Controllable Cell-Based Therapies: Regulatory Challenges & Opportunities

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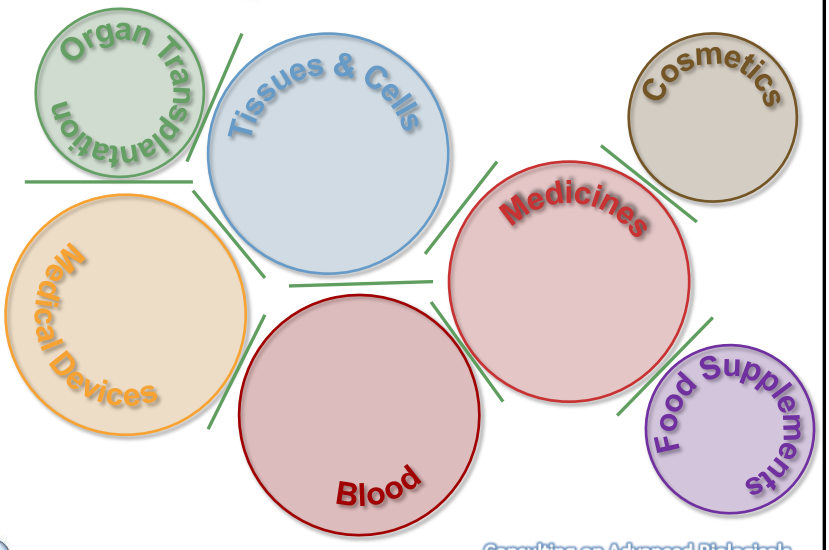
Introduction

- Regulation of Healthcare products in the EU
- Medicines – what are they?
- How do new technologies find their place?
- Regulatory challenges and opportunities
  - for discussion

Healthcare and related products:
Legal Framework



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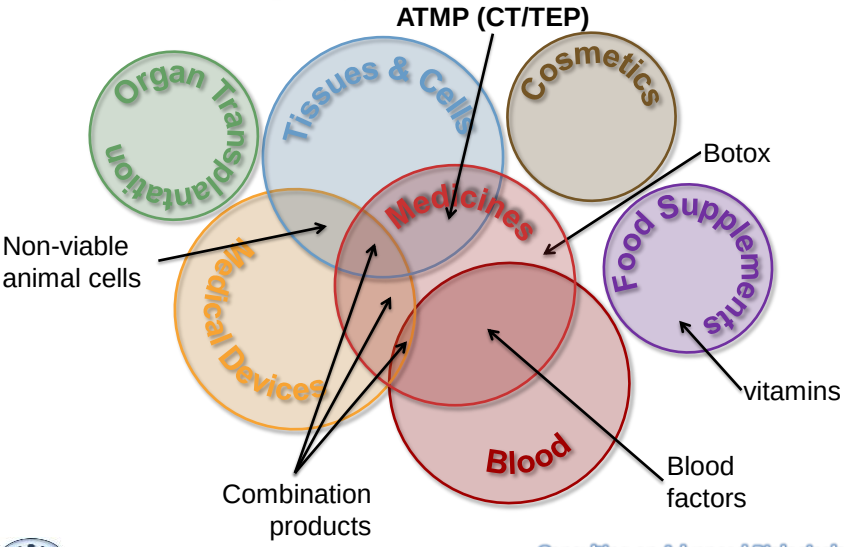
Healthcare and related products:
How it works out…



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Directive 2001/83/EC

2. Medicinal product:
(a) Any substance or combination of substances presented as having properties for treating or preventing disease in human beings;
or
(b) Any substance or combination of substances which may be **used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action**, or to making a medical diagnosis.

