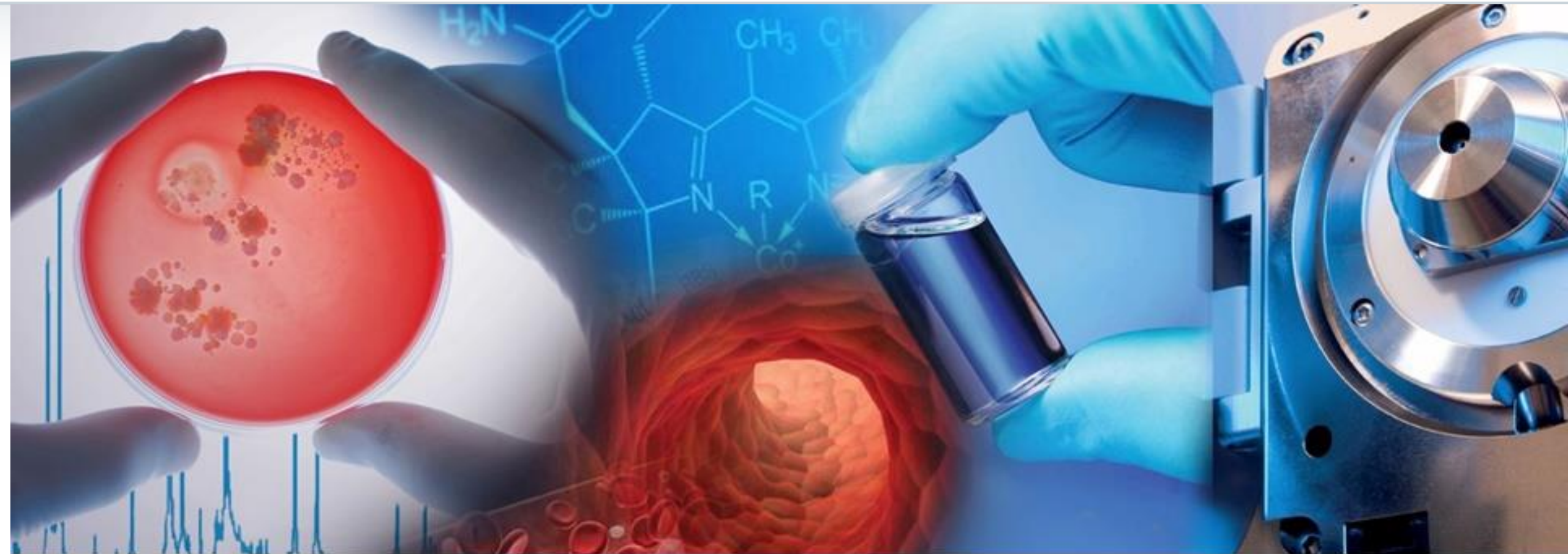


Introduction to Bruker's Products and Solutions



Jason S. Wood, Ph.D.
Regional Manager – Bio/Pharma
Bruker BioSpin Corp

Bruker Scientific Divisions



Technology Platforms

Major Applications

Bruker BioSpin

- NMR and EPR spectroscopy
 - NMR / TD-NMR
 - EPR
 - MRI
 - Analytical Services

- Analytical Chemistry
- Pharmaceuticals
- Life Science
- Food
- Metabolomics

Bruker Daltonics

- Mass Spectrometry
 - LC-TQ
 - Ion Trap
 - UHR-TOF, q-TOF, MRMS
 - MALDI-TOF
 - IMS/TIMS

- Food, Forensics, Doping control
- Chemical Analysis
- Industrial & Applied Analysis
- Petrochemistry
- Life Science Research
- Clinical Research
- Pharmaceutical Analysis

Bruker AXS

- X-ray Analysis
 - X-ray Diffraction
 - X-ray Crystallography
 - X-ray Fluorescence

- Materials Identification
- Materials Research
- Structural Proteomics
- Nanotechnology

Bruker Optics

- Vibrational Spectroscopy
 - FT-IR
 - FT-NIR
 - Raman

- PAT & Quality Control
- Materials Identification
- Materials Research
- Pharmaceuticals / Process

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Bruker Corporation

One-stop for Analytical Success!



