

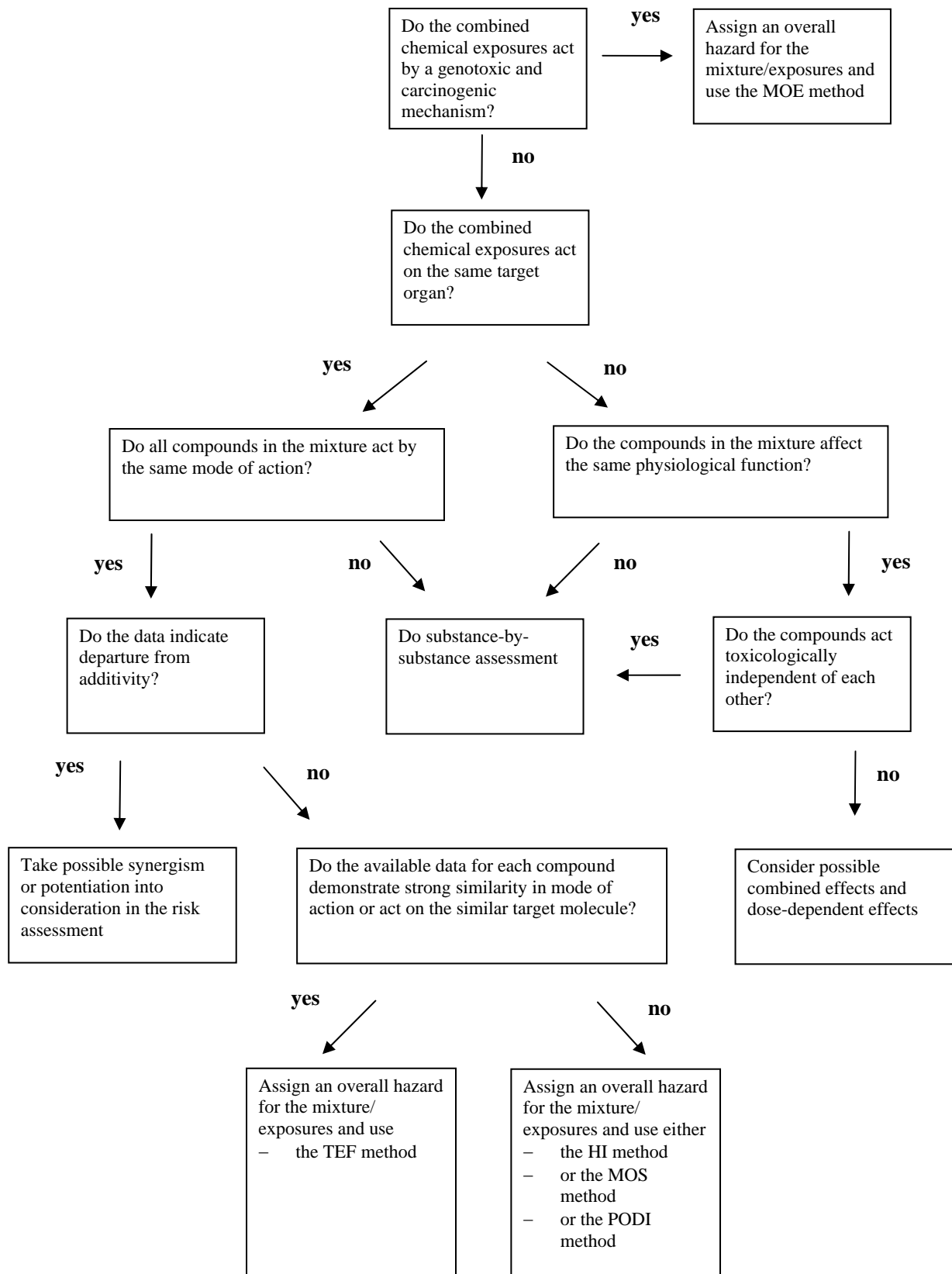


***Flow chart for use in risk assessments of multiple chemical exposures  
proposed by VKM***

*Basis for use of the flow chart:*

- The term ‘similar mode of action’ has a wider definition than the term ‘similar mechanism of action’. ‘Similar mode of action’ includes mechanisms that lead to a common effect. There may be insufficient knowledge about the precise molecular mechanisms, but the principle of dose addition may still be used.
- If exposure to all components in the mixture is below their individual NOAELs and they act by a similar mode of action, no more than additive effect is expected.
- If exposure to component(s) in the mixture is above the individual component NOAELs, combined effects due to interaction may occur.
- If there is simple similar action for all components, a common expression of the hazard can be assigned for the mixture or the concurrent exposures:
  - When ADIs are available, the HI method may be used.
  - When ADIs are not available, the MOS or PODI method may be used.
  - If there is a well-known and strong similarity in ‘mechanism of action’ for all components in the mixture, the use of an index compound and the TEF model may be considered.
- If the components act by simple dissimilar action:
  - no combined effect is expected if exposure to all components in the mixture are below their individual NOAELs
  - combined effects due to interaction may occur if exposure to component(s) in the mixture are above their individual NOAELs

Flow chart from the VKM Opinion “Combined toxic effects of multiple chemical exposures”



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