Dermatologists
- «Cosmetic on call» and «Fragrance on call» services
- Provision of samples for patch testing
  - Marketed qualities of ingredients provided free of charge to patch test manufacturers to ensure correct qualitiy
- Continual improvement of risk assessment tools
  - QRA and other activities coming from 1st and 2nd IDEA Workshops

IFRA procedures on providing information to Dermatologists

- IFRA Code of Practive requires manufcaturers to give «full assisstance to physicians in attempting to discover the causative agents of contact dermatitis»

- Guidance has been published
  - **Identification of the causes of an allergic reaction to a fragranced consumer product Cadby et al, 2010.**

- Recommends contact between dermatologist and consumer product manufacturer (or direct with fragrance house) when fragrance allergy is suspected


Patient
Patient with skin reaction to a fragranced product visits dermatologist.
Whenever possible the patient should provide a history of products used, as well as samples of the product(s) believed to have caused the problem.
Dermatologist (assisted by the consumer product manufacturer)
Identifies consumer product(s) of concern.
Patch tests patient with relevant screening material and components of the product to determine cause.*
*Manufacturer can provide samples of individual ingredients for testing.
Strong suspicion or proof that fragrance is the cause.
Dermatologist/fragrance manufacturer/consumer product manufacturer
Fragrance manufacturer in consultation with the consumer product manufacturer, where appropriate, assists with preparing and supplying appropriate fractions of the fragrance compound for testing.
Fractions are patch tested and results reported.
Several steps may be necessary to identify individual component(s)
Positive reaction to fragrance ingredient.
Patient can avoid products containing the ingredient of concern, either via inspection of the label (where relevant) or by contacting the manufacturer of the consumer product for information.
Consumer product and fragrance manufacturer are informed of dermatologist's conclusion.

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Identifying the Ingredient(s) within a Fragrance Compound Responsible for the Reaction

In order to gain detailed information about the composition of a fragrance compound, it will be necessary to contact the fragrance supplier. The identity of this supplier can be obtained from the manufacturer of the consumer product. Some of the cosmetic product manufacturers may themselves take on the task of pursuing the investigation with the help of their fragrance supplier, thus acting as an intermediary between the fragrance supplier and the dermatologist.

The expertise and knowledge regarding a specific fragrance compound from a specific manufacturer is also readily shared by the International Fragrance Association (contact details on www.ifraorg.org), which maintains a list of ex each of the different fragrance suppliers.

Guidance on Preparation of Fractions of the Fragrance

For the choice of fractions of the fragrance compound, the fragrance supplier should take into account the following: the percentage of individual ingredients in the compound and the likelihood of each to cause allergy; potential for cross-reaction of ingredients in the fragrance; the need to avoid inducing allergy during patch testing; the need to minimize false-positive and false-negative reactions; the chemical family of the ingredients; and the number of patch sites available to test. This will determine how many fractions of the fragrance need to be prepared. The fractions should be planned so as to reduce as far as practicable the number of visits required to arrive at a conclusion. These considerations are further explored below.††

Conclusions

The benefit to the consumer is that, through the measures provided by the medical community and supported by the industry, if the test procedure is successful in elucidating the cause of allergy, he/she will be able to make an informed decision by avoiding products that contain the material identified as problematic, instead of having to generally avoid all fragranced products.

For the procedure to fully benefit the community, it will require increasingly closer cooperation between industry and the medical profession. It is the experience of the industry today that very few cases of perfume allergy are directly reported to the industry's vigilance systems and few requests are received for help in in-depth investigations. A cooperative system with a more effective feedback could help guide and refine industry initiatives and the restrictive measures that it must take and would enhance the success rate of medical diagnoses and ultimately improve the well-being of the patients.