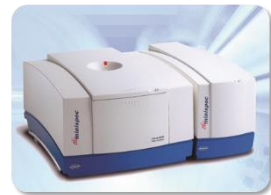
Focus on Pharmaceuticals

Solutions For Increased Quality and Productivity



- Latest Solutions and Case Studies

- **Solid Form** Determination of an API - including formulated drug substances

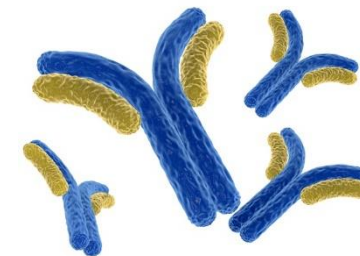


the **minispec**
Form ✓

- Determination of **Polysorbate** Degradation by EPR



- **Biologics Higher Order Structure** – Current Workflows and Practices



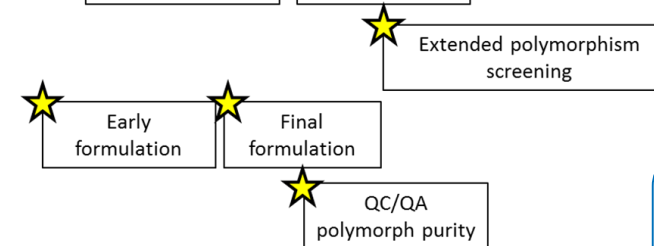
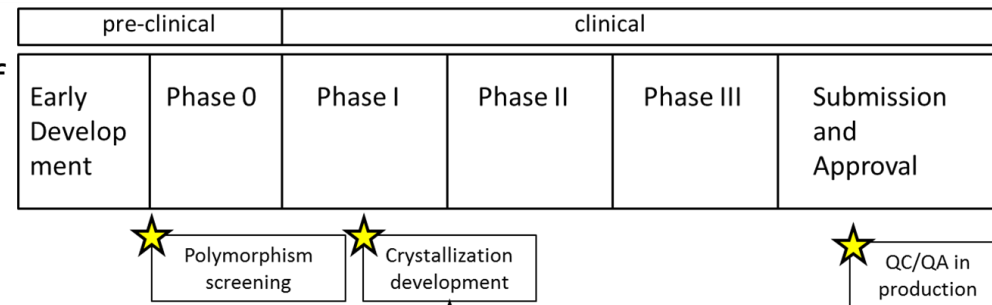
Solid Form Quantification

Pharmaceutical Drug Development



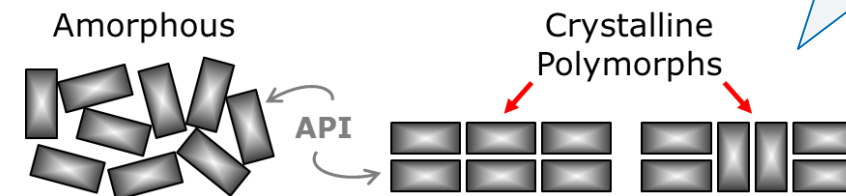
- Physical forms of *Active Pharmaceutical Ingredients* (API) play a crucial role in Drug Development

- 80% of API molecules exhibit polymorphism with a very wide range of physical and chemical properties
- Criteria: Bioavailability, processability, thermodynamic stability, etc.
- Choose best API form for development, formulation, production, storage



Polymorphism: ability of a solid material to exist in more than one form or crystal structure

- No universal technique available to quantify physical API forms in solids
- Tool box of different methods: PXRD, RAMAN & IR, TGA, DSC and solid-state NMR
- General issues: high limit of detection & low accuracy, extensive calibration, time consuming, high expertise level, amorphization



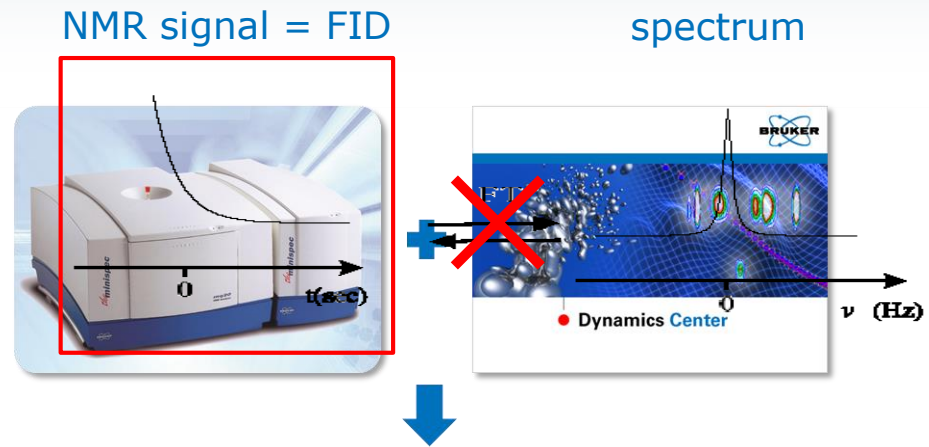
Benchtop Solution for Solid Form Quantification

