The importance of Characterisation in Immunotherapy Product Development

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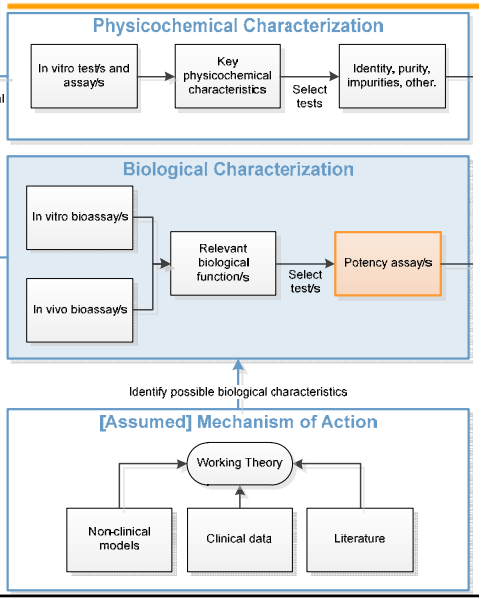
Introduction

- What should be characterised and why?
  - Physicochemical and biological approaches
- Why is characterisation so important in the long run?
- What is a potency assay?
- Why is potency so important?

Characterisation Strategy



Physicochemical characterization
Refers to the use of methods that measure physical and chemical characteristics. Eg:
Physical: size, morphology, light scattering properties, tensile strength, cell number, confluence.
Chemical: identification of phenotypic markers and secreted substances, genotype, gene expression profile.

Biological characterization
Refers to the use of methods that measure biological function, i.e. how the physicochemical characteristics influence biological systems. Eg:
Biological: *in vitro* and/or *in vivo* measurements of cytotoxicity, cell growth, de/differentiation, proliferation, migration, immunomodulation.

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The Importance of Characterisation

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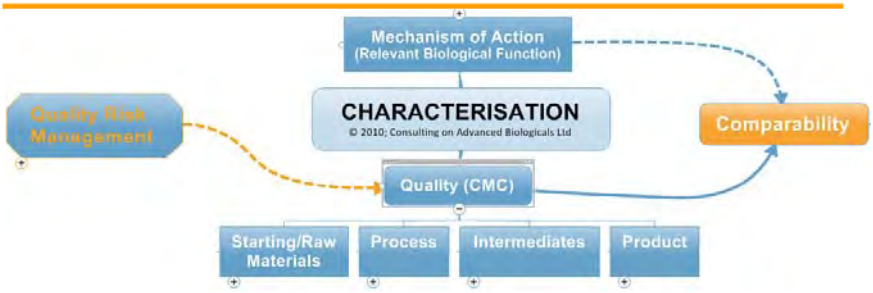

- Process knowledge enabling QRM, process optimisation, IPC, PP, process changes (comparability)
- Materials knowledge enabling QRM, acceptance criteria, shelf-life, materials substitution (comparability)
- Intermediates and (DS)/DP knowledge enabling setting of release specifications, shelf-life specifications and confirming process changes (comparability)

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Potency

Potency is the quantitative measure of biological activity based on the attribute of the product, which is linked to the relevant biological properties (ICH guideline 6QB29).

The “Human cell-based medicinal products” guideline (CHMP/410869/06) also refers to the Guideline on “Potency testing of cell based immunotherapy medicinal products for the treatment of cancer (CHMP/BWP/271475/06).

What is a potency assay?

- Biological ‘activity’ implies a change over time; so single measurements are not biological assays.
- Any assay used for biological characterisation could be a potency assay if it gives a meaningful indication the product will be ‘potent’.
- It is unlikely one single assay will capture all biological effects.
- One or more biological assays may be needed together to define potency.
- Biological characterisation will allow you to identify which assays are candidate ‘potency assays’

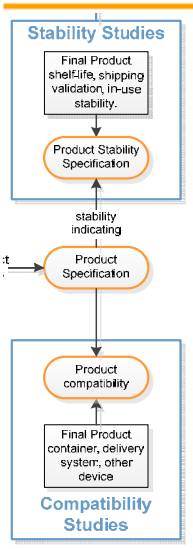
Selecting a potency assay?

