

solid form services

Importance of form selection

With an estimated 90% of organic molecules exhibiting multiple forms (polymorphs and pseudopolymorphs), the selection of a lead solid form is a critical early step in pharmaceutical development. Solid form selection involves both the chemical makeup of the solid to be manufactured as well as its crystal structure. Both the chemical and physical form determine a range of critical parameters, i.e. manufacturability, stability and bioavailability. These properties impact the development and manufacturing of both the drug substance and drug product.

About half of all marketed pharmaceutical products are salts, which often can provide both higher melting point and higher aqueous solubility. Polymorphs, solvates, and hydrates must be identified, characterized, and studied in order to develop robust manufacturing processes, ensure long-term stability, and de-risk costly changes to the drug substance, drug product, or manufacturing processes in later phases of clinical development. Many properties are affected by the solid form, whether that be a salt, hydrate, cocrystal, solvate, or polymorph.

At Lonza Solid Form Services, we have defined work flows to assess and select solid forms in a cost and time efficient manner that meets the needs of each individual program.

Key pharmaceutical properties affected by solid form selection

Critical properties affected by chemical and/or polymorphic form

Stability

- Melting and sublimation temperature
- Form stability
- Chemical stability
- Hygroscopicity

Packing

- Density
- Morphology

Purity and appearance

- Color
- Impurity profile

Bioavailability

- Solubility
- Dissolution rate

Mechanical

- Hardness
- Tensile strength
- Compactibility
- Tabletability
- Handling and filtration
- Flow and blending
- Cleavage
- Milling

Integrated development services

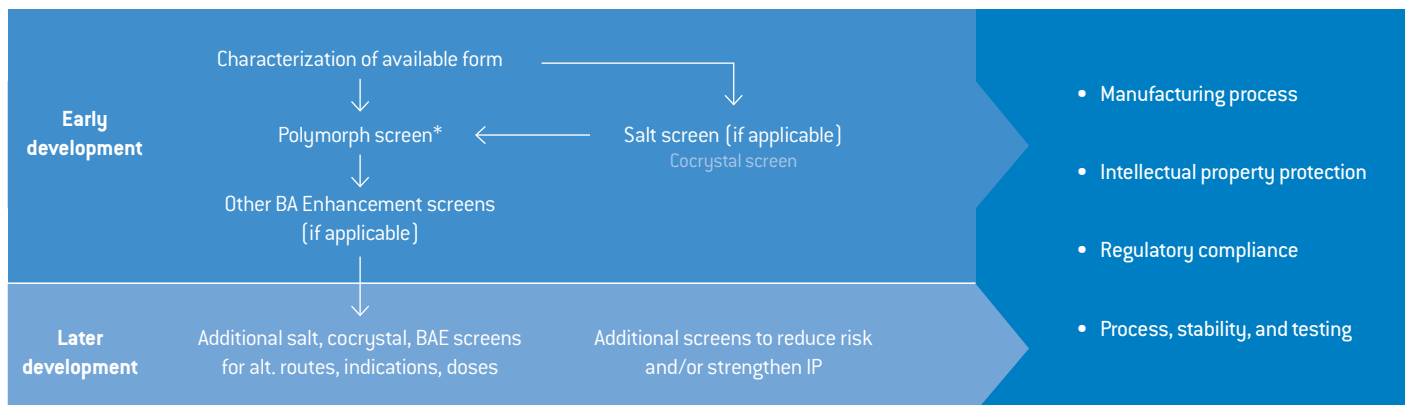
Because every molecule and problem statement is unique, the work is customized to your molecule, problem statement, and development stage to identify a suitable form. The close collaboration of the solid form services team with our drug substance and drug product development teams means that the data collected during solid form development is leveraged across all development areas.

Solid form services

Identifying and selecting a lead solid form

The selection of a lead solid involves the screening and characterization of both chemical forms (free form, salts, hydrates, solvates, cocrystals) and polymorphs of lead chemical forms. Every molecule has a different propensity for polymorphism and to form hydrates and solvates. Additionally, the physicochemical properties of the molecule

and the target product profile will determine the need for screening salts, cocrystals, or bioavailability enhancing formulations. It will also determine the key properties of any solid form, whether that be solubility, dissolution rate, or manufacturability. In all cases, physical and chemical stability of the isolated form is critical.



*Includes hydrates and solvates ["pseudopolymorphs"]

Defined work with customization

We have a wide array of characterization tools and decades of materials science experience to understand the solid form landscape of your molecule. X-ray powder diffraction (XRPD), thermogravimetric analysis (TGA), differential scanning calorimetry (DSC), and nuclear magnetic resonance (NMR) spectroscopy are the workhorses of solid form screening. These techniques allow us to identify unique forms, determine their chemical makeup, and determine thermodynamic transitions between forms. Single crystal XRD and solid state NMR are utilized to understand the detailed arrangement of molecules in a crystal. Many other characterization tools and services are available

for determining the developability, potential formulation strategies, and downstream manufacturability of solid forms.

Example screens include:

- Characterization
- Primary polymorph screen
- Stable form screen and developability assessment
- Secondary polymorph screen
- Primary salt screen
- Secondary salt screen
- Salt developability assessment
- Cocrystal screen
- Preformulation screen
- ASAP and traditional stability

| Solid state characterization | Chemical composition | Solubility and dissolution | Powder properties |
|---|---|---|--|
| <ul style="list-style-type: none"> • Powder XRD • Microscopy (PLM, Hot-stage, fluorescence, SEM, EDS, TEM*, FIB-SEM*) • Spectroscopy (FTIR, Raman, ssNMR) • Thermal analysis (TGA, mDSC, multicell DSC, isothermal calorimetry, solution calorimetry, flash DSC) • Vapor sorption (solvent, water) • Single crystal XRD* <p>*External lab</p> | <ul style="list-style-type: none"> • Chromatography (HPLC, UPLC, LC-MS, LC-CAD, GC, GC-MS) • Spectroscopy (NMR, UV-Vis, FTIR, Raman) • Solvent content (GC-headspace) • Water content (KF, water activity) • Elemental analysis* | <ul style="list-style-type: none"> • Solubility in biorelevant media and process solvents • Amorphous solubility and polymer sustainment • BCS/FaCS classification • pKa and logP profiler • Intrinsic dissolution • Biorelevant dissolution • USP dissolution and disintegration • Flux (permeation) testing for DS and DP | <ul style="list-style-type: none"> • Particle size (sieving, laser scattering, DLS, nanoparticle tracking) • Tableability (CTC profiling) • Density: (true, envelope, bulk, tapped, BET surface area/porosity) • Powder flow |

Our Solid Form Services group is located on our Bend, OR (USA) site and collaborates across our global network to provide our clients the best solid form solutions.

Contact us

small.molecules@lonza.com

The information contained herein are intended for general marketing purposes only. While Lonza makes efforts to include accurate and up-to-date information, it makes no representations or warranties, express or implied, as to the accuracy or completeness of the information provided herein and disclaim any liability for the use of this publication and that all access and use of the information contained herein are at their own risk. Lonza may change the content of this publication at any time without notice but does not assume any responsibility to update it. All trademarks belong to Lonza or its affiliates or to their respective third party owners and are only being used for informational purposes.