

ANALYSES OF PHARMACEUTICAL FORMULATIONS

Timothy G. Fawcett¹, John Faber¹, Fangling Needham¹
Camden R. Hubbard² and James A. Kaduk³

¹International Centre for Diffraction Data, Newtown Square, PA, 19073

²Oak Ridge National Laboratory, Oak Ridge, TN 37831

³Innovene USA LLC, Naperville, Illinois, 60566

In December 2002, the International Centre for Diffraction Data (ICDD) launched a new database product, PDF-4/Organics, designed to identify materials in the pharmaceutical, law enforcement, and specialty chemicals fields. The first release contained 136,895 entries that resulted from two merged databases, single crystal data from the Cambridge Structural Database (CSD) and the experimental powder data for organics from the Powder Diffraction File (PDF). It had taken approximately four years, from 1998-2002, for the ICDD editors to convert, standardize, calculate and review single crystal data from the CSD into compatible powder entries in the PDF. Since the first release there have been large annual additions to the database so that the 2006 Release PDF-4/Organics contains 286,464 entries. The ICDD teamed with global software developers to interface the database to the world's most powerful x-ray analysis software. Today the database and a wide range of analysis software are available from multiple vendors.

During the growth and development of PDF-4/Organics two fundamental questions were continuously asked. Does this new tool help solve material identification problems for the target industries? How can we make the product better? To answer the first question three separate studies were conducted by the authors over the past three years. Formulations were analyzed in a series of off-the-shelf pharmaceutical tablets, vitamin pill and health supplements, and finally a series of common fertilizer formulations. The samples represent high volume common materials with combined sales of billions of dollars. A wide variety of instruments were used for data collection ranging from a benchtop diffractometer to the synchrotron at Argonne National Laboratory. Commercial x-ray analysis programs were used to identify from three to ten phases in each specimen for 35 different formulations. Overall the results demonstrate the power of the database and analysis software to perform competitive analysis and formulation studies. As a result of this study and regular feedback from ICDD members and customers several features were added during this period. Common inorganics and excipients were added to aid in problem solving, disorder structures were analyzed and added if they passed several statistical criteria, a quality mark system was developed for evaluating calculated patterns. These have had the net result of improving the chances of identification particularly in complex multi-component formulations.