



NTP
National Toxicology Program

NTP Mold Production Contract

Concept Review
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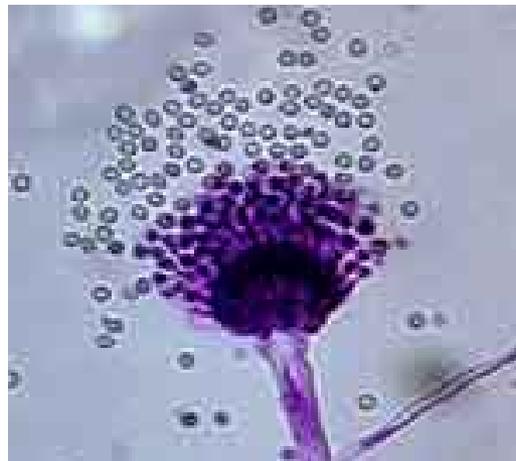
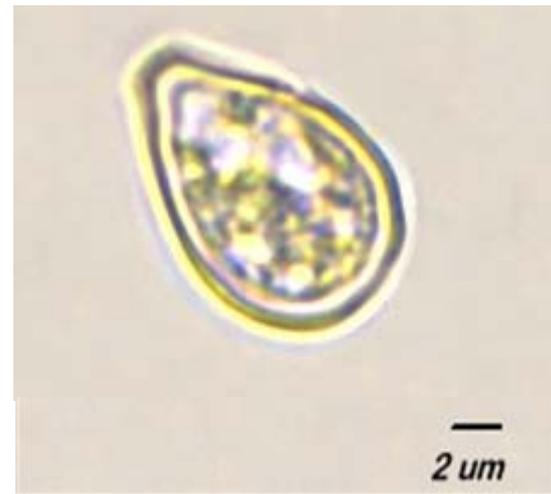


Why Are We Studying Mold?





Fungi Are Ubiquitous





Why Are We Studying Mold?

Exposure to elevated levels of indoor mold has been associated with a number of symptoms:

Allergies, asthma, hives, bleeding lungs, cancer, CNS problems, recurring colds, chronic cough, dandruff (chronic), dermatitis, skin rashes, diarrhea, eye/vision problems, fatigue, general malaise, flu-like symptoms, sudden hair loss, headaches, hemorrhagic pneumonitis, hypersensitivity pneumonitis, irritability, itching, kidney failure, learning difficulties, mental dysfunction, personality changes, memory loss.....



Nomination History

- Molds were nominated for study by a private individual
 - No specific organisms, endpoints, or health effects were suggested
- Nomination has been through multiple levels of internal and external review
 - NTP BSC and Executive committee - 2004
 - Endorsed study of molds and suggested that the program consider studying organisms commonly found in indoor air (i.e. Aspergillus and Penicillium) as well as Stachybotrys
 - NTP Concept review - 2006
 - Mold Studies Update to NTP BSC - 2007



Path Forward





NTP Toxicology Studies of Mold

- **Specific Aims**
 - Assess organ system toxicity following inhalation exposure to molds
 - Evaluate the available biomarkers of exposure and effect (both general and specific for the organisms to be studied)
 - Evaluate the contribution of different organisms to overall health effects by studying individual isolates as well as mixtures



NTP Toxicology Studies of Mold

- Proposed Approach
 - Conduct subchronic studies in rodents using inhalation as the route of exposure
 - Test two mixtures to simulate real life exposure scenarios
 - Mixed culture of molds from a water damaged building from New Orleans, Louisiana
 - Mixed culture of molds from a damp building with reported health effects (sick-building syndrome)
 - Test four isolates of individual organisms



NTP Toxicology Studies of Mold

- Proposed Approach
 - Test four isolates of individual organisms
 - *Stachybotrys chartarum* isolate 1 (macrocyclic tricothecene chemotype)
 - *Stachybotrys chartarum* isolate 2 (atranone chemotype)
 - Greenish-black fungus found worldwide
 - Colonizes high-cellulose material that becomes chronically moist or water damaged due to excessive humidity, water leaks, condensation or flooding
 - *Aspergillus versicolor*
 - Common on gypsum board, floor, carpet, mattress and upholstered-furniture dust, and damp walls.
 - *Alternaria alternata*
 - Commonly isolated from plants, soil, food, and indoor air environment
 - Important in allergy, infection and asthma severity



Purpose of the Mold Production Contract

- This contract will establish a mechanism for the procurement of materials needed to conduct toxicology studies



Specific Objectives

- Grow individual organisms and mold mixtures on relevant building materials from specific samples and/or colonies provided by the NTP
- Characterize the fungi and mold mixtures produced
 - Species and strain
 - Analytical (mycotoxins, glucans, allergens, protease activity and endotoxins)
- Confirm the viability and life-stage characteristics of the materials produced
- Supply bulk quantities of fungal materials in dry form
- Provide detailed information on the procedures used in production and characterization of the material
- Provide instructions for reconstituting the dried fungal material into a viable, growing colony

