

Summary of YPF analytical and processing capabilities in the area of Formulation Technology

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Production		
Powders and solid formulations		
Method/instrument	Type of sample	Principle, information
Spray drying, YKI-design	Powders, particle sizes 1-20 μm	Spray drying. Aqueous solutions only. Capacity: solutions from 30 ml to 1-2 L are practically feasible, but it depends on the formulation.
Spray drying for production of mesoporous silica	Powders, particle size 1-10 μm	Spray drying with drying at room temperature, followed by heat treatment in the oven. Ethanol/aqueous solutions.
Hydrothermal synthesis	10nm-100 μm	High temperature and pressure treatment of metal salts in the autoclave
Ball-milling	Powders, 0.1-10 μm	Mechanical chemical synthesis, involves the reaction activated by mechanical forces
Sol-gel	0.1-100 μm	Formation of gel and calcination, up to 300g dry powders
Colloidal process of powder coatings	0.01-500 μm	Dispersion of powders in a liquid phase and coating with polymers or other materials, up to 10 L
Freeze dryer Christ	Freeze-dried cake in vials, beakers or trays.	Freeze drying. Programmable. Probes to follow temperature in the sample.
Spray freeze drying	Pulver, particle size 1 μm – ca 300 μm	Freeze granulating of aqueous solutions/dispersions with different dual-flow nozzles which gives variation in particle size. The frozen granules are freeze dried and a powder is obtained.
Spraycoating, MiniGlatt	Powders >100 μm	5-350 g batches. Bottom spray with Wurster inset, Top-spray,
Granulering/agglomerering, MiniGlatt	Powders	30-350 g batches. Top-spray,
Tablet machine	Tablets with or without active substances	A development instrument with good control of, e.g., pressure. Capacity: ~3 – 4000 tablets/hr. Different moulds are available. Only for products not meant for human consumption.
Turbula Mixer	Powder mixing	Capacity: 50 – 1000 mL/batch
Granulation equipment MiPro	Powders	High Shear Granulator/Vacuum Dryer. 50 and 200 ml vessels.
Capsule filling	Powders, semi-solids	Semi-manual equipment. Capacity: Up to 5-10,000 capsules/day

Production		
Powders and solid formulations		
Method/instrument	Type of sample	Principle, information
Milling	Solid materials	Wet and dry. Wet milling < 1µm. Dry milling < 100 µm. Scale: 0.5-100 g
Drying/Filtrering	Solid materials	Up to 1 kg.
Christallisation	From solution/slurry.	Up to 100 L.
Chemical synthesis		Up to 100 L. 5-10 kg finished substance. "Multi-purpose" layout.

Production		
Liquid formulations (emulsions, suspensions, foams, lipid-based, gels, vesicles)		
Method/instrument	Type of sample	Principle, information
Overhead stirrers (wide range of propeller geometries) (50-500 mL)	Emulsions, Dispersions, Solutions	Preparation of suspensions, foams and emulsions. Rotation speed 200rpm-3000 rpm.
High-shear mixers Roto-stator Ultraturrax T25 (IKA, Germany) (50-500 mL)	Emulsions, dispersions	Preparation of suspensions and emulsions. Rotation speed -24000 rpm.
High-shear mixers Roto-stator Ultraturrax T25 digital (IKA, Germany) (50-500 mL)	Emulsions, dispersions	Preparation of dispersions, foams and emulsions. Rotation speed 3000-25000 rpm.
High shear mixers Roto-stator Ultraturrax (IKA, Germany) (10-500 mL)	Emulsions, dispersions	Preparation of dispersions, foams and emulsions. Rotation speed up to 20 000 rpm.
High-shear mixer Eurostar Power control visc-6000 (IKA, Germany) (500 mL-3000mL)	Foams	In combination with specially designed disk propellers and foaming vessels can be used for preparation of wet foams. Speed: 150 to 6000 rpm.