Time Domain NMR



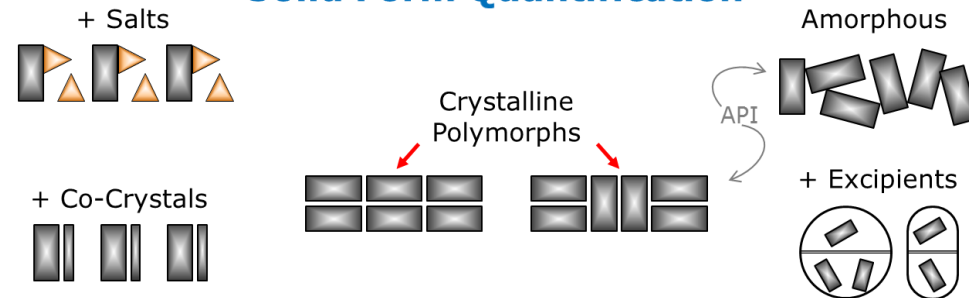
Time-Domain NMR (Relaxometry)

- Small external magnetic fields (e.g. 20 MHz)
 - No “chemical” information
- Time domain signal (FID) allows for measurement of physical properties:
 - Signal amplitude
 - Bulk Quantification
 - Solid vs liquid
 - Morphology
- Solid form quantification by combining the analytical power of NMR with an easy-to-use solution:
 - Reliable minispec mq20 benchtop system
 - Well established Dynamics Center software



