

It's Never Too Early to Put the Patient First

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Session Description and Objectives

- There is a tendency to consider patient centric formulation design as a late-stage development activity. The protracted timelines associated with some commercially approved long-acting injectables are testament to difficulties encountered when patient centricity is considered too late. This is even more critical for nanomedicines when used as targeted drug delivery systems, for which bridging is extremely challenging. It is therefore paramount to begin with a QTPP, defining end-product requirements before embarking on such a development.
 1. Have awareness of types of formulations that would benefit from the use of QTPP
 2. Have awareness of the difficulties of demonstrating bioequivalence for long acting injectables and complex medicines
 3. Consider patient needs at the heart of designing formulations by defining QTPP before embarking on development especially for long acting injectables

Biography and Contact Information

- Claire Patterson is Senior Principal Scientist at Seda
- A Pharmacy graduate (MPharm) with a Ph.D. in Pharmaceutics from the Universities of Nottingham and University College London.
- An experienced Biopharmaceutics scientist having spent 12 years with a multinational pharmaceutical company with roles in Early and Late Stage Product Development, linking in vitro to in vivo product performance.
- Current focus areas include subcutaneous and complex parenteral biopharmaceutics (including nanomedicines) and other non-oral routes of administration.
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Design Fail!



Patient Centric Formulation Design



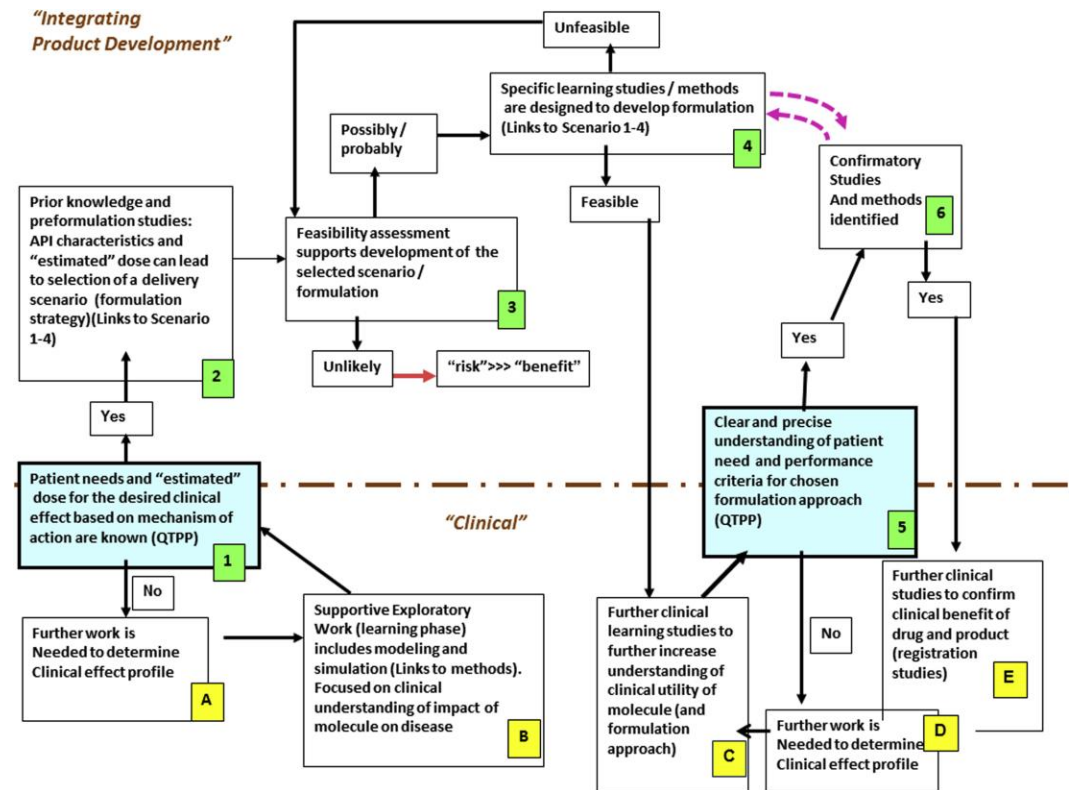
- Consider the end user experience



- Are complex parenterals a special case?