Production		
Liquid formulations (emulsions, suspensions, foams, lipid-based, gels, vesicles)		
Method/instrument	Type of sample	Principle, information
Pulp fibre disintegrant (Type 1-6, AB Lorentzen & Wettre)	Pulp/fibre dispersions	Disperser for cellulose pulp disintegration according to method ISO 5263-2 and ISO 5263-1
Dissolver Dispermat CV3 Plus (VMA-Getzman) (130mL-500mL)	Dispersions, polymer solutions	Overhead stirrer using specially designed “dissolver disks” to achieve doughnut-like flow patterns during mixing. Suited for filler dispersion, stirring, dispersing, vacuum dispersing, homogenising and fine grinding. Rotation speeds: 0-20000 rpm.
Microfluidizer: (Big microfluidizer) Model: 120E ¹ , serial: 986, with high pressure pneumatic pump (Microfluidics) (min volume ca. 150 mL to continuous)	Emulsions, Suspensions, Liposomes, Microcapsules, Cell disruption	Particle disruption/drop break-up is attained as fluids are pumped at high speeds through microchannels resulting in uniform submicron particle/droplet size. Chambers: Old: F2OY 75µm /H3OZ 200µm (upstream) /(ceramic); New: F2OY 75µm /H3OZ 200µm (upstream) /(ceramic) Pressure rage: 3 000 – 18 000 psi (206 – 1 241 bar)
Small Volume Microfluidizer Processor M-110S (Microfluidics) (min volume ca. 15 mL to continuous).	Emulsions, Suspensions	See description above. Interaction chamber: H10Z 100 µm; Pressure rage: 3 000 to 23 000 psi (204 to 1 564 bar)
Microfluidizer (Small microfluidizer) Model: 110T, serial: 687, with high pressure pneumatic pump (Microfluidics) (min volume ca. 150 mL to continuous)	Emulsions, Suspensions	See description above. Interaction chamber: H3OZ CAPM (200 µm) and H10Z CIXC (100 µm), both of ceramic type
Overhead stirrers with propellers (0.5 mL-10 L)	Emulsions, Solutions	Preparation of solution and emulsions. Rotation speed 1200 rpm.

¹ Similar to current model M-110F Reverse Flow Pneumatic

Production		
Liquid formulations (emulsions, suspensions, foams, lipid-based, gels, vesicles)		
Method/instrument	Type of sample	Principle, information
Membrane emulsification equipment LDC-1 (Micropore) (ca. 10ml to 100 mL)	Emulsion, solid-lipid or micro-gel dispersions	The liquid that is to become the dispersed phase of the emulsion is pumped at a controlled, low speed speed through a membrane located at the bottom of a vessel containing the continuous phase. The size of the resulting drops is controlled by the injection speed, the membrane pore size and the stirring rate in the vessel. Hydrophilic membranes with pore sizes 3 and 10 μm are currently available.
Planetary mixer Hobart N-50 (250-2000 mL)	All types of liquid and semisolid formulations	The beater revolves on its vertical axis at a relatively high speed while the axis is being moved around the inside of the bowl at a relatively slow speed. Particularly suited for whisking and mixing of batter-like formulations. Different beater geometries available.
High Intensity Ultrasonic Liquid Processor/Probe (VC-750 Vibra-cell, Sonics) 750 Watts; 20KHz; 10-1000 mL	Emulsions, Suspensions	Preparation of emulsions and dispersions
Ultrasonic probe (Covaris, S220; 500KHz, 15 μL -5 mL)	Emulsions, Dispersions	Focused ultrasonic beam. Preparation of emulsions and dispersions.
Ultrasonic probe (VibraCell, Sonics; 10-1000 mL)	Emulsions, Dispersions	Preparation of emulsions and dispersions
Automated dispenser/diluter (Spädautomat- Hamilton, Microlab 1000) (1-25000uL)	All types of liquid formulations.	Dual-syringe diluter/dispenser
Micro mill (Fritsch, Pulverisette Premium Line) (1mL-60mL)	Suspensions (hard, medium-hard and brittle materials) emulsions	For grinding down to a final fineness of 100 nm. Grinding can be performed dry, in suspension or in inert gas. Planetary Mills option for mixing and homogenizing emulsions and pastes or for mechanical activation and alloying in materials research.
Complete batch reactor set-ups in 0,01-100 liters size including lab automation	Manufacturing of API/Some liquid formulations	-

