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# The Authorisation of Hospital Exempt Manufacturers

*Making Gene and Cell Therapy Medicines a Reality July 11th 2012 Gibson Hotel*

Dr Patrick Costello
Blood, Tissues & Organs Manager
Irish Medicines Board

# INTRODUCTION

- What is an Advanced therapy medicinal product (ATMP)
- Tissues as starting materials
- What is a hospital exempt ATMP?
- Requirement to Authorise
  - Tissues and Cells
  - The manufacturing process
- Application Process
- Questions

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# What is an Advanced Therapy Medicinal Product (ATMP)?

- Legal definition Article 2 of Regulation EC No 1394/2007 (the 'ATMP Regulation')
  - a) 'Advanced therapy medicinal product' means any of the following medicinal products for human use:
    - a **gene therapy** medicinal product as defined in Part IV of Annex I to Directive 2001/83/EC,
    - a **somatic cell therapy** medicinal product as defined in Part IV of Annex I to Directive 2001/83/EC,
    - a **tissue engineered** product as defined in point (b).
  - (b) 'Tissue engineered product' means a product that:
    - contains or consists of engineered cells or tissues, and
    - is presented as having properties for, or is used in or administered to human beings with a view to regenerating,
    - repairing or replacing a human tissue.

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# What is an Advanced Therapy Medicinal Product (ATMP)?

- Cells or tissues shall be considered ‘engineered’ if they fulfil at least one of the following conditions:
  - the cells or tissues have been subject to **substantial manipulation**, so that biological characteristics, physiological functions or structural properties relevant for the intended regeneration, repair or replacement are achieved. The manipulations listed in Annex I, in particular, shall not be considered as substantial manipulations,
  - the cells or tissues are **not intended** to be used for the **same essential function** or functions in the recipient as in the donor.

**These products need a manufacture authorised and a centralised marketing authorisation**

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# “Engineered”

- Substantially manipulated is **not**
- cutting; grinding; shaping; centrifugation;
- soaking in antibiotic or antimicrobial solutions;
- sterilization; irradiation;
- cell separation, concentration or purification;
- filtering;
- lyophilization;
- freezing;-cryopreservation; vitrification.

**it is**

- Culture / Expansion
- Differentiation of cells
- Changing cell surface expression

**Processes that happen within a Tissue Establishment**

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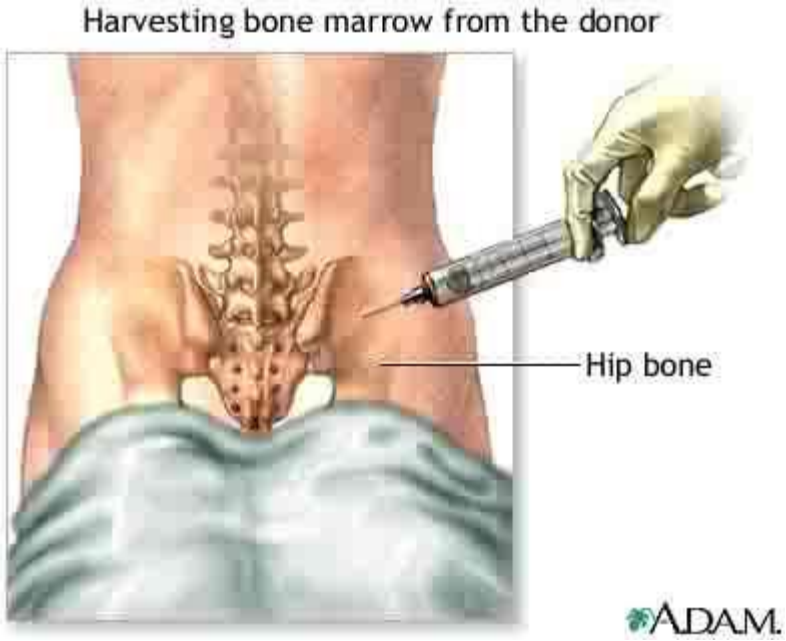
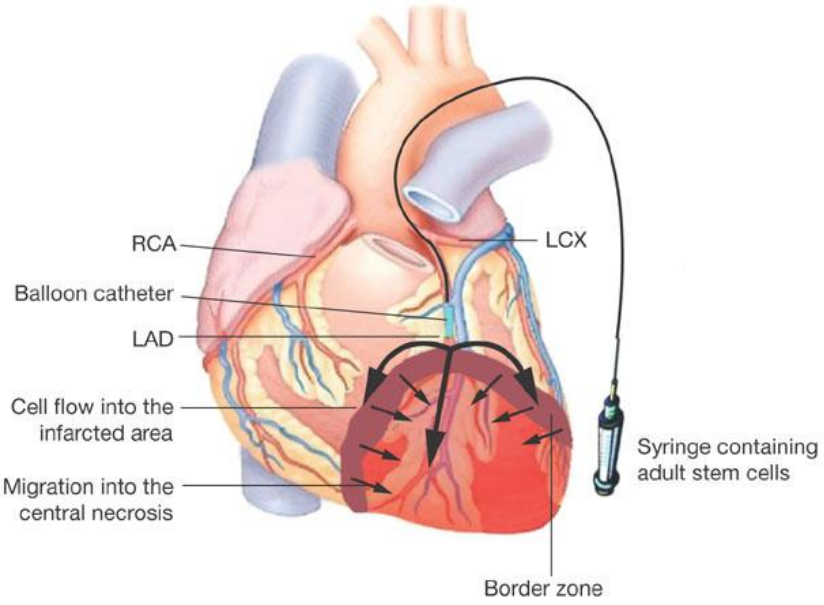
# “Engineered”

