Use of quantitative weight of evidence (QWoE) to utilise ‘omics’ data

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The rationale for the application of QWoE to omics data for hazard/risk assessment purposes

Purpose:
To provide a scientifically based, objective, transparent, quantitative and consistent framework for utilising ‘omics’ data

Application: comparison of omics:

i) With ‘traditional’ endpoints for each effect of concern
ii) For different categories of omics
iii) Between LoE’s (eg human, animal, in vitro)
iv) For adverse and adaptive changes
Steps in QWoE based hazard/risk assessment methodology for ‘omics’.

i) Define the hypothesis/effect of concern(s) and the lines of evidence (LoE) required

ii) Choose omics and ‘traditional type’ of endpoints that reflect the effect(s) of concern

iii) Identify best practice methodology for each LoE and develop scoring systems for both quality (Q) and relevance (R)

iv) Score, all papers/reports in each LoE for Q and R and calculate an average score

v) Adopt a justifiable, weighting for each LoE, combine these scores to identify extent of support for the hypothesis, and any uncertainties
Omics: best practice for scoring for quality for each LoE

Includes scoring for the:

• General experimental design to test the hypothesis
• Mode of application of the chemical to the test system
• Appropriateness of the methods for determining both omics and non-omics endpoints
• Validity of statistical interpretation of findings and comparison with historic controls
Omics: best practice for scoring for relevance for each LoE

Include scoring for:

• Dose response relationship (at relevant exposure times)
• Profile of endpoint(s) compared with controls/benchmark chemicals
• Persistence or not of the effect(s) on cessation of dosing
• Consistency of results for each type of endpoint determination
• Relationship of these endpoints to comparable ones in man
Scoring for relevance: only endpoint data available for a LoE

• Pattern of changes like well established benchmark chemicals where there is reliable linkage of omics data to the effect of concern (4)
• Consistent omics data for critical points in likely AOP for the effect of concern (3)
• Omics changes found but relevance to effect of concern not established (2)
• Inconsistent changes in omics findings/unclear whether omics changes are adverse (1)
Integration of scores for the combination of all LoE’s

Situations utilising both omics and traditional endpoint types:

• All mutually supportive (4)
• Some differences but explainable (3)
• Major differences between omics and traditional endpoint findings but changes in omics endpoints consistent (2)
• No consistency between types of omics endpoints and different LoE’s (1)