Ethics Review of Lang et al. (2008) Controlled Human Study with Formaldehyde

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Outline

1) Subject selection
2) Consent process
3) Risks and risk minimization
4) Respect for subjects
5) Independent ethics review
6) Substantive acceptance standards
7) Findings and conclusion

Subject Selection

- Recruited through online advertisements at local job offices and posting on bulletin boards at the University of Heidelberg

- 26 individuals enrolled in the study
- 21 individuals completed participation in the study
  - 11 males, 10 females
  - 19-39 years old

- Eligibility Criteria
  - Healthy nonsmoker
  - Female subjects not pregnant or nursing
  - No severe allergies/skin disease
  - Drug abuse/excessive alcohol consumption
  - Occupational or residential HCHO exposure
  - No history of diseases in the respiratory tract, heart, or metabolism
  - Not a contact lens wearer

Consent Process

- Consent process conducted through 1:1 meetings as part of the prescreening and physical exam
- Consent form notes that participation is voluntary and subjects can withdraw at anytime without penalty
- Subjects' questions were answered prior to signing the consent form
- Subjects had to wait at least 24 hours after the consent meeting to sign the form to ensure they had adequate time to consider their participation

Risks and Risk Minimization

- Formaldehyde exposure can cause eye, nose, and throat irritation
- Individuals with asthma or other breathing problems may be more sensitive to the effects of formaldehyde exposure
- Risks minimized through
  - Selection of formaldehyde levels based on existing standards and data
  - Enrolling healthy, non-smoking subjects

Respect for Subjects

- Subjects were free to withdraw at anytime without penalty
- Subjects were compensated €600 for their participation in the study
- Data were anonymized
- Subjects' confidentiality was maintained and they were not identified in the publication about the research
- Withdrawing subjects could request that their data be excluded from the study results

Independent Ethics Review

- Research was reviewed and approved by the Ethics Committee of the Medical Faculty of the University of Heidelberg
- The University of Heidelberg currently holds a Federal-Wide Assurance
- Ethics Committee members are independent in the performance of their duties

Substantive Ethics Standards

- 40 CFR §26.1703
  - Prohibits reliance on data involving intentional exposure of pregnant or nursing women or of children
- 40 CFR §26.1704
  - Prohibits EPA reliance on data if there is clear and convincing evidence that:

    (1) Conduct of the research was fundamentally unethical; or

    (2) Conduct of research was deficient relative to the ethical standards prevailing at the time the research was conducted in a way that placed participants at increased risk of harm or impaired their informed consent

Prevailing Ethical Standards

- Declaration of Helsinki
  - Research must be scientifically sound and conducted by qualified personnel
  - The research should have a clear purpose and protocol, and be reviewed and approved by an independent ethics committee
  - The importance of the study's objective must outweigh the inherent risks to subjects, and measures to minimize risks must be implemented
  - The privacy of subjects and confidentiality of their personal information must be respected
  - Participants should give prior, informed, voluntary consent and have the freedom to withdraw from the study

Findings

- All subjects were adults; pregnant and nursing women were excluded
- Research was conducted in a university setting by qualified personnel
- Research was overseen by an independent ethics body
- Risks to subjects were minimized and reasonable relative to the expected benefits of the research
- Subjects' privacy was respected
- All subjects provided written consent to participate
- Participation was voluntary and subjects were free to withdraw

Conclusion

- Available information indicates that:
  - The research is not fundamentally unethical
  - The research was not deficient relative to the ethical standards in the 1996 Declaration of Helsinki
  - The research was not conducted in a way that placed participants at increased risk of harm or impaired their informed consent

Charge Questions - Ethics

- Does available information support a determination that the conduct of the research was not fundamentally unethical?

- Does available information support a determination that the research was not deficient relative to the ethical standards prevailing at the time the research was conducted or conducted in a way that placed participants at increased risk of harm or impaired their informed consent?

Charge Question - Science

- Is the research described in the published study “Formaldehyde and chemosensory irritation in humans: A controlled human exposure study,” published in Regulatory Toxicology and Pharmacology 50: 23–36, scientifically sound, providing reliable data for use in a weight-of-evidence to determine a point of departure for acute inhalation exposures to formaldehyde?