A growing movement bringing patient centric design to the fore

- For example:
- BioRAM - A proposal to better integrate pharmaceutical and clinical development for patient benefit (J. Pharm. Sci 103: 3377-3397, 2014) by Arzu Selen, Paul A Dickinson *et al.*
- A body of case studies demonstrate that BioRAM thinking wins



Long Acting injectables (LAIs)

- Four different commercial presentations of exenatide. The final autoinjector presentation addresses the pharmaceutical, therapeutic and user factors in one elegant design
- Significant challenges associated with bridging for LAIs
 - Long time to steady state leads to high drop out rates, high risk of BE failure
- Without the ‘right’ product, can lose significant market share



2005



2012



2014

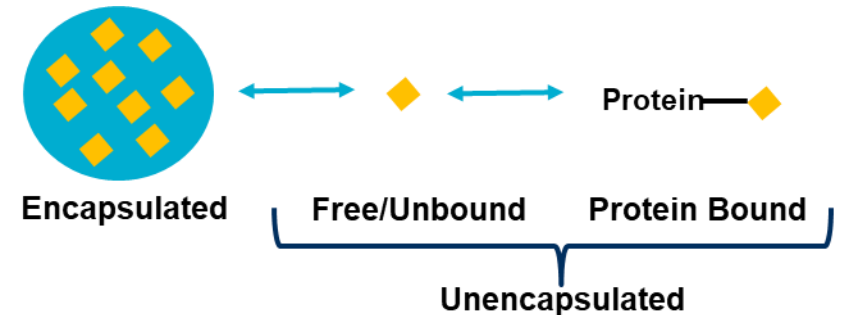


2017

Nanomedicines and Targeted Delivery

Bridging is an even bigger issue for complex parenterals!

- Systemic PK is rarely representative of efficacy/safety outcomes
- Significant challenges associated with bioanalysis
 - Sample stability (continued release of drug in sample post collection)
 - Process induced artefacts (cross contamination, nanoparticle rupture)
 - Differentiation between protein bound and encapsulated drug
- Need to frontload activities to increase chances of successful translation from preclinical to clinical and through scale up



Delicate Balance between short term and longer term aims



- Heavy price to pay if left too late
- A bit of foresight can help tip the balance in your favour

Start with the end in mind!

- Simple tools can be used to integrate pharmaceutical and clinical development
- Cross functional discussions are essential
- Develop target profiles:
 - Target product profile (TPP)
 - Candidate drug Target Profile (CDTP)
 - and Quality Target Product Profile (QTPP)
- Think about bridging strategy when designing the clinical programme – including the bridge from preclinical to clinical to commercial



With a view to commercial presentation(s) (including device)

Defining the TPP

2. Example for pain associated with diabetic neuropathy:

Product Properties	Minimum Acceptable Result	Ideal Results
Primary Product Indication	Relief of pain symptoms in diabetic neuropathy	Relief of symptoms in neuropathic pain syndromes
Patient Population	Adults with diabetes who experience moderate to severe pain	Adults with diabetes who experience moderate to severe pain
Treatment Duration	Chronic	Chronic
Delivery Mode	Subcutaneous injections	Subcutaneous injections
Dosage Form	Prefilled vials with liquid	Prefilled vials with liquid
Regimen	Once every month	Once every 2 months
Efficacy	A 40% decrease in pain score in 30% of patients	A 70% decrease in pain score in 50% of patients
Risk/Side Effect	Devoid of local injection effect and clinically significant CNS side effect	Devoid of local injection effect and any CNS side effect
Therapeutic modality	Antibody	

[CREATE Bio Example: Target Product Profile \(TPP\) | National Institute of Neurological Disorders and Stroke \(nih.gov\)](#)

Key considerations about the patient experience are often missed.

These factors should be considered at project inception

- Route of administration
- Frequency of administration
- Treatment scenario – at home or in GP surgery/clinic/hospital
- Need for drug delivery

These are fundamental to selecting an appropriate lead candidate (CDTP) and in designing the product presentation (QTPP).

Selecting the right candidate (CDTP)



- Candidate must be able to fulfil the TPP
- Ability to cross biological barriers
- Suitability for dosage form
- Dose
 - Potency, bioavailability at site of action
 - Biological stability

Design assay cascade accordingly!

Designing the Product (eQTPP)

- Not a late stage activity!
- This is your design brief to ensure your product meets the TPP
- Takes place during preclinical development, PRIOR to formulation feasibility studies
- Include formulation AND device i.e. final product presentation
- It may be very costly (or impossible!) to course correct later on
- Focus on performance related aspects

	Attribute
General	Specific patient needs relating to patient demographic and disease implications
	Route of administration
	Dose and frequency of administration
	Release profile
	Injection Volume
Formulation	Excipient precedence/Tolerability
	Viscosity
	Osmolality Range
	Stability
Device	Dose Preparation (single component or multi)
	Steps-to-injection
	Overall Size of Device
	Dose Rate
	Needle gauge

Concluding Remarks

- Tools like BioRAM and QTPP, in combination with specific patient profiles should be used early to ‘start with the end in mind’
- Embark on phase appropriate activities, mindful of value inflection points, but don’t neglect to consider final product presentation and how you will navigate the path to commercial
- The patient experience should be up there with efficacy and safety to maximise your chances of success
- It’s never too early to put the patient first, but it may well be too late!



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Questions

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