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Medical Devices
Directive 93/42/EEC

'medical device' means any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application intended by the manufacturer to be used for human beings for the purpose of:

- *diagnosis, prevention, monitoring, treatment or alleviation of disease,*
- *diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,*
- *investigation, replacement or modification of the anatomy or of a physiological process,*
- *control of conception,*

*and which **does not** achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means;*

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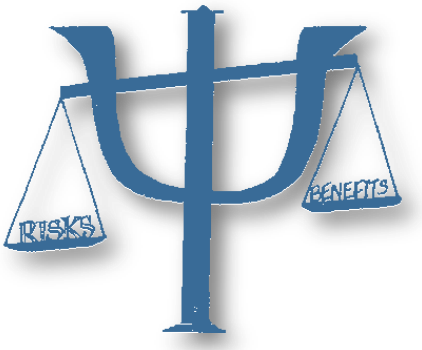
What are the Objectives of Medicines Regulation?

- Safeguarding public health
  - Medicines can be dangerous
  - Unacceptable toxicity
  - Disease transmission (biological materials/medicines)
- Consumer protection
  - Fit for purpose
  - Learn from mistakes
- Consumer confidence
  - Knowing they are regulated.

What are the Basic Requirements for Medicines?

- Quality
  - Consistent
  - Pure or few (and safe) levels of impurities
- Safety
  - Risks identified and mitigated as far as reasonable
  - Safety evaluated such that risks understood/controlled
- Efficacy
  - It works (when you follow the instructions) within the limitations stated.
  - Risk/benefit

Risk/Benefit



- Toxicity/side effects
- Risk of disease transmission
- Treatment/cure of disease/symptoms
- Secondary benefits

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The Rest is Science

- Core Directives give definition and scope
- Technical Annexes gives high level data requirements (but not prescriptive)
- Regulatory guidelines are mandatory – but most are procedural
- Pharmacopoeia
  - monographs mandatory (give or take)
  - general chapters are guidance
- Scientific guidelines are just that
  - convey principles
  - reflect on agency experience to date
  - Nearly always *'…unless otherwise justified'*

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Regulatory Pathway
What this means to Regulatory Professionals

- Legal framework
  - Which legal framework applies?
  - Medicine, device etc. (or >1)
- Legal basis for approval
  - Medicine
    - Full dossier
    - Abridged dossier
      - Generic, biosimilar etc
  - Medical Device
    - Implantable, IVD, active implantable etc
    - Class I, IIa, IIb, III.

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Regulatory Pathway
What this means to Developers

- What do I need to do?
- Regulatory Translation:
  - **What are the Data Requirements?**

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Regulatory Pathway
What are the Data Requirements?

- Depends on the science.
  - But you need to establish Q/S/E somehow
- The regulators will not have the answers at the beginning
  - Why? Because its new!
- What should I do?
  - Early discussion of new technology with regulators
    - Warning! Premature discussion can backfire
      - Scare the regulators
      - Confuse the regulators
      - Slow progress (uncertain if safe to proceed)
  - Consider early discussion with regulatory professionals

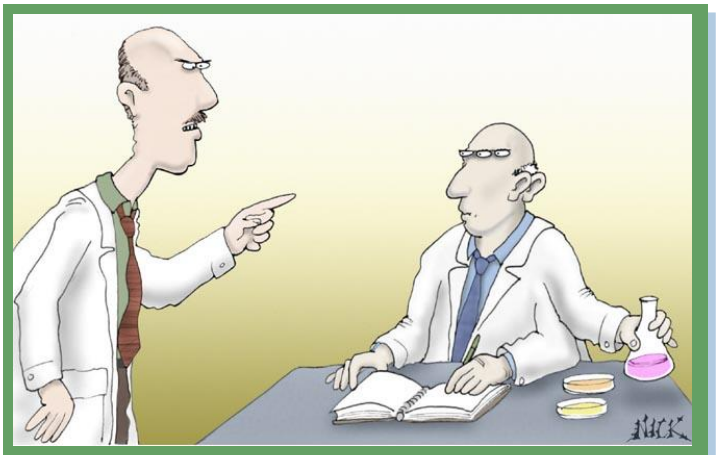
Regulatory Pathway
What are the Data Requirements?

