DRAFT Protocol: Study on the Effectiveness of the QRA

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“Prospective Study”

- Not designed to be the only study done; considered to be used with additional studies
- Study design must include a pilot study to test the methodology, reliability and feasibility of the protocol, study population recruitment and retention, study design and assess human subjects protection issues

Key Conclusions from Last WG Meeting February 15th, 2017

- **The WG is supportive of clinical work complementary to the surveillance system, favoring establishment of an approach which would minimize confounding factors (i.e. prospective study).**

- **Given a number of open protocol questions, the working group proposed a pilot study. A protocol for such a pilot study will be developed by the group of interested volunteers from the IDEA working group.**

Objective

- To measure the effectiveness of QRA2 in preventing the induction of contact allergy, in comparison to the original risk assessment method used by RIFM and IFRA
- Use a patch test before and following controlled exposure to a novel fragrance ingredient that has not been marketed and with no intention of marketing the material.

Study Design

- Randomized controlled trial
  - 3 Test Groups
  - Target Material
  - Initial Patch Test
  - Product Use - for at least 6 months
  - Final Patch Test
- Final study design based on pilot study outcome

Test Groups

- **Group 1**
  - use products containing this target fragrance ingredient at QRA2 levels.
- **Group 2**
  - use same products with the target material at levels designated by the methodology used prior to the introduction of QRA methodology.
- **Group 3**
  - (control group) will use the exact same formulation of products without the target fragrance ingredient.

What is the study testing?

1. **Testing the effectiveness of the QRA2 in protecting the induction of sensitization compared to the Control Group**

2. **Testing (secondary hypothesis) whether the QRA2 results in fewer subjects developing a contact allergy than the original risk assessment method used by RIFM and IFRA**

Target Material

- **From the last WG meeting:**

  “Rather than the weak fragrance allergen proposed (dimethyl citraconate), it was suggested that it would be better to use a strong sensitiser such as diphencyclopropenone (DPCP) as a marker allergen and replace the ‘control group’ by knowledge of the ability of the material to sensitize people.”

Initial Patch Test

- **Every subject will participate in a patch test with the target material. Any subject who reacts positively to this initial patch test will not participate in the full study.**

Study Population

- Male and female subjects from the general population that are not DPCP sensitive?
- Size of population needed in each group to test the hypotheses?
  - What assumptions about the population, detectable difference between QRA2 and control group, power, and type 1 error rate will be made?
  - Use a sensitive population
    - Less subjects, but will the results still be interpretable? – discouraged at the last WG Meeting
- Random selection of subjects with documented procedure

Final Patch Test

- **The study will conclude with a final patch test.**

Selection of Products

- **Recommend products to include focus on underarm and palms/hands**
  - **Deodorant type product**
  - **Liquid hand soap**
  - **Moisturizer type product**

Product Use

- Use products for at least 6 months
- Need to control exposure by advising subjects of expected use and measuring use
  - Subjects will need to come to a lab on a regular basis
  - Need regular dermatological examinations
  - Consider other information needed to document to be able to describe compliance to the protocol
    - Detailed history administered by trained personnel
    - Details on other fragranced consumer products used

Ethical Review

- **From the last WG Meeting:**

  “There was both concern and debate generally about the ethics of inducing contact allergy in this study, even though doing so would be essential for the study to be meaningful. “

Ethical Review

- An expert in clinical review board was consulted.
  - Dr. Christopher Coch, U Hospital Bonn
- It was believed that the objective of gaining an early understanding of whether the QRA process had the potential or, importantly, finding that it did not have the potential to reduce the incidence of skin contact allergy was a legitimate scientific objective for a study.
- Combining this with the fact that the risks were low and that adverse effects could be treated, it was felt that if these benefits were well articulated to an ethics committee, approval to run the study would likely be forthcoming.

To Summarize:

- A simpler study design that hopefully allows a quicker evaluation of the effectiveness of QRA2 but:
- Need protocol approval from an Ethical Review Board – emphasize the benefits of the study very clearly
- Study design must include a pilot study to test the methodology, reliability and feasibility of the design
  - Is the study feasible? Size of population needed?
  - Assist in detailing timing of clinical visits

More Information

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