s6.m22.o1 **In Memoriam of Jacek M. Grochowski**
Michal Markiewicz

s6.m22.o2 **VCD Spectroscopic Determination of Absolute Stereochemistry as a Complementary Technique for Investigation of Chiral Drugs.**
Helen Turner,[a] Christopher Frampton,[b] Andrea Russell,[a] Mike Claybourn[c] and Ron Roberts[c], [a]*University of Southampton, UK,* [b]*Bruker Nonius, Europe, and* [c]*AstraZeneca, UK. E-mail: hlt298@soton.ac.uk*

Keywords: Absolute Stereochemistry; VCD; Single Crystal XRD

Chirality plays a major role within the pharmaceutical industry, with more than one third of all drugs marketed being sold in a single enantiomeric form. The FDA requires for regulatory submission that the absolute stereochemistry be proven by single crystal X-ray diffraction. This allows comparison of the functionality, activity and safety of different enantiomers of the active pharmaceutical ingredient. However, the route to determination of absolute stereochemistry is not always an easy one, especially where pharmaceuticals are concerned. Single crystal X-ray diffraction using the anomalous dispersion method is a well established technique, but requires good quality crystals as a pre-requisite, which are not always possible to obtain. Vibrational circular dichroism (VCD) spectroscopy can provide a complementary route to accurate absolute stereochemistry determination and can be performed on both liquids and solutions. This technique operates in the infrared region of the spectrum and is based on the differential interaction of the enantiomers with left-handed and right-handed circularly polarised light.

Captopril ($C_9H_{15}NO_3S$) is an angiotensin converting enzyme (ACE) inhibitor used in the treatment of high blood pressure and heart failure. It was the first potent and orally active ACE inhibitor. Atenolol ($C_{14}H_{22}N_2O_3$) is a beta blocker and it can be used to treat hypertension (high blood pressure). Cholestane ($C_{27}H_{48}$) is a hydrocarbon and is the parent structure of all mammalian steroids. These three compounds present increasing levels of difficulty for traditional absolute stereochemistry determination by single crystal X-ray diffraction using the anomalous dispersion technique. We show here how VCD spectroscopy can be used in these situations to provide complementary evidence for accurate absolute stereochemistry determination.