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Form ✓

Solid Form Quantification

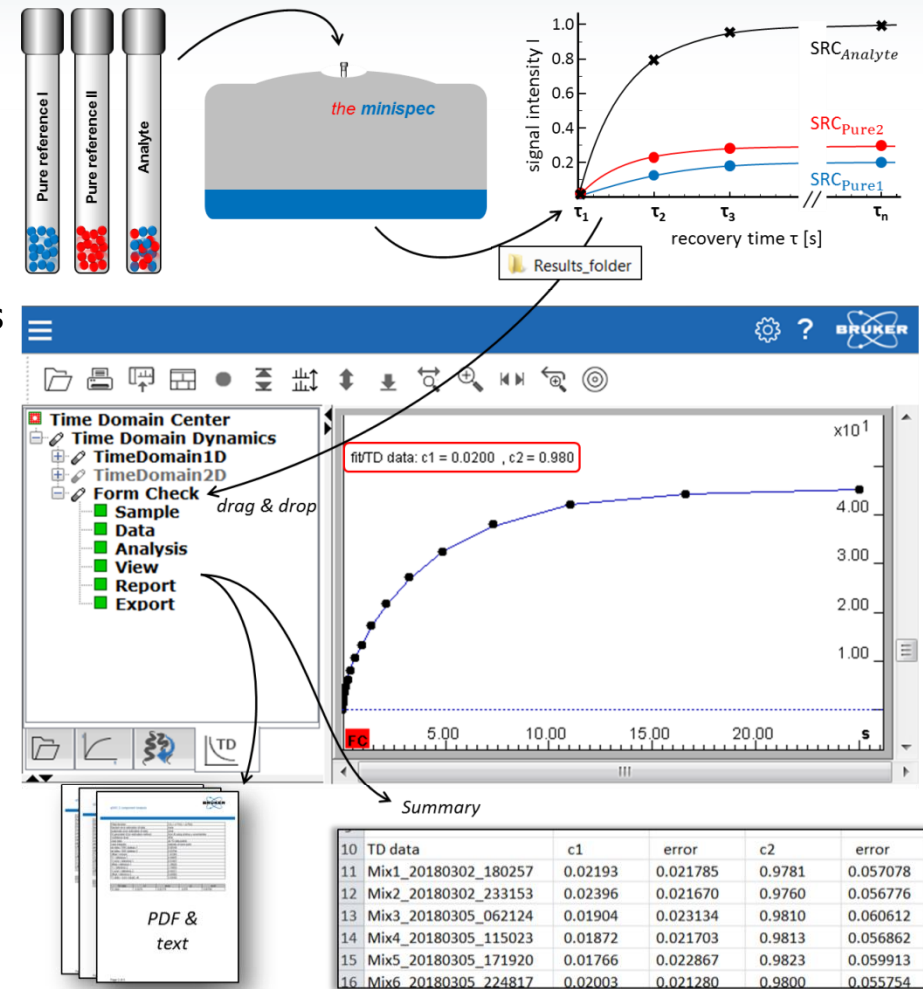


Solid Form Quantification



● the minispec Form Check

- **Analyte** = blend of two components with unknown quantities
- **Pure component 1** = reference I
- **Pure component 2** = reference II
- Calibration = fingerprint-measurements of both pure components (T_1 saturation recovery curves (SRCs))
- Data of analyte = linear combination of the two fingerprints
- Automated analysis within seconds via drag & drop of 'Results' folders into the Dynamics Center:
 - ✓ Summary of all results
 - ✓ PDF & text reports for each analyte
- Results given in relative mass percentages of pure components in an analyte
- Patent pending



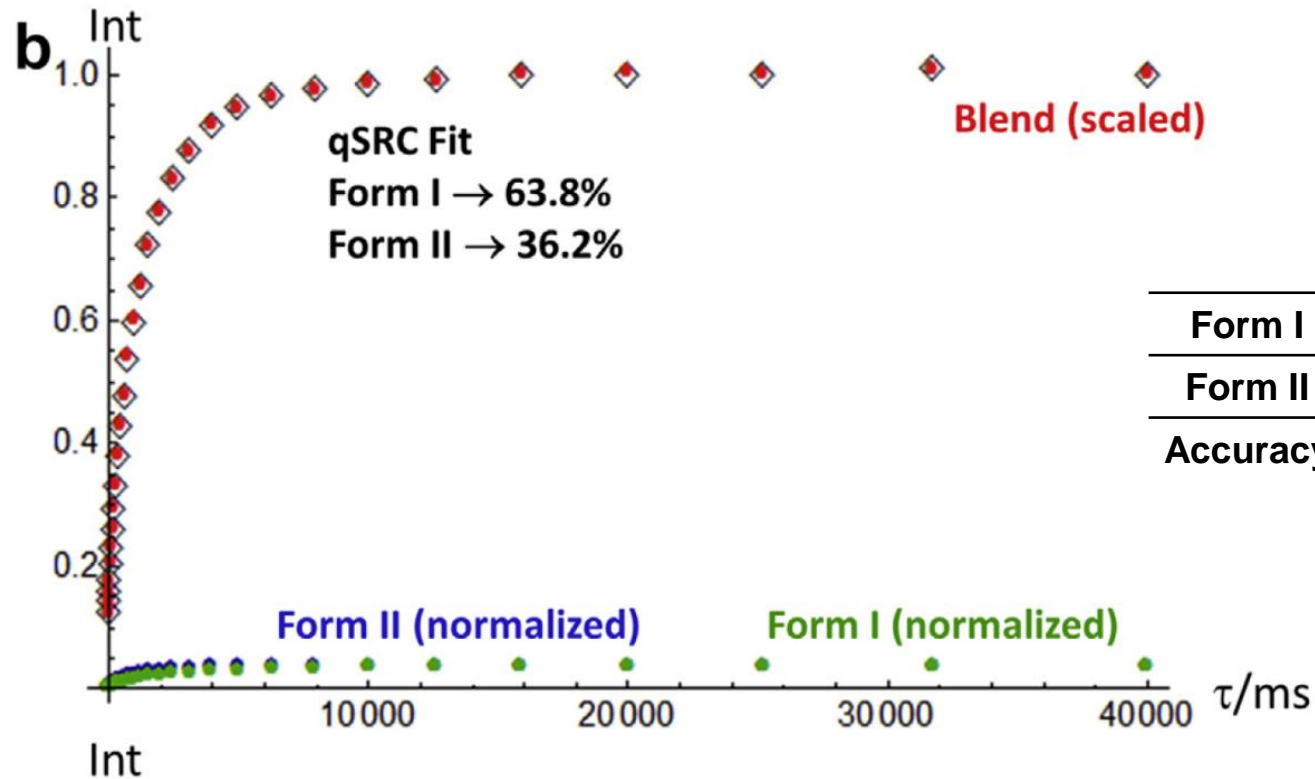
Case Study

Anhydrous HCV Drug Polymorphs



● the minispec **Form Check**

- Anhydrous HCV drug polymorphs I & II (MSD)