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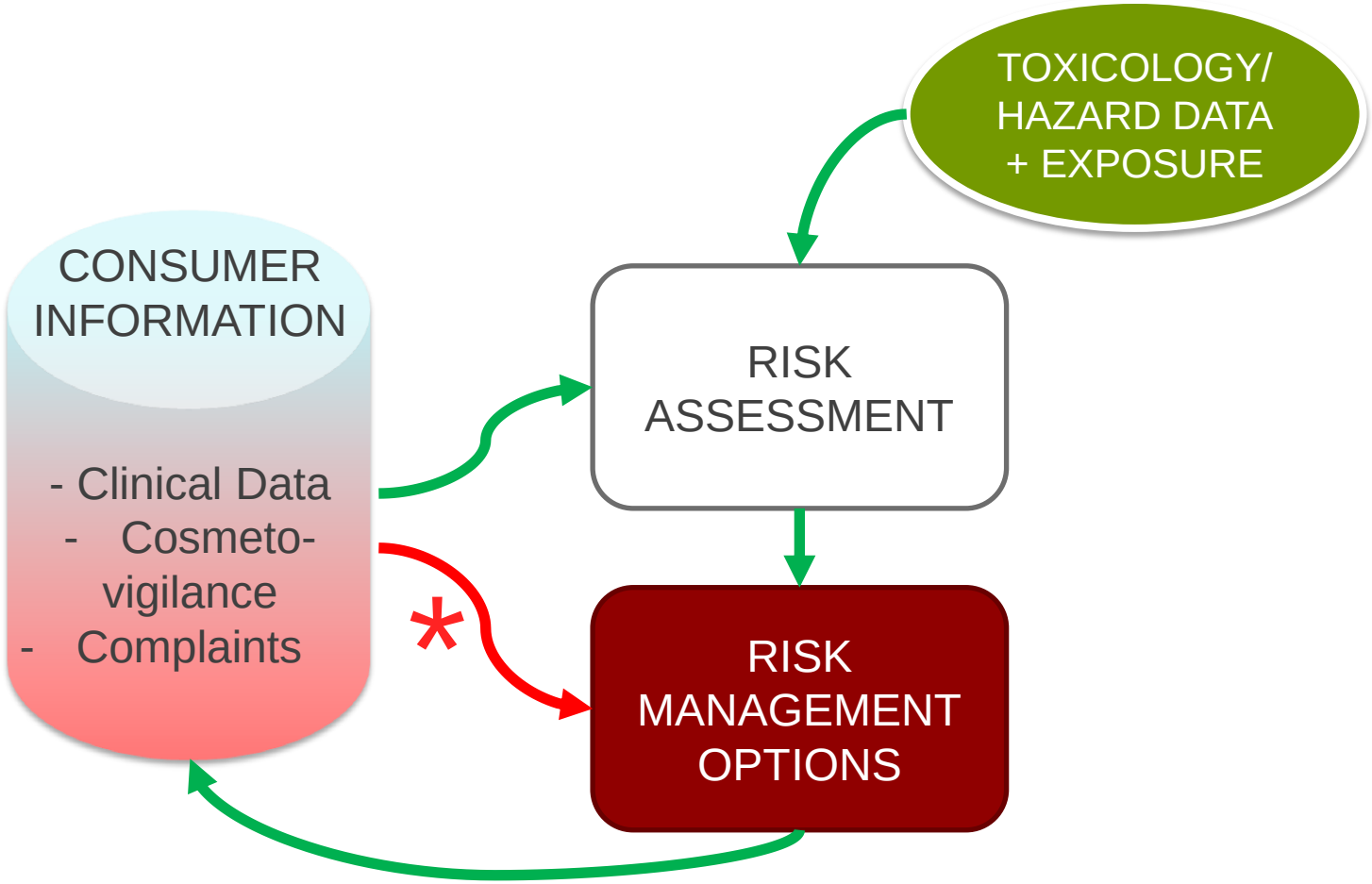
The perspective of an industry risk assessor/manager



* Allergen of specific concern?

