Centre for Process Innovation and Material Science challenges when developing an oral mAb product

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Presentation Topics

- Who Am I ?
- Who are CPI and what do they do/offer ?
- Material science challenges when developing an oral mAB product
  - Project Soteria®

Who Am I ?

- Joined CPI Particles Team as Senior Research Engineer in Sept 2018
- Prior to CPI I worked as a Process Design Engineer at Procter & Gamble for 30 years in the Dry Laundry Powder sector
    - Process design, scale up and manufacturing roll out and troubleshooting.

Who are CPI and what do they offer ?

We help companies to develop, prove, scale-up and commercialise new products and processes

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www.uk-cpi.com

Creating a **healthier** society, **cleaner** environment and a **vibrant** UK economy...

...by ensuring **every** great invention gets the **best** opportunity to become a successfully marketed product.

cpi

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We help deliver, de-risk and accelerate...

...your concepts into successful products

...using our integrated innovation services

Industry relevant expertise and assets

Delivering product development, proof of concept, and scale-up services.

Expertise in securing funding for partners and clients

Enabling the right partnerships, connections, and funding routes at the right time.

Knowledge and application of innovation processes

Business services and consultancy to reduce risk and speed up time to market.

Biotechnology

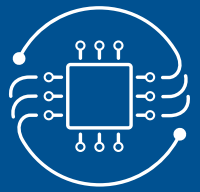
Biotherapeutics

Formulation and materials

Pharmaceutical processing

Photonics

Printed electronics



Flexible hybrid electronics

Digital

...with our expertise and core capabilities

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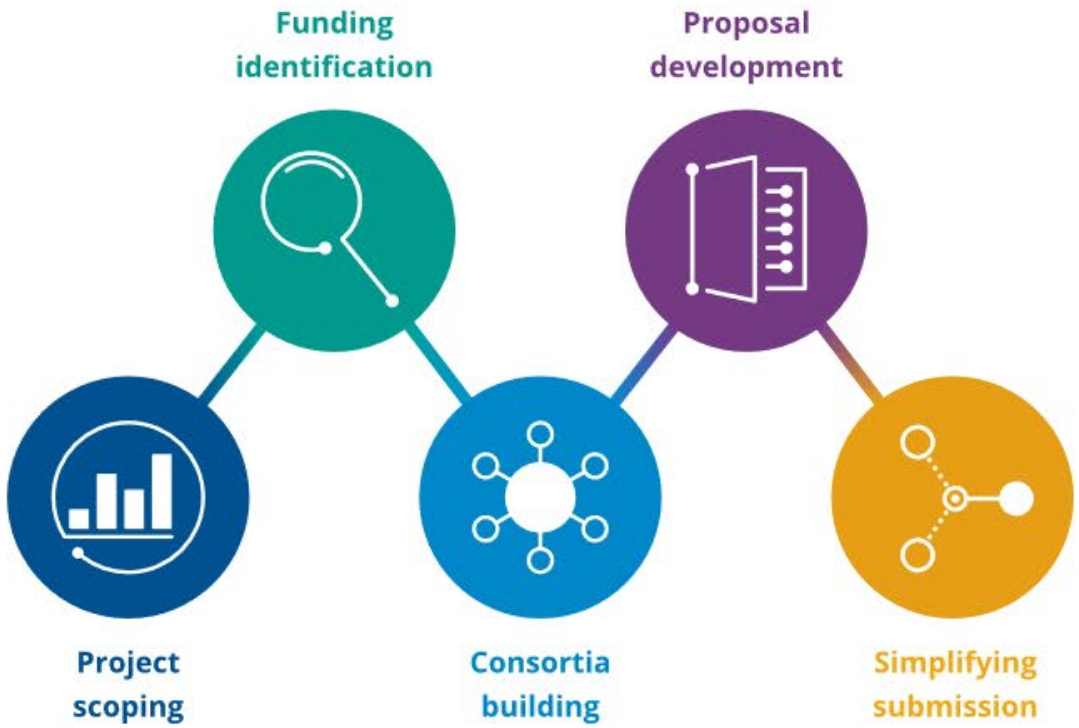
Supporting collaboration and grant applications...



