The process of structural identification is often dynamic, requiring multiple revisions of partial structures before arriving at the final structure. A process coupling the capabilities of mass spectrometry, NMR, and other techniques is described.

How do you represent, store, and revise potential structures throughout the process of elucidation, and ultimately report and communicate these structures to your spectrometrists, chemists and biologists? One does not always have enough information to provide an absolute identification of analytes or their isomeric forms in the early stages of structure identification, in which case one’s interpretation will correspond to a set of possible chemical structures. If several of these compounds have a common scaffold, this collection can be represented succinctly through a generic structure representation rather than trying to draw each potential case individually. One form of generic structure representation utilized by the patenting group is the Markush representation — enabling the attachment of one or more substituents to multiple potential connection points but still communicating valuable structural information. Such a feature is ideal for the representation of structure throughout the structural elucidation phase.

Method
Markush structures are particularly useful in the study of degradants, impurities, and metabolites that are routinely studied by mass spectrometry. Using ACD/MS Manager Suite, which incorporates the structure drawing package (ACD/ChemSketch), allows you to draw, attach, database, search, and report using partial, Markush, or absolute structure to your chromatographic and spectral data. The classical representation of Markush as in Figure 1 (left) does not permit the unambiguous location of the possible chlorination site. In the event that the Markush attachment is made to a phenyl, for example, it is implied that the attachment is in all available positions on the ring structure. When the attachment extends beyond the ring, the identification is unclear. Using the ACD/Labs shaded Markush representation (right) clearly identifies the exact sites of substituent attachment, and thus, interpretation of the likely structure is definitive.

During the elucidation of the structure by mass spectrometry, the shaded Markush structure representations can be attached to both spectra and chromatograms, as depicted in Figure 2.

The chromatograms and spectra with associated structures can then be added to the database and enabled for structure searching by structure, substructure, and similarity.

Conclusion
The process of structural identification is one where the analyst narrows a list of structural possibilities. These possibilities can often be represented more concisely and accurately by site specific Markush structure representation, namely shading. Markush structure allows you to accurately describe the current state of interpretation and permits one to better communicate mass spectrometric, NMR, and other analytical technique information.