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Pathogen Safety Data Sheet: Infectious Substances – *Cryptococcus neoformans*

SECTION I - INFECTIOUS AGENT

NAME: *Cryptococcus neoformans*

SYNONYM OR CROSS REFERENCE: *C. neoformans* var *neoformans,* cryptococcosis, cryptococcal infections, cryptococci, torulosis, European blastomycosis [1-3].

CHARACTERISTICS: *C. neoformans* is a spherical yeast, 4-6 µm in diameter, that produces a capsule containing glucoronoxylomannan (GXM), extending the overall diameter to 25 µm or more [4-6]. *C. neoformans* usually has a single bud that pinched off at the mature stage [4]. *C. neoformans* may also exist in pseudohyphal form. *C. neoformans* var *neoformans* contains serotypes A and D [1]. *C. neoformans* can differentiate into several complicated morphological forms, including yeast, chlamydospores, pseudohyphae and hyphae, and is typically present in the yeast form during infections. Small-sized basidiospores (1.8 to 3.0 µm) can turn into yeast cells, the form preferred at 37°C, or can form dikaryotic hyphae which are favoured at 24°C [8]. This organism exists as a yeast form in the environment [9].

SECTION II - HAZARD IDENTIFICATION

PATHOGENICITY/TOXICITY: *C. neoformans* causes various diseases in immunocompromised and immunocompetent hosts [10]. Diseases include meningoencephalitis (77.2%), pulmonary cryptococcosis (mostly in immunocompromised hosts, 8.2%), and several other diseases. Disseminated cryptococcosis is a complication and may occur in 91.8% of cases [11]. Cryptococcosis may be fatal if untreated. Spores or desiccated yeast cells of *C. neoformans* enter the host respiratory tract by inhalation [1,2]. Pulmonary infection disseminates most commonly to the brain and the skin [2]. *C. neoformans* can cause systemic infection, including fatal meningitis (meningoencephalitis) in normal, diabetic, and immunocompromised hosts [13]. The infection from *C. neoformans* in the brain can be fatal if untreated [8].

CNS infection: Cryptococcosis of the CNS presents mostly in the form of acute, subacute, and chronic meningitis, with symptoms of persistent headache, nausea, dizziness, ataxia, impaired memory and judgment, irritability, somnolence, clumsiness, and confusion [6, 10]. Patients may or may not have fever, and most have minimal or no nuchal rigidity. As the disease progresses, seizures may occur. CNS infection may also present as a brain abscess (cryptococcomas), subdural effusion, dementia, isolated cranial nerve lesion, spinal cord lesion, and ischaemic stroke. If cryptococal meningitis occurs, mortality rate is between 10-30% [14].

Respiratory infection: Pulmonary cryptococcosis may present as cough, dyspnea, blood-streaked sputum, and a dull ache in the chest [6]. Other respiratory system infections include pneumonia, cavitation, endobronchial masses, empyema, nodules, sinusitis, mediastinitis, bronchiolitis obliterans, and pneumothorax [10].

Cutaneous infection: Skin lesions may be single or multiple and commonly begin as painless lesions of the face or scalp [6]. Skin lesions may take the form of erythematous or umbilicated papules, pustules, acneiform lesions, indurated plaques, palpable purpura, soft subcutaneous masses, sinus tracts, cellulitis, vesicles, or large ulcers with undetermined edges.

Rarer presentations include lymphadenitis, pancreatitis, hepatitis, peritonitis, oesophagitis, osteomyelitis, septic arthritis, myositis, endophthalmitis, papilloedema, optic nerve atrophy, pyelonephritis, prostatitis, endocarditis, fungaemia, myocarditis, pericaditis, Cushing's syndrome, adrenal insufficiency, adrenal mass lesions, and thyroiditis [10].

EPIDEMIOLOGY: There are differences in number of cases in different strains of *C. neoformans* [1]. *C. neoformans* serotypes A and D are distributed worldwide and cause the vast majority of cryptococcal infections, predominately in immunocompromised individuals. Serotype A is responsible for over 95% of cryptococcosis cases worldwide [1]. *C. neoformans* serotype A appears to be implicated in 99% of AIDS patients with cryptococcosis worldwide, except in France where serotype A is responsible for around 80% of the infections [12]. More frequent cases of serotype A and D have been reported in Europe where cryptococcosis is associated with 77% of HIV patients. Cryptococcal meningitis, caused by the fungus *C. neoformans*, can cause up to 30% mortality in AIDS patients in resource-poor regions such as Southeast Asia [1]. It is estimated that 6% to 10% of patients with AIDS in the United States, Western Europe, and Australia and 0% to 50% of AIDS patients in sub-Saharan Africa are infected with life-threatening cryptococcal meningitis [12]. By the 1990s, *C. neoformans* had become the leading cause of culture-positive meningitis in many regions, including New York City. Cryptococcal meningitis alone kills about 624,000 people each year [1].

HOST RANGE: Humans and various domestic and wild animals (e.g., cats, birds) [1, 7].

INFECTIOUS DOSE: Unknown.

MODE OF TRANSMISSION: Spores are inhaled from the environment as the organism is found in the soil [1, 15].

INCUBATION PERIOD: Unknown, *C. neoformans* can colonize in the host respiratory tract for months to years without causing any clinical symptoms [1].

COMMUNICABILITY: Person-to-person transmission has not been documented other than through transplanted organs [6].

