

9th October 2017 – Joint COC, COM, COT Workshop

Paper 1

**COMMITTEES ON CARCINOGENICITY, MUTAGENICITY AND TOXICITY OF
CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT
(COC, COM and COT)**

Use of epigenetics in chemical risk assessment

1. Epigenetics and the use of epigenetics in chemical risk assessment has been discussed by the three Committees a number of times in the last 10 years, and as such it was considered to be a relevant item for discussion as part of a joint meeting.
2. Annex A to this paper contains previous Committee statements or discussion papers and associated minutes; Annex B provides reports of recent expert workshops on epigenetics; and Annex C provides recent peer-reviewed articles to support the discussion at the meeting.

Questions

3. Participants are invited to consider the following questions:

Overarching Question: Whether epigenetics should be included in chemical risk assessment?

Supplementary Questions:

- i. What is normal epigenetic variability and adaptation?
- ii. How can epigenetic change be linked to adverse outcome and adverse outcome pathways?
- iii. What are the next steps to enable epigenetic change to be interpreted for incorporation in chemical risk assessment?

**Secretariat
September 2017**

These papers are attached. They are not being made publicly available for copyright reasons.

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Paper 1 – Annex A

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Previous Committee statements or discussion papers and minutes

COT Statement 2008/03 – Statement on the COT workshop on transgenerational epigenetics

CC/2013/05 – Epigenetics and carcinogenesis

CC/2013/06 – Epigenetic changes induced by carcinogens

CC/MIN/2013/01 Item 5 – Minutes of discussion of CC/2013/05 and CC/2013/06

MUT/2016/05 – Environmentally induced epigenetic toxicity: potential public health concerns

MUT/MIN/2016/02 Items 6&7 – Minutes of discussion of presentation and MUT/2016/05

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Paper 1 – Annex B

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Expert workshop reports

1) ECETOC Workshop Report 30: The Role of Epigenetics in Reproductive Toxicity. Available here: <http://www.ecetoc.org/publication/workshop-report-no-30-role-epigenetics-reproductive-toxicity/> (accessed 21/09/2017)

2) ECETOC Workshop Report 32: Noncoding RNAs and Risk Assessment Science. Available here: <http://www.ecetoc.org/publication/workshop-report-no-32-noncoding-rnas-risk-assessment-science-3-4-march-2016-malaga/> (accessed 21/09/2017)

And peer-reviewed paper Aigner A, Buesen R, Gant T, Gooderham N, Greim H, Hackermüller J, Hubesch B, Laffont M, Marczylo E, Meister G, Petrick JS, Rasoulpour RJ, Sauer UG, Schmidt K, Seitz H, Slack F, Sukata T, van der View SM, Verhaert J, Witwer KW and Poole A (2016) Advancing the use of noncoding RNA in regulatory toxicology: report of an ECETOC workshop. Regulatory Toxicology and Pharmacology, 82, 127-139.

3) EFSA Scientific Colloquium 22 – Epigenetics and Risk Assessment: Where do we stand? Available here: <http://www.efsa.europa.eu/en/supporting/pub/1129e> and here: <http://onlinelibrary.wiley.com/doi/10.2903/sp.efsa.2016.EN-1129/full> (accessed 21/09/2017)

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Paper 1 – Annex C

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Selected published peer-reviewed papers

- 1) Greally JM and Jacobs MN (2013) *In Vitro* and *In Vivo* Testing Methods of Epigenomic Endpoints for Evaluating Endocrine Disruptors. ALTEX, 30(4), 445-471.
- 2) Marczylo EL, Jacobs MN and Gant TW (2016) Environmentally induced epigenetic toxicity: potential public health concerns. Critical Reviews in Toxicology, 46(8), 676-700.
- 3) Jacobs MN, Marczylo EL, Guerrero-Bosagna C and Rüegg J (2017) Marked for Life: Epigenetic Effects of Endocrine Disrupting Chemicals. Annual Review of Environment and Resources, 42, 23.1-23.56. (advanced in press version)
- 4) Vandenberg MP, Vandenberg DJ and Vandenberg JG (2017) Beyond Lamack: The Implications of Epigenetics for Environmental Law. Vanderbilt University Law School, Legal Studies Research Paper Series, Working Paper Number 17-30. Available from: https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2974409 (accessed 26/09/2017)
- 5) Moggs JG, MacLachlan T, Martus H-J and Bentley P (2016) Derisking Drug-Induced Carcinogenicity for Novel Therapeutics. Trends in Cancer, 2(8), 398-408.
- 6) Miousse IR, Currie R, Datta K, Ellinger-Ziegelbauer H, French JE, Harrill AH, Koturbash I, Lawton M, Mann D, Meehan RR, Moggs JG, O'Lone R, Rasoulpour RJ, Reijo Pera RA and Thompson K (2015) Importance of investigating epigenetic alterations from industry and regulators: An appraisal of current efforts by the Health and Environmental Sciences Institute. Toxicology, 335, 11-19.
- 7) Goodman JI (2017) Incorporation of an epigenetic evaluation into safety assessment: What we first need to know. Current Opinion in Toxicology, 3, 20-24.
- 8) Terranova R, Vitobello A, Del Rio Espinola A, Wolf CR, Schwarz M, Thomson J, Meehan R and Moggs J (2017) Progress in identifying epigenetic mechanisms of xenobiotic-induced non-genotoxic carcinogenesis. Current Opinion in Toxicology, 3, 62-70.

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