It is estimated that about 80-90% of the active pharmaceutical ingredients (API) are actually marketed in the form of solid state (tablets, powder inhalations), since an oral administration of drugs is the most comfortable for patients. However, a given compound may exists in the different crystal forms, which are further called the polymorphs. The different structure is the reason for considerable differences in the physicochemical properties of APIs, including different melting points, density and rate of dissolution and so forth, which are directly related to their biopharmaceutical classification.

Over the last few decades, an enormous interest in polymorphism of APIs has been observed, having implications in the biopharmaceutical properties, formulation/processing or intellectual property aspects. Probably, the most known example is an anti-HIV agent, Ritonavir, where the decreased bioavailability of the - unexpectedly emerged - polymorphic form led to withdrawal of the extant formulated products from the market. From the regulatory perspectives, clear understanding of polymorphism and its impact on drug product is therefore essential.

The bioavailability of a given active ingredient - determining the effectiveness of therapy - is directly related to the dissolution rate of an API in solid form. It has been proved that polymorphic forms, differing in the rate of solubility, can be used by organism to a different degree. It can happen that one of the forms is pharmacologically active, while the others are not. In such a case, because of the poorer solubility - and thus a lower rate of absorption - they could not reach the concentration in the blood required for the therapeutic effect.

However, the substances in amorphous phase are usually characterised by a higher rate of dissolution rate than those in crystalline state, which implies the administration of possibly smaller doses of the drug and, thus, reducing the risk of unwanted side effects. The amorphous substances show disordered internal structure but not fully random as there is a short-range ordering.

While the case of Ritonavir changed the view of pharmaceutical scientists towards the polymorphism, it is, however, even more intriguing to note that, much attention has already been paid to the unexpected polymorphism of amorphous substances, the so-called polyamorphism. So far the phenomenon of polyamorphism has been observed and studied in more detail for inorganic APIs than organic ones. Thus, in view of the fact that analysis of this phenomenon is very important for therapeutic effects, the interest in determination of polyamorphism for organic APIs has been recently increasing.

Amorphous substances can be obtained by different methods, e.g. by fast cooling of molten substance, vapour condensation, precipitation from solutions, milling of crystalline substances, lyophilisation or spray drying. Nevertheless, the use of amorphous substances is related to the problems following from their low physicochemical stability. The amorphous form is less thermodynamically stable so it is more vulnerable to transformations upon certain particular technological processes, since the changes in temperature, pressure or humidity can further induce the phase transitions.

In technology of dosage forms the influence of particular processes taking place in the drug formulation must be considered. Changes in the condition of the formulation process or storage of drug dosage forms can induce polymorphic transformations. API and the auxiliary substances must be obtained in strictly defined and chemically pure form at all stages of production and storage.

The majority of amorphous substances show a tendency to crystallisation, which implies the appearance of disappearance of a certain form of solid state. In API is can have serious pharmaceutical and therapeutic consequences. That is why investigation of polymorphic and amorphous species of pharmaceutic substances and their phase transitions in solid state is of key importance for development of new formulations and for the process of their production. Although a broad spectrum of experimental methods can be applied for analysis of crystalline substances, including differential scanning calorimetry (DSC), infrared spectroscopy (FT-IR), solid state nuclear magnetic resonance (SSNMR) and X-ray powder diffraction (XRPD), investigation of amorphous forms still remains an analytical challenge.

The properties of amorphous substances depend not only on the structure but also on the molecular dynamics, so analysis of the latter aspect is an important element of amorphous bodies characterisation. It is generally believed that determination of reorientations and internal mobility of amorphous species can be of key importance for understanding of their physicochemical properties and for development of methods for enhancement of their physicochemical stability.

The study of molecular reorientations planned in this project, especially the study of amorphous systems incorporated into a silica matrix and subjected to high pressure, have an innovative character which could shed more light on the relation between the structural and dynamic aspects affecting the stability and biopharmaceutical properties.