	Expected	Experimental
Form I	63.2 %	63.8 %
Form II	36.8 %	36.2 %
Accuracy	0.6 %	

D. Stueber, S. Jehle, J Pharm Sci., 106, 1828-1838 (2017)

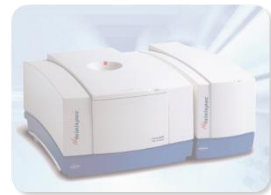
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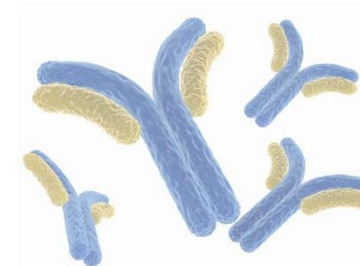


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Form ✓

- Determination of Polysorbate Degradation by EPR



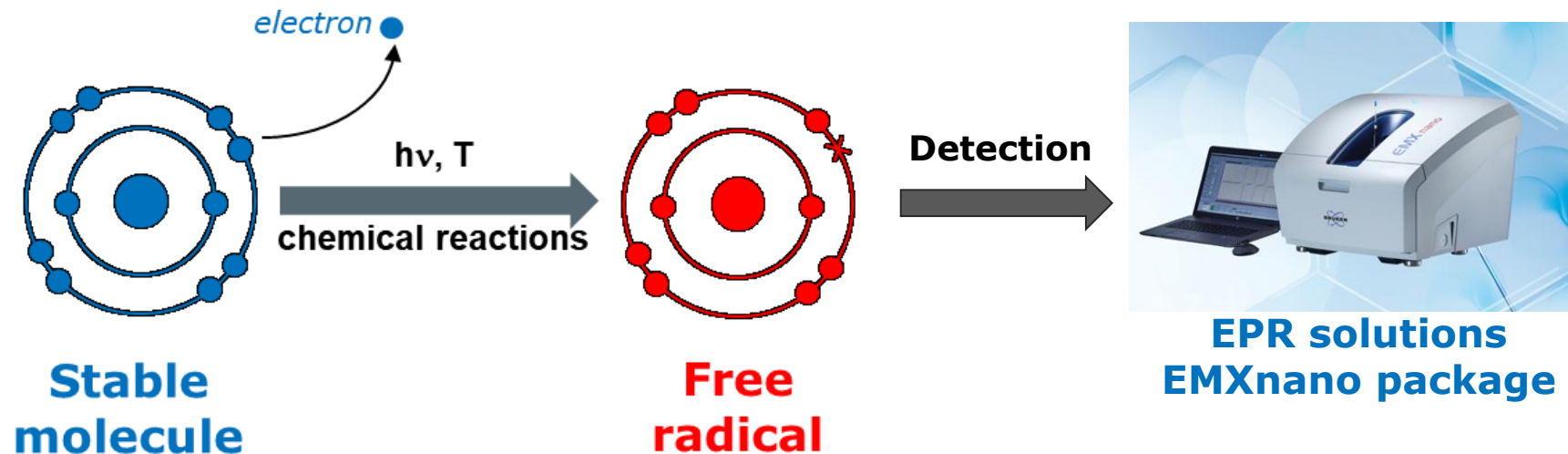
- Biologics Higher Order Structure – Current Workflows and Practices



What is EPR?



- EPR is a magnetic resonance technique that detects **unpaired electrons**
- **Unpaired electrons** occur in **free radicals** and many **transition metals**
- **Free radicals** and **transition metal ions** are often present in APIs, excipients, and complete formulations

