Code Number and Title:
LRI-AIMT6: Eye irritation testing in vitro in practice – Database and testing strategy

Background
The existence of several validated and accepted *in vitro* tests for the detection of severe eye irritants (tests with OECD Guideline) and the absence of validated and accepted *in vitro* tests for the detection of moderate irritants (no OECD Guideline yet) and non-irritants (only OECD 437/438) renders the evaluation of a reliable and meaningful testing strategy for *in vitro* eye irritation difficult. Industrial chemical companies are forced to establish their own 'optimal' testing strategy on an often poor scientific knowledge. This becomes even more of a challenge since *in vivo* testing is/will be restricted.
To overcome this issue, in 2012/13 toxicologists from some companies within the VCI have joined efforts to collect in-house data of 'real-life' test substances, focussing in a first step on data with the BCOP assay (Bovine Cornea Opacity and Permeability, OECD 437). In parallel, corresponding *in vivo* test results and results of other *in vitro* eye corrosion/irritation tests (e.g. EpiOcular, HET-CAM) for the test compounds were gathered where available.
The assessment of the collected data set was astonishing. No clear messages could be obtained for the development of a concerted testing strategy. There was no clear consistency among the *in vitro* tests within a battery approach, and/or some *in vitro* test results were in conflict with the available *in vivo* data.
Since the number of chemicals to be assessed solely based on *in vitro* data e.g. under REACH will strongly rise in the next years, it is urgent to establish reliable *in vitro* testing strategies, which require more knowledge on the applicability domain and the limitations of each *in vitro* test system. Thus, the data base with *in vitro* eye irritation/severe irritation tests should be enlarged for chemicals with reliable, existing *in vivo* data for eye irritation as a basis for further validation and for the establishment of reliable testing strategies specific to given chemical classes.

Objectives
This project is looking to establish a substantial data base of *in vitro* eye irritation/severe eye irritation tests for chemicals with reliable, existing *in vivo* data. The ECETOC Eye Irritation Reference Chemicals Data Bank (ECETOC TR 48(2), 1998) or the Master Chemicals List currently established by Cosmetics Europe (Barroso et al, SOT Annual Meeting 2014, The Toxicologist 138, p. 268, No. 1027, 2014) could serve as a basis for the choice of test substances. Test systems being supposed are at least the BCOP assay and the ICE test for the detection of severe eye irritation and the HCE test and EpiOcular test for the detection of slight to moderate eye irritation.

The project's objectives are to:
1. Define applicability domain and strenghts/limitations of the different *in vitro* systems included (in support of preparation of new OECD Guidelines or revision of existing OECD Guidelines)
2. Help to assess the reliability of the different *in vitro* eye irritation tests, e.g. with depending on different chemical classes, where applicable
3. Provide a first proposal for tiered testing strategies which enable industry to establish reliable *in vitro* test batteries for eye irritation assessment, specific to given chemical classes if appropriate, to ensure adequate classification & labelling, to improve eye irritation assessment based on in vitro data for C&L and e.g. REACH.

Scope

- Determine *in vitro* eye irritation/severe eye irritation test systems of interest to be included in the project (proposal: BCOP, ICE, HCE, EpiOcular; further tests may be considered); studies should be conducted GLP-like (full GLP status not necessarily needed)
- Determine chemicals of different chemical classes and with different eye irritating properties to be included in the project e.g. based on the ECETOC Eye Irritation Reference Chemicals Data Bank (ECETOC TR 48(2), 1998) or the Master Chemicals List currently established by Cosmetics Europe (Barroso et al, SOT Annual Meeting 2014, The Toxicologist 138, p. 268, No. 1027, 2014)
- Determine fitting with ongoing stakeholder activities in this field to avoid overlap
- Determine laboratories to perform the given tests
- Test the chemicals chosen in the determined *in vitro* test systems (under GLP conditions and according to OECD Guidelines, if available, or according to the most recent standards); among selected laboratories test protocols must be harmonized to allow a comparison of the results
- Transfer results to ECVAM to promote validation with respect to the applicability domains of the respective test systems
- Establish testing strategies specific to given chemical classes, if possible

Deliverables

The final report shall contain an executive summary (2 pages max), a main part (max. 50 pages) and a detailed bibliography. It is expected that the findings will be developed into at least one peer reviewed publication, following postering(s) and presentation(s) at suitable scientific conference(s).

Cost and Timing

Start in early 2015
Duration – depending on number of test substances and test systems (e.g. 12 months).
Budget in the order of 500 k€, depending on number of test substances and test systems (e.g. 50 substances in 5 tests for about 500 k€; key aspect is 5 tests per substance)

Partnering/Co-funding

Applicants should provide an indication of additional partners and funding opportunities that can be appropriately leveraged as part of their proposal. Partners can include, but are not limited to industry, government/regulatory organizations, research institutes, etc. Statements from potential partners should be included in the proposal package.

Fit with LRI objectives/Possible regulatory and policy impact involvements/ Dissemination

Applicants should provide information on the fit of their proposal with LRI objectives and an indication on how and where they could play a role in the regulatory and policy areas. Dissemination plans should also be laid down.

DEADLINE FOR SUBMISSIONS: August 31, 2014

Please visit www.cefic-lri.org for general information about the LRI funding programme, guidelines for grant applications and links to application documents.

For further assistance do not hesitate to contact the LRI Secretariat by e-mail at lri@cefic.be or by phone on 0032 (0)2 676 7368.