QRA Methodology Update (QRA2) and evaluating its effectiveness in consumer protection

Ian R. White

IDEA Annual Review 2016
Luxembourg, March 6, 2017

Work by IDEA 2016

Completion of QRA2 dossier

- Response by IDEA to SCCS and JRC comments and the subsequent Annual Review met the deadline of October 30, 2015.
- Additional editing included on ‘foreseeable use’ and more detailed information on the incorporation of the aggregate exposure model.
- Final dossier submission to DG Grow October 2, 2016.

Work undertaken in 2016

- Details in next presentations

IDEA
International Dialogue for the Evaluation of Allergens

- Integration of Alternatives to Animal Testing (non-animal data) into QRA2 – WG meeting on April 26, 2016.

- Pre- and pro- hapten assessment:
  - Development of framework for integration into QRA2 - WG meeting Dec. 13, 2016 on identification, understanding of formation and exposure assessment.
  - Development of an analytical method for detection and quantification of hydroperoxides .
    - progress report on the development of analytical method.

Critical importance of surveillance

- The scientific community / EU Commission (particular SCCS) / dermatologists require the assessment of the effectiveness of the revised QRA2.
  - In order to do this a reliable surveillance system must be in operation.
  - Inclusion of ‘new’ fragrance substances.

IDEA Surveillance 2015-2016

Surveillance system draft proposal, spring 2015:

- Developed from that used for monitoring isothiazolinone 'crisis' in Europe.
- Presented and discussed at IDEA WG meeting on April 6, 2016.

Key conclusions of this meeting:

- Support for the surveillance system to assess prevalence of contact allergy in eczema patients as recommended by the dermatologists.
- The surveillance system alone may not verify whether the QRA2 is effective due to confounding factors.
- Work in parallel is, therefore, recommended and will be subject to further discussion.

Surveillance: discussions

Meetings to pursue recommendations, develop protocols, engaging with clinics/dermatologists, examining size and duration of studies and detailed planning:

- Meeting in Malmö (Sweden), May 23rd 2016 with M Bruze and colleagues and Chemotechnique Diagnostics (allergen preparation manufacturer).
- Meeting in Erlangen (Germany) with W Uter, expert in study design and data treatment (July 7th , 2016 and February 1st , 2017).
- The context and the plan for an IDEA surveillance study presented (IR White) at the September 2016 ESCD meeting.
- Internal industry discussions on preparing a meaningful surveillance system continued.

Priorities for surveillance

For surveillance of 'routine' fragrance substances, the choices are:

- Only include FMI and II and its constituents (+ some screening materials).
  - **FMI** (introduced in 1977):

    amyl cinnamal
    eugenol
    Evernia prunastri (Oak moss)
    geraniol
    isoeugenol
    hydroxycitronellal
    cinnamyl alcohol
    cinnamal

  - **FMII** (introduced in 2004):

    citral
    farnesol
    hexyl cinnamal
    citronellol
    coumarin
    HICC

- Testing all 26 fragrance substances requiring labelling on cosmetic products

Other allergens in the 26: amyl cinnamyl alcohol, anise alcohol, benzyl alcohol, benzyl benzoate, benzyl cinnamate, benzyl salicylate, butylphenyl methylpropional, **d-limonene**, **linalool**, methyl 2-octynoate, α-*iso*-methyl ionone, *Evernia furfuracea* (Tree moss)

Surveillance of new ingredients

IDEA
International Dialogue for the Evaluation of Allergens
International Dialogue for the Evaluation of Allergens

Recommendation to first look at additional materials identified by the SCCS in its 2012 opinion:

> *For other fragrance substances identified by the SCCS as (potential) allergens in humans, routine testing of groups of substances over blocks of time should provide information on the prevalence and relative importance of them as allergens (information on consumer exposure is required).*

- In discussions with stakeholders, the inclusion of 'new ingredients' is recognized as a crucial point for the further development of surveillance system.
- Stringent criteria to select new ingredients to reduce confounding factors.

Effectiveness of QRA2: critical work

- For the proposed surveillance studies to be effective, considerable effort and engagement by clinical dermatologists is required.
  - All clinical dermatology centres test with FMI+II (present in European baseline series).
  - Some centres additionally test all patients with individual ingredients of FMI+II.
  - Few centres test with all 26 labelled substances as well as FMI+II.

  Clear information on when QRA2 fully incorporated for each substance on the market.

  Assuming QRA2 is fully utilised for all labelled fragrance substances, should we anticipate a reduction in clinical sensitisation, whatever the confounding factors?

- Testing with 'new' fragrance materials as they are introduced onto the consumer market will show what is happening in the naïve population
  - Meeting is planned for end 2017 for agreement.