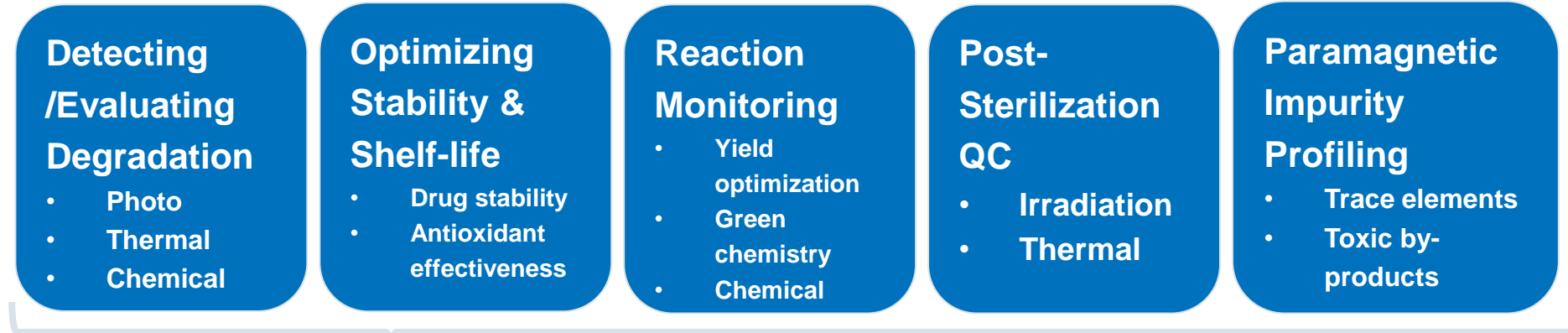


EPR Solutions for Pharma

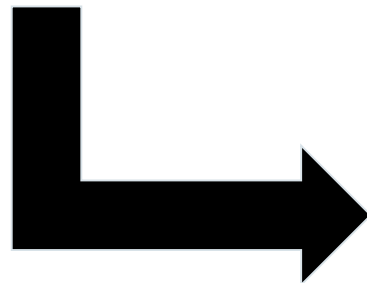
Why EPR? – Solutions!



- There are at least 5 areas of interest where EPR spectroscopy is beneficial:



Free radicals & Transition metals



**EPR solutions
EMXnano package**



EPR Solutions for Pharma

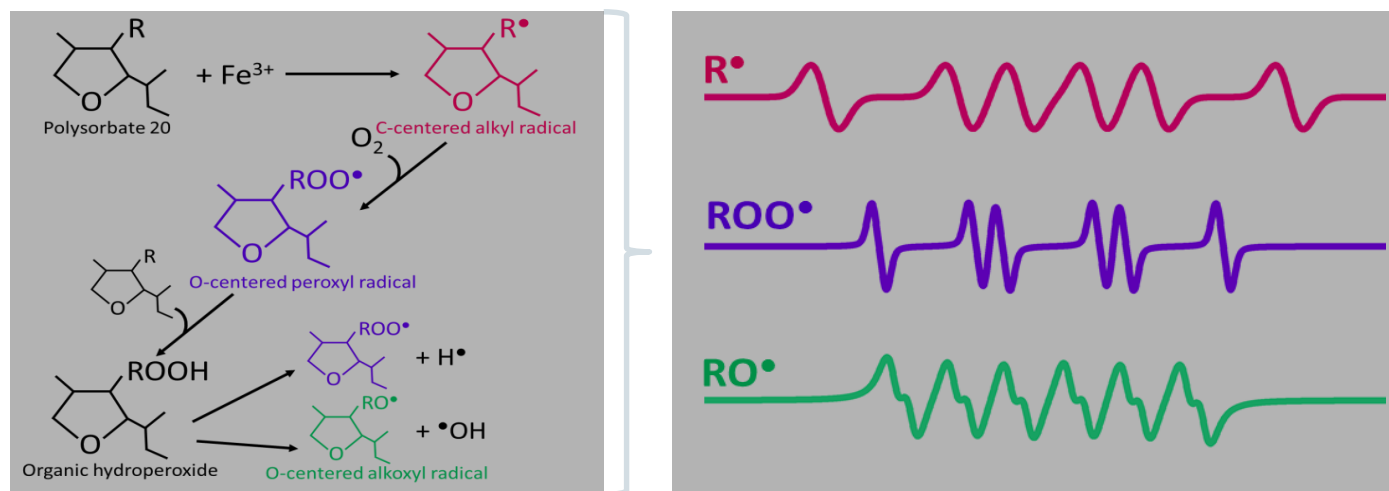
Polysorbate Degradation



Impurity profiling - EPR is able to detect **free radicals** and **transition metals** traces down to **parts per billion** levels!!!

An example: Polysorbate autoxidation

- Polysorbates used in drug formulation as a stabilizer undergoes autoxidation
- Autoxidation is catalyzed by **transition metal ions** and results in side-chain cleavage and **free radical** formation
- EPR detected, identified and quantified the three different **free radical impurities**



Lam X.E. et al.(Genentech Inc.), *Pharm. Res.* (2011) 28 2543

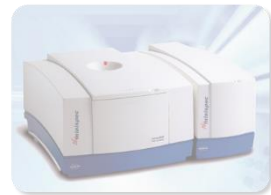
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