

ANALYSIS OF LEACHABLE BIS DI-TERT-BUTYL PHENYL PHOSPHATE (BDTBPP) IN BIOPROCESSING FILMS

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The analysis of extractable and leachable compounds from medical grade plastics is a complex issue that is compounded by the presence of many chemical species that are either direct or indirect reaction and/or degradation products of additives, process aids and polymer agents. These compounds may be present at various levels and the potential for adverse effects on cell growth remains to be determined and warrants further investigation. Since many of these films undergo aggressive processing steps, such as, thermal extrusion and gamma irradiation there is the potential for many unknown degradation products to be formed at each step of the processing. In addition, the absolute identification of many of these chemical compounds remains unknown. Within the various applications of single-use disposable bioprocessing, the presence of bis di-tert butyl phenyl phosphate (bDtBPP), a common gamma irradiation degradation product of tris (2,4-ditert-butylphenyl) phosphite (TBPP), has been shown to have a profoundly negative impact on cell growth for certain lines. The presence of bDtBPP even at low levels (on the order of 10ppb) has been shown to inhibit cell growth performance percentages in some lines by as much as 30-50% [1].

The quantitative analysis of this compound becomes increasingly difficult at lower levels due to either; 1) irreversible binding of strongly charged phosphate groups to glassware and other labware used in processing samples, or 2) hydrolytic degradation in aqueous solutions, or 3) any combination of the two. Losses from either of these conditions has been show to give rise to variations in quantitative analysis results as high as 50% when testing ranges are set between 5-100 parts per billion (ppb) in water. To this end, we have investigated the fate of this compound at part per billion levels to gain insight into possible mechanisms associated the variations observed. The hydrolytic degradation as well as irreversible binding to various substrates such as HPLC vials, pipette tips, etc. has been investigated extensively. We propose mitigation strategies which allow for low level quantitative analysis of this compound to achieve a coefficient of variation (CV) within the range of 10-20%, for bDtBPP in water within concentration ranges of 5-100 ppb.

References

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