Detecting errors and inconsistencies in the structure determination of pharmaceutical compounds: wrong structures, twinning, disorder and modulation.

Graciela Díaz de Delgado,[1] María Cecilia Dávila,[1] Analio Dugarte,[1] Estefany Hernández,[1] Astrid Mora,[1] Miguel Ramírez,[1] Hernando Camargo,[2] José Antonio Henao,[3] Robert Toro,[3] José Miguel Delgado.[1]

[1] Laboratorio de Cristalografía-LNDRX, Universidad de Los Andes, Mérida, Venezuela, [2] Facultad de Química Ambiental, Universidad Santo Tomás, Florida Blanca, Colombia, [3] GIQUE, Universidad Industrial de Santander, Bucaramanga, Colombia.

The final stages of a structure determination and refinement process include a series of validation procedures to detect inconsistencies and errors before publication and deposition of the results into the different crystallographic databases. Richard E. Marsh's legendary work on identifying missed symmetry and incorrectly described structures has been a major driving force in the development of structure validation tools that are now available to the crystallographer. In this contribution, we will discuss several examples of compounds recently studied in our laboratory where careful analysis and validation indicated the need for a re-determination, a new refinement, or the presence of interesting unidentified features. The examples include the identification of a new polymorph of Diclofenac methyl ester (wrong structure reported), re-determination of the structure of a polymorph of enalapril maleate (using diffraction data from a multi-crystal composed of two concomitant polymorphs), commensurate modulation in the structures of clorpheniramine maleate and a Cu-complex of γ-aminobutyric acid, and incommensurate modulation in the structures of ciprofloxacin and valproic acid derivatives.