# Successful approaches to the Ethical Review by accredited units in Europe:

## Philip Morris Research Laboratories bvba Belgium

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# Philip Morris Research Laboratories bvba

- Conducts research on the impact of test substances (usually aerosols or parts thereof) on living cells and laboratory animals (rodents only) to assess biological activity as part of safety evaluation, risk assessment, and disease mechanism understanding. Key domains of research are the respiratory system and the cardiovascular system.
  - *In vivo* sub-chronic (90-day) toxicological inhalation studies and genotoxicity studies
  - Mechanistic understanding of cigarette-smoking-related diseases
- GLP-certified since 1995
- AAALAC-accredited since 2001

# Installation of ethical committee

- Kick-off in December 2000 with internal members; later extended to include external members
- Lowest common multiple to meet ‘Guide for Care and Use of Laboratory Animals’ (‘Guide’) and Belgian legislation
- Major improvements following AAALAC site visit in 2004

# Ethical committees in Belgium

- Institutional ethical committees* established in 1995 by modification of Law of 1986 concerning animal welfare and protection and implemented by Royal Decree in 2001 which specifies:
  - tasks and responsibilities of ethical committee and its members
  - minimal requirements regarding committee composition
  - confidentiality
- 35 local ethical committees for 384 laboratories using laboratory animals; 1050 projects per year

* also referred to as Institutional Animal Care and Use Committee (IACUC)

# Meeting the 'Guide' and Belgian legislation: Composition of the Ethical Committee

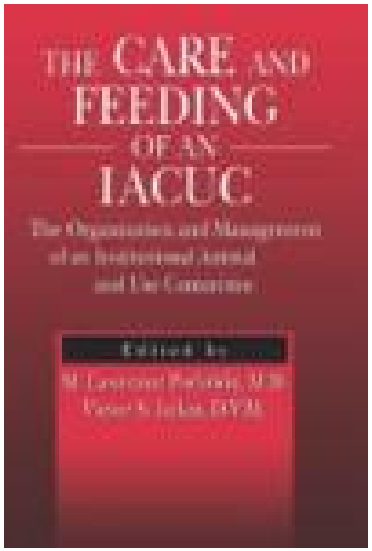
| | **'Guide'** | **Belgian legislation** |
|---|---|---|
| Number of members | Minimum 3 | Minimum 6 |
| Animal Welfare Officer | X<br>DVM, ACLAM certified or having training or experience in LAS or LAM | X<br>Not necessarily a veterinarian |
| Study Director/ principal investigator | X | X |
| Public/independent member | X | X |
| Laboratory director | - | X |
| Lab animal technician | - | X |
| Veterinary Inspector | - | X<br>PFS Public Health, Div. Animal Welfare & Cites |

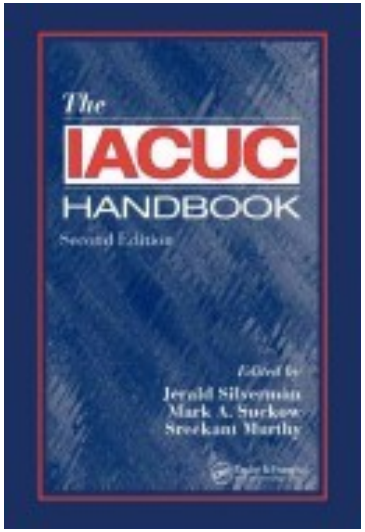
# Meeting the 'Guide' and Belgian legislation: Tasks and Responsibilities of the Ethical Committee

| | 'Guide' | Belgian legislation |
|---|---|---|
| Evaluating the ethical aspects of the experiments planned and executed | X | X |
| Establishing the ethical criteria concerning animal experiments | X | X |
| Advising the director of the laboratory, the study directors, and technicians concerning the ethical aspects of animal experiments | X | X |
| Advising the supervisory authority concerning the ethical aspects of animal experiments | | X |
| Oversight and evaluation of the Animal Care and Use Program (review 2x/year) | X | (X) |
| Inspections of the buildings and the infrastructure and inspections of the animals on the premises (2x/year) | X | |

# Meeting the 'Guide' and Belgian legislation: Running of the Ethical Committee

- Left to the discretion of the ethical committee and not legally imposed
  - Internal regulations
  - Based on input from other ethical committees, literature, and own learnings



# Major improvements after site visit and deferred accreditation in 2004

- Deficiencies identified: possible conflict of interest during the abbreviated ethical review process, and lack of documentation of committee deliberations
- Corrective actions taken:
  - Full review of all projects by the entire ethical committee before the start of the animal procedures
  - Addition of external member(s)
  - Separation of functions of animal welfare officer and study director to avoid potential conflict of interest
  - Implementation of ethical matrix
- Result of corrective actions: full accreditation (2004)
- No deficiencies identified during 2007 site visit

# Updated review process

- Scientific quality review and PMI Animal Welfare Committee review performed before applications are reviewed by the ethical committee.
- Applications submitted to ethical committee secretary at least 3 weeks prior to study start.
- Applications distributed to all members, usually in electronic format, for review. Reviewers have a minimum of 7 days to return comments.
- Comments and replies are shared among all members (later archived).
- If any reviewer requests a full meeting, it will take place within 7 days.
- Committee strives for a consensus; minority opinions are documented.
  - If no consensus can be reached, vote by simple majority.
- Committee decision ("approved", "approved under certain conditions", "temporarily approved" or "approval refused“) handed over to study director
  - In general, low percentage of disapprovals.
- Study director and committee members may appeal any committee decision to the Deontological Committee (National committee), whose decision is binding.

# Updated composition and functions

- Conflict of interest:
  - Better definition of role of animal welfare officer

- Addition of external members:
  - Extended to 2 external members
    - independent of PMI
    - with qualified knowledge of ethics and animal welfare

# Ethical Matrix

- Guidance document (2004)
  - Requests a detailed description of the objectives and social and scientific relevance of the animal experiments and of the research projects in a broader context.
  - Provides tools to balance the ‘benefits’ and ‘costs’ (in terms of animal suffering) of the animal experiments.
  - The pain, stress, and suffering of the animals and the implementation of the 3 Rs (replacement, reduction, refinement) are evaluated using different sources of information.
    - links to sources available in the document
    - sources used need to be identified
  - No scoring system used.
- Reviewed in 2008

# Challenges and Outlook

- Closing discussions and voting on project:
  dedicated eRoom
- Review of Animal Care and Use Program and animal-related Standard Operating Procedures
- Getting prepared for changes in EU-directive 86/609
  - Post-experimental review of protocols
  - Transparency and public information