

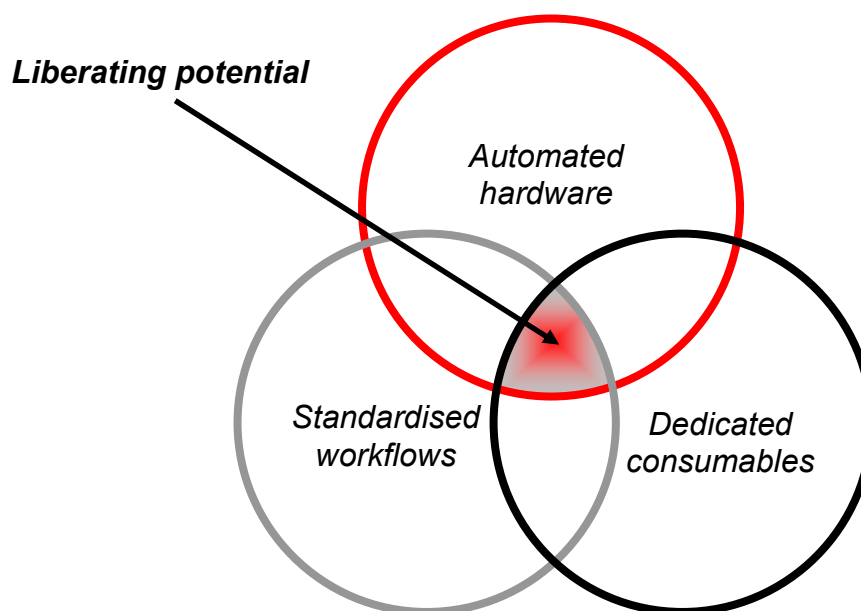


Preformulation and formulation support

Introduction

The scientifically based development of a new drug formulation is a challenging and complex task. Most companies, therefore, have elaborated a stage-plan-based approach starting with the development and physico-chemical characterisation of the solid state, followed by compatibility studies, formulation prototypes and finally market formulation. However, all of these activities are time-consuming and expensive. Therefore, in most cases, preformulation and formulation programmes are reduced as far as possible, which on the other hand increases the risk of pitfalls in later stages of development.

RPD TOOL offers a range of products dedicated to liberating the potential of your drug by selecting the best formulation candidate. Our answer to the above-mentioned time and cost issues consists in the balanced use of highly automated proprietary hardware platforms, dedicated consumables and standardised workflows. The combination of these elements ensures that **the potential of your drug is liberated**. Reduced preformulation or formulation programmes or other compromises no longer have to be accepted in order to meet both the requirements of fast and cost-effective drug development and the market's demand for high-quality products.



Plot 1: The balanced use of automated hardware, standardised workflows and dedicated consumables are today's answer to the latest pharmaceutical needs.

Automated hardware products

RPD TOOL has developed a set of lab automation platforms to provide the required sample throughput at the highest level of quality. These are:

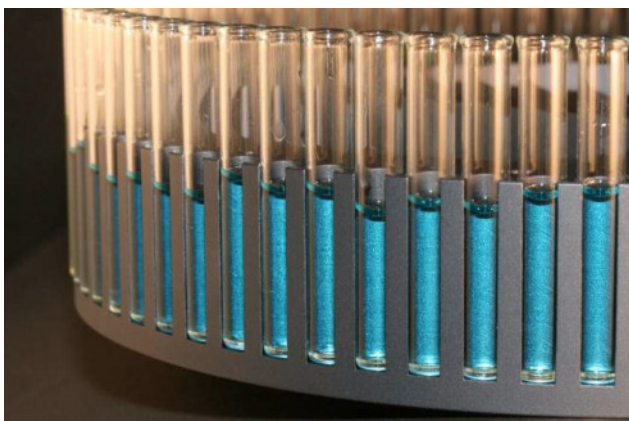
- **PreFormulation Mate:** *PreFormulation Mate is a flexible platform for performing important preformulation and formulation workflows, such as salt, polymorphism and co-crystal screening, as well as the determination of solubility and solubilisation/dissolution rate.*
- **SpecScreen xHTS:** *SpecScreen xHTS enables the fully automated performance of physical storage stability studies under a wide range of storage conditions. The robot system is equipped with a set of dedicated analytical tools (Raman-, NIR-spectrometer and camera) which enable an in-depth investigation of storage time and conditions in important physical parameters, such as (pseudo)morphological stability, hygroscopicity visual appearance, solubility and solubilisation rate.*
- **ChromScreen xHTS:** *ChromScreen xHTS enables the fully automated performance of chemical storage stability studies. The system contains sophisticated tools for sample preparation and chromatographic analysis of all formulation samples stored under a wide range of conditions. ChromScreen xHTS provides detailed answers as to the effects of storage time and conditions (temperature, light, humidity) on the formation of by-products, as well as racemisation and epimerisation of the drug substance.*
- **StabScreen xHTS:** *StabScreen xHTS is a combined platform for the fully automated assessment of the physical and chemical storage stability of new drugs and formulations. The system enables a large number of samples to be stored under a wider range of conditions (light, temperature, humidity) and contains all the analytical modules of SpecScreen xHTS and ChromScreen xHTS.*

