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IMPACT OF A TOXIC SINGLE-USE BIO-PROCESS CONTAINER FILM LEACHABLE ON CHINESE HAMSTER OVARY CELLS

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Key Words: Leachables, cytotoxicity, CHO cells, single-use systems

A high-throughput cell-based assay (HT-CBA) was developed to investigate the impacts of the polymer films used to construct single-use bio-processing equipment such as bio-process containers (BPCs) and single-use bioreactors (SUBs) on the growth and health of Chinese hamster ovary (CHO) cells. Cell growth media were incubated in BPCs constructed from several different films, and the media thus treated was used to culture CHO cells in 24 deep-well plates. Multiple films negatively impacted culture growth and viability. The compound bis(2,4-di-tert-butylphenyl)phosphate (bDtBPP) which leaches at low levels from these films was shown to be highly detrimental to cell growth. The toxic compound is derived from the breakdown of tris(2,4-di-tert-butylphenyl)phosphite (trade name Irgafos 168®), a common antioxidant additive present in many formulations of polyethylene (one of the polymers commonly used as the fluid contact layer of BPCs). Cell growth experiments with multiple recombinant protein-expressing CHO cell lines show a 50% reduction in culture growth at bDtBPP concentrations below the parts-per-million range for all cell lines. Cell specific productivity was not impacted. Cellular response to bDtBPP is rapid with a significant decrease in mitochondrial membrane potential within minutes of compound spiking. The CHO cells recover growth and health when returned to culture medium free of bDtBPP.

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