Production		
Liquid formulations (emulsions, suspensions, foams, lipid-based, gels, vesicles)		
Method/instrument	Type of sample	Principle, information
Equipment for continuous process development: micro reactor, counter-current extraction column, centrifugal extractor	Manufacturing of API/Some liquid formulations	-
Equipment for scale-up of unit operations: pressure filters, dryers, membrane filter technology and distillation equipment	Manufacturing of API	-

Production		
Biologics		
Method/instrument	Type of sample	Principle, information
LAF-bench	Bacteria formulations /incubation	Minimises contamination from the environment
Autoclave	Sterilisation of solutions and formulations	Vapor sterilisation max capacity 4x1L Duran flasks

Production		
Diverse		
Method/instrument	Type of sample	Principle, information
Manual capsule filling equipment	Powders, semi-solids	Semi-manual equipment. Capacity up to 5-10000 capsules/day.

Capsule sealing (Schaefer Technologies Inc, Lab-Top Sealing Machine)	Powders, semi-solids	-
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Characterisation		
Physicochemical Properties		
General		
Method/instrument	Type of sample	Principle, information
XPS (x-ray photoelectron spectroscopy). Also known as ESCA (electron spectroscopy for chemical analysis)	Powder, solid samples with low vapour pressure	Surface chemical characterization under high vacuum. Analysis depth 2-5 nm. Quantitative data on elemental composition and functional groups obtained straightforwardly (no need for reference samples). Adsorbed amount, thickness of adsorbed layer, effect of surface modification, adhesion issues, cleaning/ contamination /spots on surfaces, etc.
SEM/ESEM/EDX	Solids, liquids, wet, dry	Electron microscopy for morphology information. Through EDX is also possible to determine element content. The effect of moisture on structures can be studied with ESEM.
AFM (Atomic Force Microscopy)	Solids	Topography and surface morphology. Nano mechanical surface properties (e.g. dissipation and adhesion). Surface force interactions and frictional properties.
Polarisation Microscopy	Powders, suspensions	Determining whether a substance is crystalline or amorphous. Determining optical properties of crystalline materials, for example their refractive index.
Laser Diffraction Particle Size 0.2-2000 µm Malvern MasterSizer 3000 (Sthlm), 2000 (S-tälje)	Solids, wet, dry	Gives information about the particle size distribution of powders, suspensions, emulsions etc.
Dynamic Light Scattering Particle Size 0.001 – 6 µm ZetaSizer Nano	Powders, dispersions	Gives information about the particle size distribution of powders, suspensions, emulsion, molecules, etc., as well as z-potential.
DSC – Differential Scanning Calorimetry”	Solid, wet, suspensions	For determining temperature and heat content during different phase conversions. Can also be used for purity analysis.

Characterisation		
Physicochemical Properties		
General		
Method/instrument	Type of sample	Principle, information
TGA – Thermal Gravimetric Analysis.	Solid, wet	Weight as a function of temperature, for example, for determining the amount of solvent in a solid or the amount of CO ₂ in a carbonate. Connected to an IR-spectrometer (Sthlm)
DVS – Dynamic Vapour Sorption	Solid, wet	Weight as a function of humidity, volatile organic substances, and temperature.
TAM – Thermal Analysis Monitor.	Solid, wet, fluids	Extra sensitive calorimeter. Equipped with a titration attachment for ITC measurements (Isothermal Titration Calorimeter)
Theoretical calculations	-	Calculation clusters for difficult calculations, e.g., “fluid dynamics”
Vibrational spectroscopy	Solid, wet	Raman/IR
Vibrational spectroscopy	Solid, wet	IR
ToF-SIMS	Powders, particle size >10 µm	Surface chemistry analysis in a strong vacuum. Qualitative composition (molecular species). Imaging with resolution of approx. 0.2 µm, but more difficult on powder than on flat surfaces. Analysis depth: 1 nm
Competence within images and neutron scattering connected to MAXIV	Solids, semi-solids, fluids, gases	Chemical information, form and structure of proteins, particles and solid materials, the interaction between drugs and carriers, or between bacteria/cell-like membranes.
Confokal Raman Microscopy	Solid, semi-solids, fluids, powders particle size >10 µm	Imaging based on Raman-spectrometry. Horizontal or vertical optical incisions. No sample preparation, but some materials auto-fluoresce which can worsen/obstruct analysis. Qualitative composition and localisation in the sample.
Transmission Electron Microscope (TEM)	Particle size and morphology, chemical composition	TEM, EELS, EDS

