

Triads XRPD Indexing Algorithm and Its Use in Pharmaceutical Development

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X-ray powder diffraction (XRPD) pattern indexing is the process of determining the size, shape, and symmetry of the unit cell and assigning the Miller index labels (h,k,l) of each of the peaks in a XRPD pattern given the peak list $\{2\theta_i\}$ or $\{d_i\}$. Indexing is a mathematically well-posed problem involving both real and integer unknowns. It is relatively easy to verify whether a proposed solution is consistent with an XRPD pattern, but surprisingly difficult to generate suitable candidate solutions. There are several software packages available for XRPD pattern indexing, any one of which is adequate for indexing of good quality XRPD patterns for materials with high-symmetry unit cells (cubic, tetragonal, hexagonal, and trigonal) commonly adopted by inorganic materials. None of the available algorithms is particularly well suited to the low-symmetry unit cells (triclinic, monoclinic, and orthorhombic) commonly adopted by solid forms of active pharmaceutical ingredients (APIs).

Details of a novel indexing algorithm called the Triads Indexing Algorithm will be presented. The algorithm provides an efficient, deterministic means of generating candidate structures in a form that is convenient for evaluation of the candidate solutions. The Triads Indexing Algorithm has been used routinely for over a year at SSCI, a division of Aptuit. Illustrations of the utility of indexing in pharmaceutical development will be given. Performance comparisons of the Triads Indexing Algorithm to other algorithms in terms of success rate and computation time will be provided.

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