...for the right funding at the right time

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Material Science challenges when developing an oral monoclonal Antibody (mAb) product

Soteria®, a revolutionary platform technology for oral delivery of antibodies for GI inflammatory diseases

Introduction to Soteria®

- All antibody therapeutics for GI diseases like IBD are currently injected at high doses
- This leads to significant adverse effects and loss of response due to development of anti-drug antibodies in >50% of patients
- Soteria® technology is a combination of gut stabilization excipients in the core and proprietary enteric coating on the outside of the pill to allow targeted delivery of antibodies to the site of disease with minimal systemic exposure
- CPI Specific Objective: Transform the Antibody + gut stabilization excipients into a free flowing, stable and uniform blend that can be used in clinical studies and then scaled up for commercialization

Who are the Partners ?

Technology Owner

Intract Pharma

Formulation/Process Development

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Scale Up post CPI (GMP)

QuayPharma

Clinical Testing Coordination

pharmidex

Product Design Overview

- Drug - Infliximab
- Multi Functional excipients (Soteria®) - Protect antibody from degradation in the gut leading to enhanced tissue levels
- Additional Excipients – needed for improved blend flowability and ongoing processability
- Phloral®– unique dual-trigger enteric coating relying on pH and microbiome of the colon to release antibody at the site of disease

Process Development Thought Process & Challenges

- when working with large molecule mAb's

- Large molecules typically more complex and more chemically/physically unstable versus small molecules

Small molecule

large molecule

If I want to do anything with the large house I know it's going to be more of a challenge/carries more risk.

- Many mAb's come in a lyophilised form which are typically hygroscopic, hence more challenging to handle and work with.

However, the development thought process is no different for small versus large molecules.
- It may mean that there may be more a detailed work plan and more challenges to overcome as a result

Material Characterisation

– The importance of knowing about the materials you are working with

- Need to understand the physical properties of the materials, such as
    - Particle size – blend uniformity/segregation
    - Density – linked to capsule/die filling and dosage
    - Hygroscopicity – moisture pick up and the impact on physical properties/handleability
    - Flow – handleability throughout the process
    - Thermal stability – degradation points

Bottom line – flags potential risks that need to be addressed to ensure overall product quality

Material Characterisation

– The importance of knowing about the materials you are working with

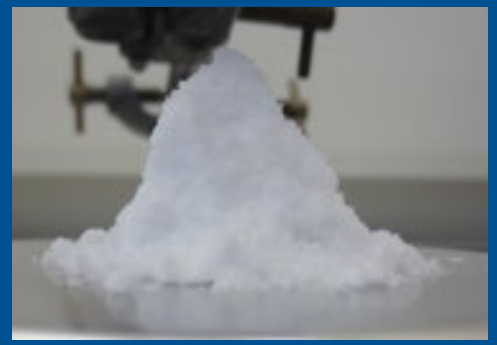
What does knowing the above enable

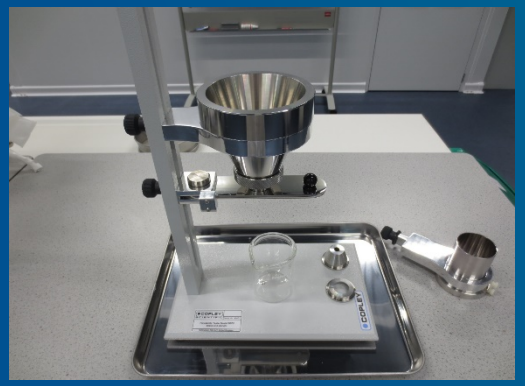
- Excipient choice – matching certain physicals is important for blend uniformity
- Helps estimate formula design early – gages the ballpark for the amount of additional excipients
  - Do I need 1-3% of a flow aid or do I need 10-20%
- Highlights potential needs for specific process control
  - Do we need a low humidity/temperature environment – dry air/chilled air system
- Do we potentially need additional process steps to overcome problems
  - Dry granulation/compaction to boost flow and density