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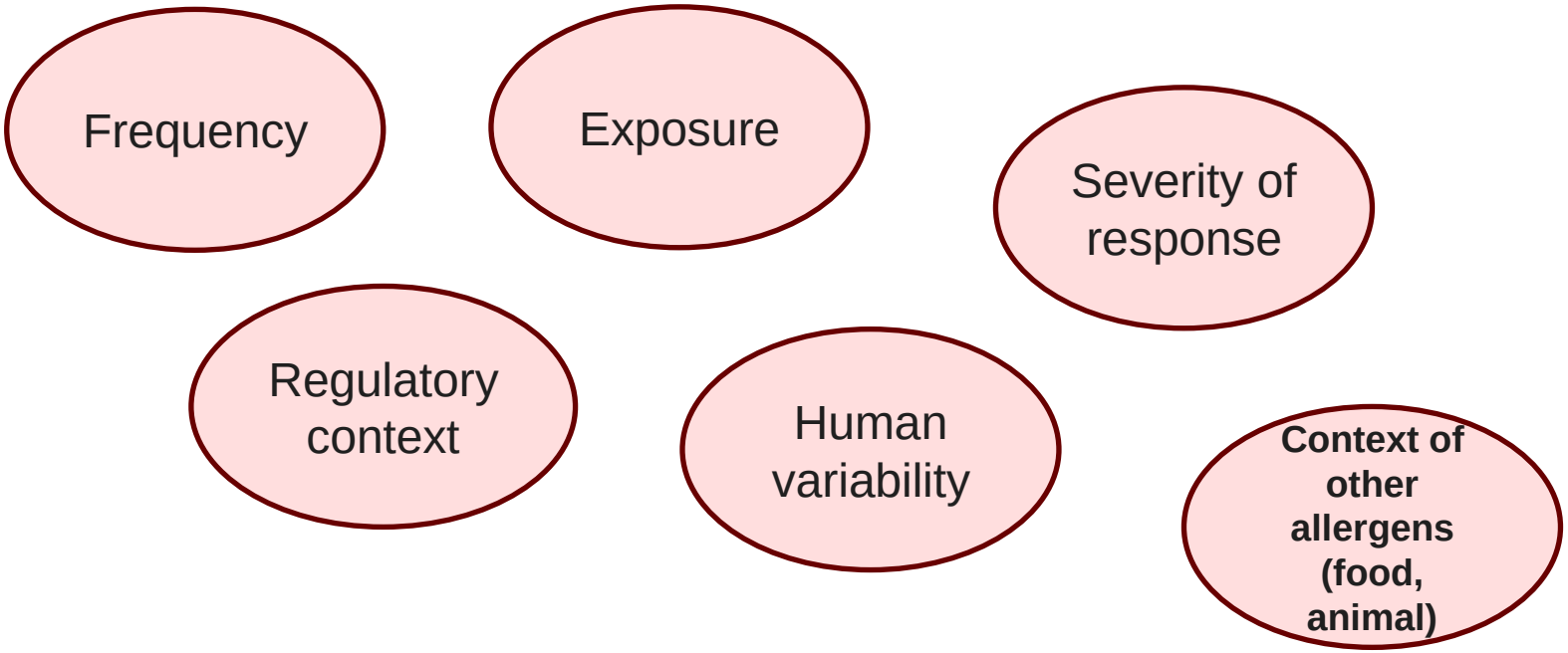
How much is significant?



Early detection — Issue — High concern

Risk management options

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Industry goal re. «allergens of specific concern»

- A fragrance allergen of specific concern may be considered as a normal fragrance allergen for which appropriate risk management measures were taken too late (or innefective)
- Consequently, the substance sensitized a significant proportion of the general population and special risk management measures (such as consumer information) are necessary to prevent elicitation
- Acting more quickly and taking pro-active risk management measures may have avoided the problem
- **The industry goal is to solve the problem at the earliest stage – for the greatest benefit of the consumer (who is not sensitized) and the industry (which avoids unnecessary bans and labeling)**

How can the diagnostic process be improved to enhance industry reactivity?

- Greater level of information and closer collaboration from diagnostic process would allow better refinement of risk control tools
- Consumer prduct companies/fragrance houses are available to provide detailed information on fragrance
- Information on patients relevant to risk assessment – source of reaction, site, relevance etc would be the ideal but often not available
- High level information (i.e. without clinical relevance, causal link to product) is useful in a non-specific way (e.g. trend indicator)
- Goal to avoid having allergens of specifc concern through early identification and corrective actions (and avoid unnecessarily restricting perfumery creativity)

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