SECTION III - DISSEMINATION

RESERVOIR: *C. neoformans* may be found in humans and various domestic and wild animals [1, 7]. Soil and decaying vegetation is also a reservoir for serotypes A and D [1]. *C. neoformans* is associated with various environmental niches, especially avian guano [1, 9].

ZOONOSIS: Although *C. neoformans* may be encountered in animals, direct transmission from animals to persons has not been proven [17].

VECTOR: None.

SECTION IV: STABILITY AND VIABILITY

DRUG SUSCEPTIBILITY/RESISTANCE: Amphotericin B or itraconazole with or without flucytosine or fluconazole [15].

DRUG RESISTANCE: *C. neoformans* can develop resistance to flucytosine when used alone [5].

SUCEPTIBILITY TO DISINFECTANTS: *C. neoformans* is effectively killed by 70% ethyl alcohol and is susceptible to phenolic compounds, formaldehyde, glutaraldehyde, iodophors, and sodium hypochloride (1%) [18, 19].

PHYSICAL INACTIVATION: Photodynamic therapy (PDT), which combines methylene blue (MB) with a low-power red laser can inactivate *C. neoformans* [20]. PDT can be performed using 150 µM MB and 100mW red laser with a florescence at 180J/cm2 for 9 min. *C. neoformans* can be inactivated by UV, microwave, gamma radiation, moist heat (121°C for at least 20 min), and dry heat (165-170°C for 2 h) [21-24].

SURVIVAL OUTSIDE HOST: Unknown; however, the main reservoir for *C. neoformans* is the environment, including the soil, bird guano, and trees [1, 9].

SECTION V – FIRST AID / MEDICAL

SURVEILLANCE: Monitor for symptoms and confirm by culture and histopathology and serologically. Nested PCR may be used [4, 5, 15, 25].

Note: All diagnostic methods are not necessarily available in all countries.

FIRST AID TREATMENT: Give appropriate antifungal therapy [6].

IMMUNIZATION: No immunization is currently available [15]; however, some vaccines are currently in clinical trials, including GXM conjugated to tetanus toxoid vaccine, which has been shown to be effective in immunocompetent individuals in clinical trials [12].

PROPHYLAXIS: HIV patients may receive antifungal therapy such as fluconazole when no symptoms of infections are present [9].

SECTION VI - LABORATORY HAZARDS

LABORATORY ACQUIRED INFECTIONS: There is 1 reported case of laboratory exposure to *C. neoformans* from a laceration by a contaminated scalpel blade [26]. There are 2 reported cases of eye infections related to surgical procedure from *C. neoformans* [9]. Cryptococcosis from a needle puncture to the thumb during blood collection from an AIDS patient with cryptococcal fungemia and two percutaneous cryptococcal inoculations from needlestick have been reported.

SOURCES/SPECIMENS: *C. neoformans* may be found in soil, bird guano, blood, urine, and specimens from bone marrow, brain, CSF, eye, respiratory sites, skin, and mucous membranes [1, 4, 26].

PRIMARY HAZARD: Inhalation of basidiospores and desiccated yeast cells could be infectious for the lab workers and should be regarded as potentially serious airborne hazards [9]. Accidental parenteral inoculation of infectious materials may also occur [9, 26].

SPECIAL HAZARD: Bites from infected lab mice and manipulation of infectious environmental materials (e.g. pigeon dropping) may be a potential hazard [26].

SECTION VII – EXPOSURE CONTROLS / PERSONAL PROTECTION

RISK GROUP CLASSIFICATION: Risk Group 2 [27].

CONTAINMENT REQUIREMENTS: Containment Level 2 facilities, equipment, and operational practices for work involving infectious or potentially infectious materials, animals, or cultures [28].

PROTECTIVE CLOTHING: Lab coat. Gloves when direct skin contact with infected materials or animals is unavoidable. Eye protection must be used where there is a known or potential risk of exposure to splashes [28].

OTHER PRECAUTIONS: All procedures that may produce aerosols, or involve high concentrations or large volumes should be conducted in a biological safety cabinet (BSC). The use of needles, syringes, and other sharp objects should be strictly limited. Additional precautions should be considered with work involving animals or large scale activities [28].

SECTION VIII – HANDLING AND STORAGE

SPILLS: Allow aerosols to settle. Wearing protective clothing, gently cover spill with paper towels and apply an appropriate disinfectant, starting at perimeter and working towards the centre; allow sufficient contact time before clean up.

DISPOSAL: Decontaminate all wastes that contain or have come in contact with the infectious organism by autoclave, chemical disinfection, gamma irradiation, or incineration before disposing.

STORAGE: The infectious agent should be stored in leak-proof containers that are appropriately labelled.

SECTION IX – REGULATORY AND OTHER INFORMATION

REGULATORY INFORMATION: The import, transport, and use of pathogens in Canada is regulated under many regulatory bodies, including the Public Health Agency of Canada, Health Canada, Canadian Food Inspection Agency, Environment Canada, and Transport Canada. Users are responsible for ensuring they are compliant with all relevant acts, regulations, guidelines, and standards.

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Although the information, opinions and recommendations contained in this Pathogen Safety Data Sheet are compiled from sources believed to be reliable, we accept no responsibility for the accuracy, sufficiency, or reliability or for any loss or injury resulting from the use of the information. Newly discovered hazards are frequent and this information may not be completely up to date.

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