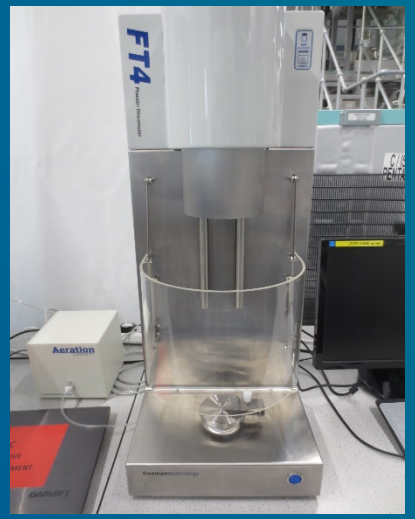
Examples of challenges faced on Soteria ®

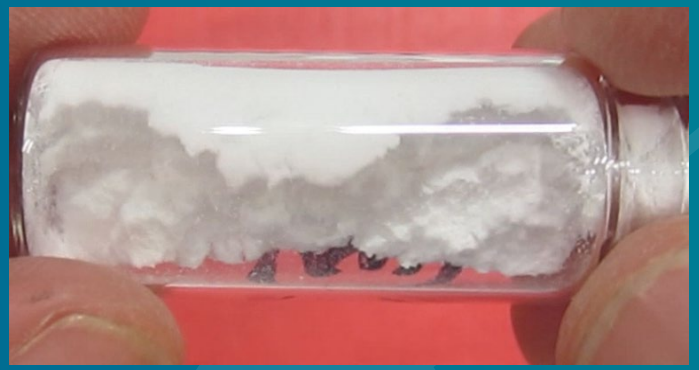
Material Supply

- Limited material hence unable to do the optimum level of characterisation
- Need careful decisions on what analysis to do or what can be done – out of the box ideas
    - Visual assessments and gut feel versus hard analysis/data
        - carries a level of risk
        - ensure stakeholders are aware of risks before moving to next stage or scale up
    - Use of placebos
        - often difficult to find suitable candidate
        - also carries a level of risk







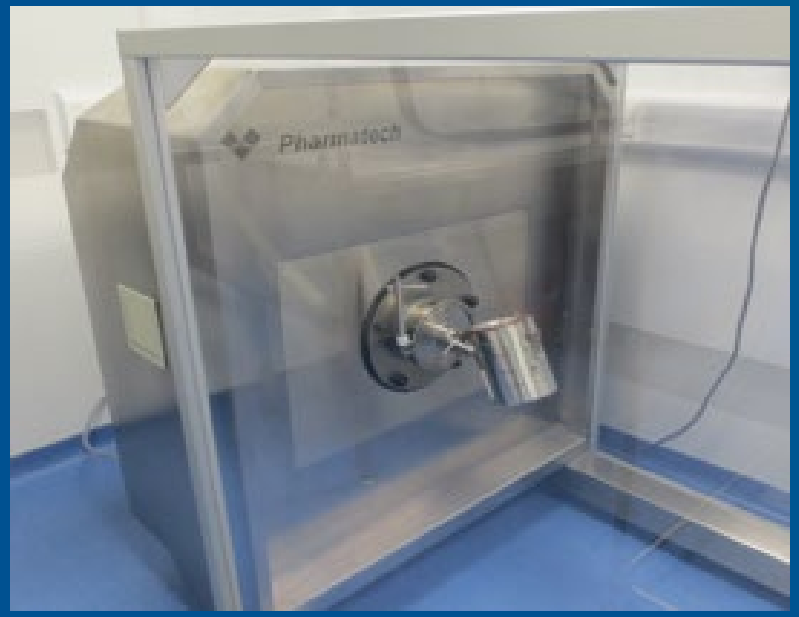


Ideal is Angle of Repose, Flow Through Orifice, Flow Function using 5-100g versus visually rolling in a vial using <1g

Examples of challenges faced on Soteria ®

Material Supply

- Limited material and how to ensure blend uniformity
  - Scale down mixing approach utilising existing capability



Utilise standard
Pharmatech MB100
mixer to mix
1-2g sample
(30lt to 4ml)

4ml vial packed into 2lt vessel
- the rotational mixing and mix time is what's important irrespective of vessel size

Examples of challenges faced on Soteria ®

Materials Form

- Lyophilised cakes
- Materials with large hard lumps present

Need to convert these into a usable powder form via grinding, grating, sieving - using whatever you can

Standard Tyler Mesh

Comil (U5)