- Practicalities will necessarily limit those that could be used for product release, e.g. An in vivo assay (e.g. Botox) is unlikely to be possible for cell therapy release testing.
- Where time or material mean a true potency assay would not be possible, a surrogate measure can be used, e.g.
  - ChondroCelect – expression of gene markers
  - Provenge – Expression of CD54

Warning!

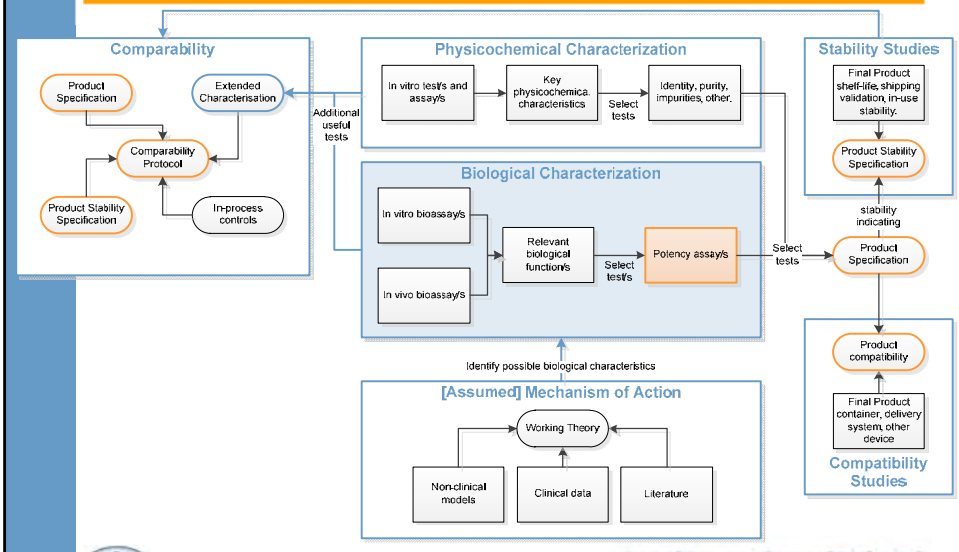
- These surrogates for potency are only valid if correlated to other bioassays and/or *in vivo* effects relevant to the MoA.

The Importance of Potency



- You cannot confirm stability without a potency assay
  - Biological function may be lost before viability
- Viability alone doesn't confirm the product is effective, you need a potency assay.
- Compatibility of the product with devices (e.g. syringes, containers, etc) or other biomaterials (or potentially drugs) cannot be confirmed without a potency assay.
  - Although generally minor issue

The Importance of Potency



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Further Reading

- PAS-83:2012 Developing human cells for clinical applications in the European Union and the United States of America. Guide.
  - Free Download

http://www.bsigroup.com/en/sectorsandservices/Forms/Download-PAS-83/

  - Purchase hardcopy

http://shop.bsigroup.com/en/ProductDetail/?pid=000000000030218727

- PAS 84:2012 (BSI) Cell Therapy Regenerative medicine. Glossary
  - Free Download

http://www.futuremedicine.com/doi/pdfplus/10.2217/rme.12.38

- PAS 93:2011 (BSI) Characterization of human cells for clinical applications. Guide
  - Free Download

http://www.bsigroup.com/en/sectorsandservices/Forms/PAS-93-Form-page/.

- Potency Assay Development for Cellular Therapy Products
  Cytotherapy, Submitted.

Interactive mindmaps available at: www.advbiols.com/resources

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Further Reading

Interface focus | FirstCite e-publishing | J. R. Soc. Interface doi:10.1098/rsif.2010.0442.focus Published online

REVIEW

Regulating interface science healthcare products: myths and uncertainties

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Whenever new technology emerges it brings with it concerns and uncertainties about whether or how it will need to be regulated, particularly when it is applied to human healthcare. Drawing on the recent history in the European Union (EU) of the regulation of cell-based medicinal products, and in particular tissue-engineered products, this paper explores the myths that persist around their regulation and speculates on whether the existing regulatory landscape in the EU is flexible enough to incorporate nanotechnology and other new technologies into healthcare products. By untangling these myths a number of clear conclusions are revealed that, when considered in the context of risk–benefit, make it clear that what hinders the uptake of new technology is not regulatory process but basic science.

Keywords: biomaterials; healthcare; regulation

http://rsif.royalsocietypublishing.org/content/early/2010/09/14/rsif.2010.0442.focus

Note: Free Access

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