These four automation platforms are designed to operate with RPD TOOL's dedicated consumables and workflows as described in the following section and ensure that the various workflows during preformulation and formulation development are cost-effective.

Disposable consumables

In addition to the above-mentioned hardware tools, a set of disposable consumables has been developed in order to guarantee the most efficient workflows and the highest reproducibility and quality of results. The set of consumables covers a volume range from a few microlitres to 100 ml. Typical examples of our consumables are our tailored glass vials for 96 well plates (20 to 1000 μ l volume range) and 24 well plates (1 to 10 ml volume range) which can be used for a variety of applications such as:

- Automated chemical and physical storage stability studies of powder, compacts, semi-solid and liquid substances and formulations under different environmental conditions (temperature, humidity, light) on our screening platforms.
- Automated photodegradation and oxygenation studies.
- Salt formation, polymorphism and co-crystallisation studies.
- Automated solubility determination in the mg scale.
- Determination of physical parameters such as log P, pKa or hygroscopicity.
- Automated HPLC sample preparation.

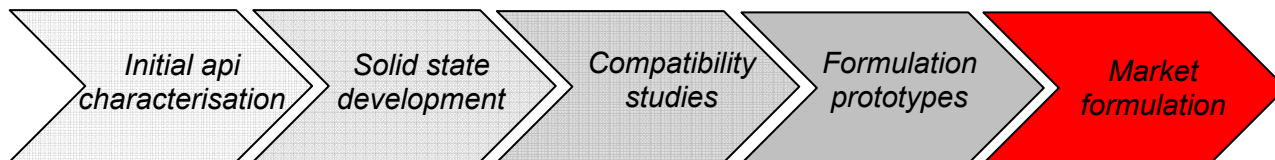


Plot 2: Disposable 96 well glass vials: Left: During crystallisation experiments in our automated hardware platform. Right: Arrangement of different applications. From left to right: For storage stability studies of compacts under humidity-controlled conditions; for storage stability studies of powders under humidity-controlled conditions; for storage stability studies of powders under dry conditions; for HPLC sample preparation; equipped with a magnetic stirrer for solubility determination; equipped with an FEB liner for automated slow evaporation experiments during polymorphism screening experiments.

Cost-effective disposable consumables are also available in the 10 to 100 ml volume range for scale-up of solid formation experiments, automated dissolution studies or fully automated HPLC sample preparation. All consumables can be equipped with RFID tags for automated sample tracking during both automated and manual workflows.

Physico-chemical characterisation and standardised workflows

Our highly automated standardised workflows can be performed from initial preformulation activities to final market formulation:



Picture 2: Stages of pharmaceutical drug development. .

Examples of workflows and physico-chemical characterisations in different development states are:

Physico-chemical characterisation

- Solubility and log P
- Solubilisation/dissolution rate
- Hygroscopicity
- Initial physical and chemical stability
- DSC, TGA, particle size distribution

Solid-state development

- Salt screening
- Polymorphism screening
- Co-crystal screening
- Amorphous form screening
- Physical and chemical stability

Compatibility studies

- Chemical storage stability
- Physical storage stability
- Physico-chemical characterisation of stored samples

Formulation development

- Chemical storage stability
- Physical storage stability
- Physico-chemical characterisation of stored samples

Benefit

We are committed to setting new standards in formulation R & D by providing dedicated hardware, consumables and workflows. You can either benefit from our products or our services to accelerate your development process by parallel processing of automated workflows.

Please do not hesitate to **liberate the potential of your drug** and contact us for further details of our unique technology!

Your RPD TOOL Team.