A major advantage of human cell and tissue culture models is (Resp Sens?)... or asthma in humans.

The Abstract Sifter was populated with chemicals retrieved from the EPA literature database by querying with MeSH terms related to respiratory sensitization (e.g., Asthma, Bronchial Hyperreactivity, and Respiratory hypersensitivity). The literature for these candidate chemicals was further queried, sifted, tagged, and evaluated to identify publications relevant to respiratory chemical allergy or asthma in humans.

This approach successfully identified twenty-eight compounds as respiratory sensitizers based on well-defined clinical diagnostic criteria. This output will be used along with other available data to establish a reference list of respiratory sensitizers, irritants, and non-sensitizers, to update existing risk assessment approaches and evaluate the accuracy of new approaches for this key endpoint.

Comparison of the protein binding mechanisms of our identified "in silico" respiratory sensitizers suggests acylation is a prevalent protein binding mechanism, in contrast to Michael addition and Schiff base formation common to skin sensitizers.

Overall, this approach provides an exemplary method to evaluate and apply human clinical data as part of the weight-of-evidence towards establishing reference chemical lists.

Central Query: Has this compound been shown to cause respiratory sensitization in clinical literature?

NO INFORMATION: There is no information to evaluate the compound's sensitizing potential

EQUIVOCAL: There is clinical evidence of respiratory symptoms after exposure, but available evidence does not conclusively demonstrate sensitization, either:

- There is no evidence of immune-mediated response to distinguish respiratory sensitization from respiratory irritation
- There is conflicting evidence of immune-mediated responses and/or confounding exposures

YES: There is significant clinical evidence that the compound has caused respiratory sensitization in at least one case, as defined by either:

- Patient history of exposure with positive nonspecific bronchial challenge, combined with evidence of specific IgE and/or IgG immune-mediated response
- Patient history of exposure with positive non-specific bronchial challenge, combined with evidence of IgE and/or IgG immune-mediated response, when paired with appropriate negative controls to eliminate confounding exposures

Clinical evidence was tabulated for review. Abstract Sifter was utilized to collect and prioritize relevant literature reports for evaluation. The collected literature was systematically evaluated for clinical evidence that indicated allergic asthma caused by low-molecular weight chemical exposure.

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PubMed search with Abstract Sifter

Clinical Evaluation Criteria

Establish a high-confidence reference set of low molecular weight respiratory sensitizers based on clinically verified case reports of occupational asthma.