# A Force Field for Halogenated Active Pharmaceutical Ingredients

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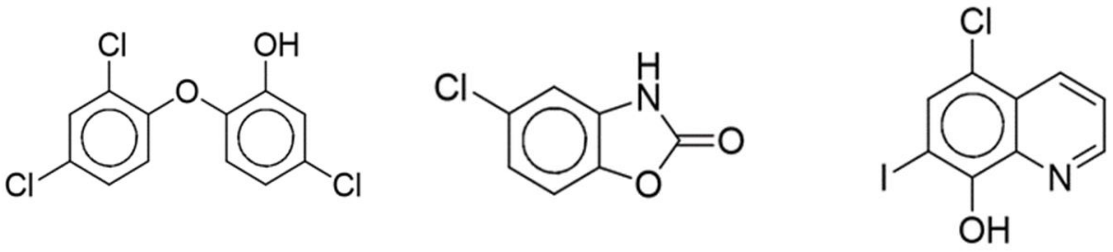
The discovery of a new active pharmaceutical ingredient (API) that is effective for a specific disease is a very costly and time-consuming process. Many interesting APIs in development pipelines fail to reach the market because of problems that have a negative impact in the production and performance of a drug, such as low solubility, polymorphism, and incompatibilities with excipients. For example, low solubility often implies a low bioavailability, and polymorphism, the ability of a molecule to adopt more than one crystal structure, frequently leads to differences in physical properties that hinder the production of drugs with highly reproducible performance.

Molecular dynamics (MD) simulations have become increasingly more familiar to pharmaceutical developers as a powerful tool to rationalize and forecast the properties of prospective APIs that are critical for an a priori evaluation of negative impacts on production and performance. A critical aspect of the use o MD simulations is the development of force fields that are able to accurately capture the energetic (e.g. lattice energy) and structural (e.g. unit cell dimensions) characteristics of an as large as possible class of substances. Here we describe the parameterization and validation of a force field suitable halogenated molecules, based on the study of three marketed APIs (Figure 1): triclosan, (b) chlorzoxazone and (c) clioquinol




(a) (b) (c)

**Figure 1.** Halogenated APIs selected to develop this work: (a) triclosan, (b) chlorzoxazone and (c) clioquinol.