Usable powder

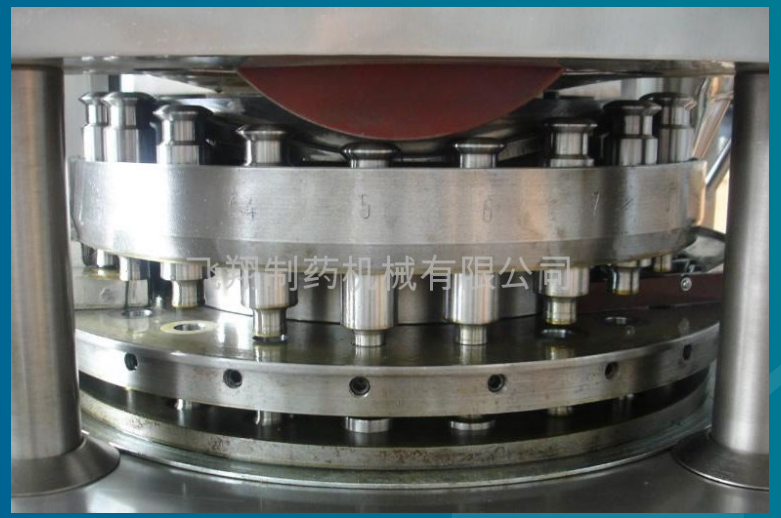
Examples of challenges faced on Soteria ®

Poor Flow and Low Density Materials

- Poor Flow – unable to fill capsules or dies for tabletting at manufacturing scale
- Low Density – unable to get sufficient product into capsule/tablet hence low dosage delivery

Fix – Compaction via Roller Compaction/Tabletting then milling

- Right to succeed proven via manual small scale compaction press (existing capability)



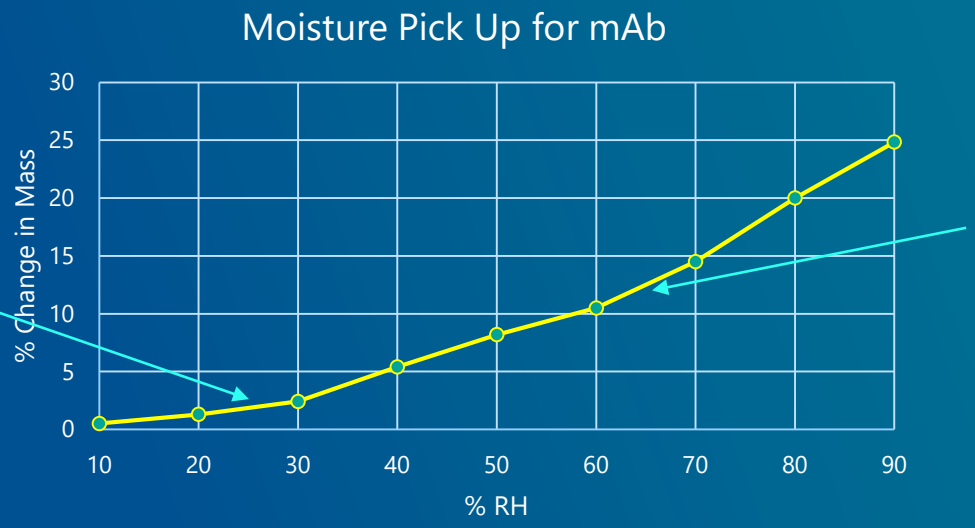
Future CPI in-house capability

Examples of challenges faced on Soteria ®

Hygroscopic Materials

- Moisture pick up can have a huge impact on material properties
  - to the point where you can't handle them without engineering controls such as dry air

March 2019
Relative Humidity ~27%
Low risk



July 2019
Relative Humidity ~65%
High risk
mAb caking - unmanageable

- Needed to work in a glovebox with dry air feed to reduce RH (not ideal)

Need to factor in climatic/seasonal changes in environmental conditions
- they can play a huge part in processability

In summary

- There is no need to reinvent the wheel
- Build up your material data library
- Where possible obtain the maximum quantity of material to do the appropriate level of characterisation
- Utilise the capability you have
- You will always encounter challenges and problems
  - deal with and overcome them as best you can, the sooner the better

Thank you

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