ESRF	**Experiment title:** Measurement of diffuse scattering of the active pharmaceutical ingredient Aspirin	**Experiment number**: CH-2798
Beamline: BM01A	**Date of experiment**: from: 11 June 2009 to: 15 June 2009	**Date of report**: 27.1.2010
Shifts: 12	**Local contact(s)**: Phil Pattison, Dmitry Chernyshov	*Received at ESRF:*

Names and affiliations of applicants (* indicates experimentalists in attendance):

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Report:

Facilities used: MAR-345 detector for all measurements, wavelength 0.7021 Å, 21 runs.

Aspirin: The aim of the project was to obtain diffuse scattering data on mixed polymorph crystals of Forms I and II of Aspirin. High-quality crystals of the mixed polymorphs are by their very nature very difficult to obtain. Although we brought several prescreened samples with us, the intense synchrotron radiation revealed that the crystals were generally not of sufficient quality to be of use for the experiment. Furthermore, we found that such crystals are extremely delicate and sensitive to mechanical influences and even transferring one good crystal to a different mount rendered it unusable. After several hours, and investigation of all of our aspirin crystals, we switched to our backup project.

α-$NaLuF_4$: This material was initially studied during our visit to BM01A in Nov. 2008 (report HS-3639). At that time, we made the unexpected discovery that the crystals display evidence of six-fold twinning, quite sharp satellite reflections and extensive diffuse scattering. In addition, crystals from different parts of the melt ampoule (obtained by the Bridgman technique) displayed different diffraction patterns, indicating that the ampoule was not a single phase. As that ampoule had been synthesized some months prior to the experiment and crystals taken from some regions of the ampoule seemed to crumble over time, it was uncertain if the different phases were a function of decomposition or slow annealing of some regions of the ampoule. Our aim was to build on the experience gained and shortfalls experienced during the HS-3639 experiment and collect improved Bragg, satellite and diffuse scattering data (fast, medium, slow data collections) at room temperature from several crystals chipped off different parts of a newly synthesized ampoule. We also wished to obtain data sets at two additional temperatures (100 and 200 K) to be able to follow the temperature evolution of the atomic displacement parameters of the average structure and thus to separate dynamic from positional disorder.

Fourteen data sets were collected from different crystals of α-$NaLuF_4$. All crystals from various parts of the freshly synthesized ampoule showed the same diffraction pattern, so the ampoule was only a single phase. Rapid cooling of a crystal from the new ampoule resulted in crystal damage, as seen by split reflections in the reciprocal space reconstructions. Slowly cooling another crystal averted this problem, and we now have data sets at 290, 200 and 100K from the same crystal.

A distinctly different diffaction pattern was observed with one sample that came from the old ampoule (as seen previously), thus confirming that the old ampoule was indeed composed of at least two phases (lest we had mixed up samples previously).

The processing of the obtained data has occupied most of our time since. We have put a lot of energy into optimising the data integration for the main and satellite reflections. This has been complicated by the closely overlapping reflections from six twin domains, which caused difficulties in obtaining, for example, correct orientation matrices, appropriate integration box sizes, etc. We now believe we have, after many months, obtained the best data integration possible, and are proceeding with the structure refinements, first in an orthorhombic C-lattice using just the main reflections from the six twin components, then in the five times c-axis supercell. Once this has been done we will have good models for the average and modulated structures and can then proceed with interpretation of the diffuse scattering. See the previous report (HS-3639) and the summary below for a description of our interpretation of the structure thus far. We have not yet really progressed beyond this point in developing our models or understanding the structure, because of the time spend overcoming the challenges of the data integration.

- The crystals do not have cubic symmetry, but tetragonal at the most, as the reflections along some lines in reciprocal space are not collinear, but alternate slightly each side of the mean line.
- The reciprocal space maps show satellite reflections indicating a commensurately modulated structure. If the cubic unit cell is transformed to *C*-orthorhombic, the satellites align along *c* with q = 0.2.
- If the satellites are treated as Bragg peaks, one can derive an orthorhombic cell with space group *Cmmm*. The structure could be solved easily in the 5-fold supercell using Superflip[1] and an initial comparison with the average structure derived from the "cubic" Bragg data showed close agreement of atomic positions and modulation of the site occupations of the shared Na/Lu sites in one column through the structure and possible positional displacements of similar sites in other columns through the structure. Subsequent treatment of the satellite data in terms of modulation vectors will simplify refinement.
- The apparent cubic lattice symmetry and systematic reflection "presences" in the orthorhombic setting can be explained in terms of 6-fold twinning.
- The α-$NaLuF_4$ sample seems identical with one characterised in 1966 by powder diffraction for which no structural model was reported.[2]

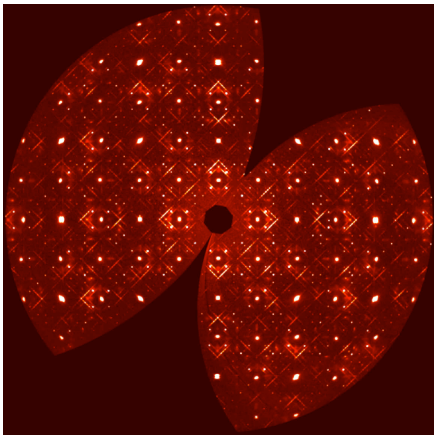
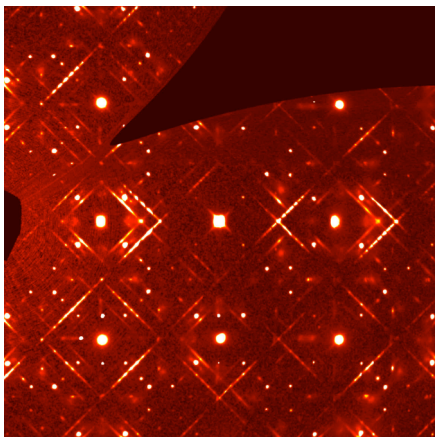
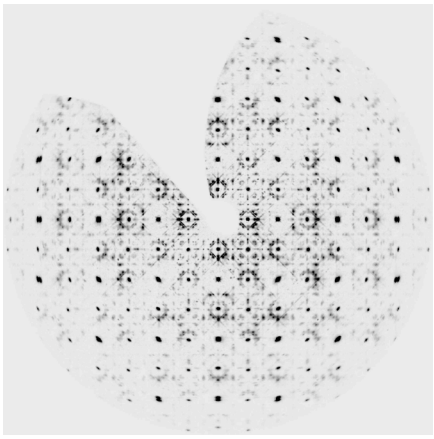
a)  b)  c) 

Fig. 1. *a*) The (*h*0*l*) layer from a fresh crystal of α-$NaLuF_4$ on beamline BM01A, showing Bragg peaks, satellite peaks and weak diffuse scattering; *b*) A close-up centred on 200 shoing the richness of the diffraction pattern; *c*) The (*h*0*l*) layer from the second phase of α-$NaLuF_4$ (beamline BM01A Nov. 2008).

1. L. Palatinus, G. Chapuis, *J. Appl. Crystallogr*. **40** (2007) 786.
2. R.E. Thoma, H. Insley, G. M.Hebert, *Inorg. Chem*. **5** (1966) 1222.