- Depends on the science.
  - But you need to establish Q/S/E somehow
- Early pioneers need to work it out
  - Every medicine is case-by-case to some degree
  - Understand what you are trying to achieve
    - Asking basic questions of regulators will not make a good impression
    - make sure you understand the regulatory framework/s and principles
  - Formulate a plan to do this (several stages)
  - Discuss the plan with regulators
    - Only when you are certain it's a good plan
    - One step at a time

CONCLUSIONS

- Current legal framework is logical and elegant
- Legal framework avoids specifics
- Specific scientific principles provided as guidelines
  - not prescriptive
  - easily updated
- Upside ‘considerable flexibility’
- Downside ‘moving target’
- Early adopters of new technology need to work with the regulators to figure out the data requirements.

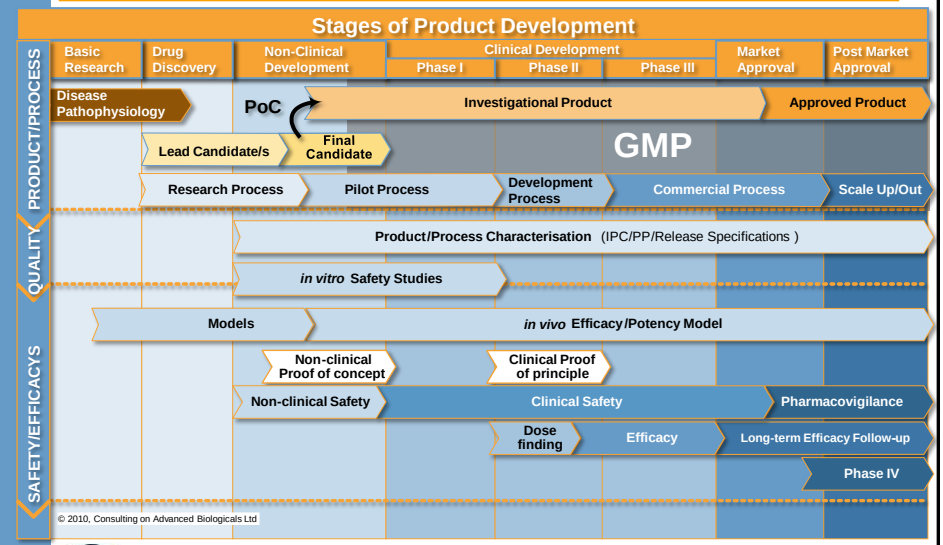
THANK YOU



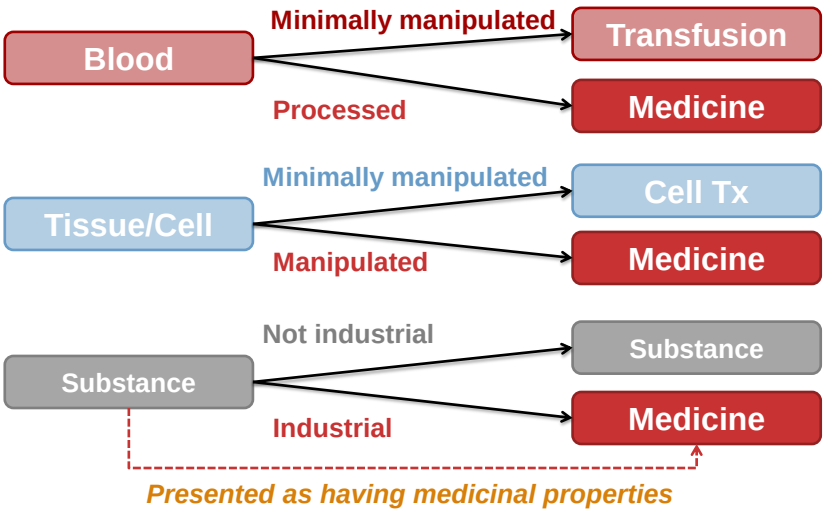
“You’re a selfish man, Lewis! Those stem-cell lines were meant for people who’ve LOST an organ!”

Back-up Slides

Product Development



Analogous approaches



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