Characterisation		
Physicochemical Properties		
General		
Method/instrument	Type of sample	Principle, information
Wide range of chromatography techniques (HPLC, UPLC, GC, ion chromatography) coupled to different detection techniques (UV, ELSD, FID, AED)	Chemical analysis of all types of formulations	-
Wide range of chromatography coupled to mass spectrometry (LCMS, GCMS, HRMS)	Chemical analysis of all types of formulations	-

Characterisation		
Physicochemical Properties		
Powders		
Method/instrument	Type of sample	Principle, information
X-ray powder diffraction (XRPD).	Solids, wet, suspensions	Gives the fingerprint of crystalline materials and can even indicate if a material is amorphous. The degree of crystallinity can also be determined.
Tablet hardness instrument < 50 kN	Tablets	Standardised Pharmacopoeia method for testing tablet hardness.
Bulk density	Powders	Determining unstamped and stamped bulk density (volume weight)
Specific surface area	Solids	With gas sorption. Determination of specific surface with N ₂ (as well as Kr, CO ₂)
Porosity	Solids	With gas sorption. Micro- and mesopores with N ₂ and/or Ar Mikro < 2 nm and meso 2-50 nm.

Characterisation		
Physicochemical Properties		
Powders		
Method/instrument	Type of sample	Principle, information
Chemisorption/ Physisorption	Solids	Chemical: H ₂ and/or CO Physical: Any volatile compound (e.g., alcohols, alkanes etc.)
Absolute density He-Pyknometer	Powders, pellets, tablets	Determining the density of the smallest particles in a solid material
Polymorphism screening	Solids	A combination of different techniques for evaluation of the tendency for a substance to form different crystalline phases.
Salt Screen	Solids	Evaluation of tendency of a substance to form salts
Co-crystal screen	Solids	Evaluation of the tendency of a substance to co-crystallise
Phase diagrams	Solids	Determining a phase diagram for solid materials in equilibrium with saturated solutions. This is very important in, among other things, the development of crystallization methods.
Single crystal X-ray diffraction (SXR)	Powders, solid material	Determination of crystal- and chemical structure, as well as absolute configuration in some cases.
Powder wetting	Powders	The apparent contact angle on powder beds. A contact angle machine is used.
Powder wetting	Powders	Penetration of moisture in powder beds. Own construction.

Characterisation		
Physicochemical properties		
Liquid formulations (emulsions, suspensions, foams, lipid-based, gels, vesicles)		
Method/instrument	Type of sample	Principle, information
Stability analysis /Turbiscan Ageing System (TAGS) (Formulation, France)	Emulsions, Suspensions, Foams	Automated monitoring of separation phenomena (sedimentation, creaming, coalescence, agglomeration, phase separation over time)

Characterisation		
Physicochemical properties		
Liquid formulations (emulsions, suspensions, foams, lipid-based, gels, vesicles)		
Metod/instrument	Type of sample	Principle, information
Accelerated Stability analysis /LUMiFuge) (LUM, Germany)	Emulsions, Suspensions, Foams, Gels	Monitoring of separation phenomena (sedimentation, creaming, coalescence, agglomeration, phase separation over time) under accelerated conditions (6–2300 times compared to gravity).
Foam analysis/ Dynamic Foam Analyzer DFA100 (Krüss, Germany)	Foams	Measuring foamability, foam stability, drainage, liquid content of foams
Ross Miles Foam Tests Apparatus	Foams	Allows to test foamability and foam stability in accordance with ASTM D 1173.
Polarisation Microscopy	All types of fluid/semisolid formulations	Identification of the presence of crystalline and/or liquid crystalline structures.
Rotational shear rheometer (Kinexus, Malvern)	All types of fluid/semisolid formulations	Determines rheological properties such as flow curves and visco-elastic properties.
Viscometers (ReoLogika, StressTech och Physica, Rheolab MC1)	All types of fluid/semisolid formulations	Determines rheological properties such as flow curves and visco-elastic properties.
Extensional rheometer (Haake CaBER 1, Thermo electron corporation)	All type of liquid/semisolid formulations	Capillary breakup extensional rheometer which allows to quantify elongational properties of fluids or semi-solids.
Texture Analysis Stable Micro Systems Texture Analyser TA-Xtplus	All type of liquid/semisolid formulations	Measuring mechanical properties such as firmness, elasticity, adhesion, compressibility, rupture of gels, emulsions and foams

Characterisation		
Physicochemical properties		
Liquid formulations (emulsions, suspensions, foams, lipid-based, gels, vesicles)		
Metod/instrument	Type of sample	Principle, information
Interfacial/surface tension and/or dilational rheometry Oscillating drop tensiometry Dataphysics	Liquids	Measuring interfacial tension and interfacial rheology at air/liquid and liquid/liquid interfaces, providing insight into stability of emulsions and foams.
Wilhelmy plate tensiometry	Liquids	Measuring interfacial (liquid/liquid) or surface tension (air/liquid).
Osmometer (Fiske, Micro-Osmometer 210)	All types of liquid formulations	Measuring the osmotic strength of solutions, colloids, or compounds.

Characterisation		
Physicochemical Properties		
Biologics		
Metod/instrument	Type of sample	Principle, information
Plate-reader VarioscanLUX Thermo Scientific	Liquid	UV/Vis and fluorescence measurements in 12-384 well plates for assessing release assay or content of peptides and proteins, etc.

Characterisation		
Functional properties		
Diverse		
Method/instrument	Type of sample	Principle, information
Release of active /UV-vis spectroscopy	Solid, wet, liquid	Set-up for determination of release rate and amount of actives from encapsulation system.
Diffusion cell (PermeGear, V6A-02)	Suspension, liquid	Franz diffusion cells for release studies. Permeability over skin/biological membranes.
µDiss (PION)	Solid	Miniaturized dissolution equipment with on-line UV absorption detection
Dissolution (USP2 baths, 900 mL)/HPLC	Solid	In vitro drug release
Climate and light cabinets for shelf-life and stability studies	Solid, wet, liquid	Stability studies (GMP according to ICH guidelines for drug substance)

Characterisation		
Functional properties		
Diverse		
Method/instrument	Type of sample	Principle, information
Flow cell (mucoadhesion of soft gels) (in-house development)	Semisolid gels	Adhesion of formulations (gels) to biological surfaces such as mucosa is measured as the gel retention towards liquid flow. E.g. the retention of gels on a mucosa surfaces upon flushing with saliva.
Mini traction machine (tribology)	Liquids, semisolids (gels, pastes, dispersions...)	Lubrication assessment method; friction at different loads, moving speeds and rolling to sliding ratio accessible. Suitable as well as bio-lubrication assessment method in combination with soft (compliant), e.g. PDMS substrates.
Force board (sliding friction + normal forces, friction coefficients)	Liquid, solid and semisolid	Static and dynamic friction of two interacting surfaces in relative motion; Tactile friction, i.e. the friction between a human finger and any material/surface. Friction measured between a human finger and cream-treated model skin.
QCM-D (adsorbed amount, layer thickness, and viscoelastic properties of a film/coating)	Liquid	Adsorbed amount, thickness and changes in viscoelastic properties. Surface interactions of e.g. polymers, surfactants, peptides, and proteins with a large number of solid surfaces. The cleaning efficiency of a formulation can be verified by following the desorption kinetics.