- Non- homologous use




http://sicklecell-ourvoice.blogspot.ie/2009/12/part-2-stem-cell-transplant.html




http://www.forbes.com/sites/stevensalzberg/2011/12/04/stem-cells-show-promise-for-repairing-damaged-hearts/

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# Starting **materials** for ATMP manufacture

- Human tissues and cells
  - Stem cells
  - Amnion / amniotic membranes
  - Cornea
  - Cartilage

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# What is a hospital exempt ATMP?

- Legal definition Article 28 of Regulation EC No 1394/2007 (the 'ATMP Regulation')
  - *Any advanced therapy medicinal product, as defined in Regulation (EC) No 1394/2007, which is prepared on a* ***non-routine basis*** *according to* ***specific quality standards****, and used* ***within the same Member State*** *in a hospital under the exclusive professional responsibility of a* ***medical practitioner****, in order to comply with an individual* ***medical prescription*** *for a custom-made product for an* ***individual patient****. – paragraph 1*

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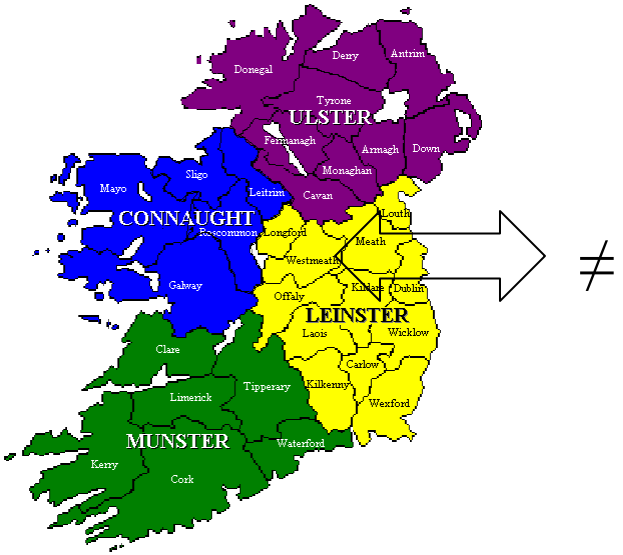
# What is a hospital exempt ATMP?

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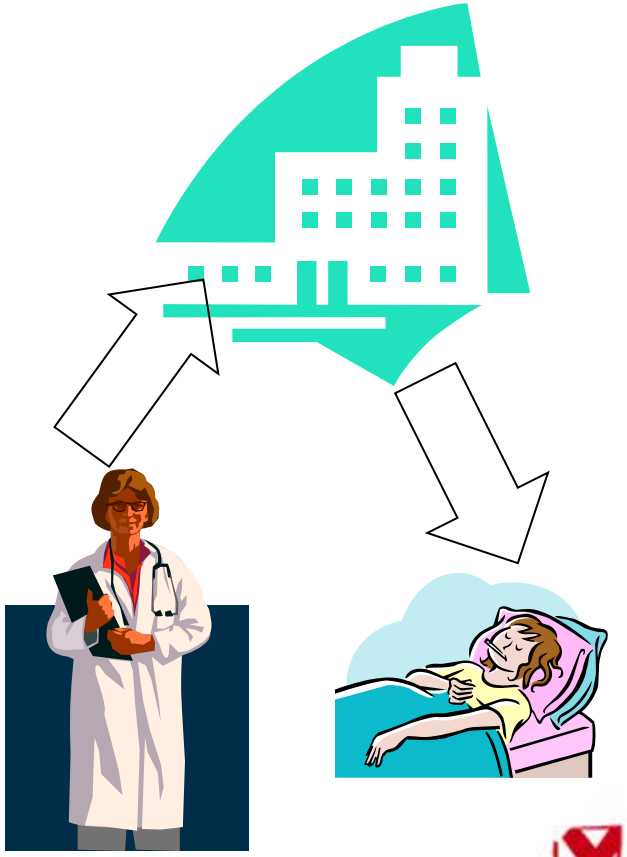

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# What is a hospital exempt ATMP?

- Legal definition Article 28 of Regulation EC No 1394/2007 (the 'ATMP Regulation')
  - ***Manufacturing*** *of these products* ***shall be authorised*** *by the competent authority of the Member State. Member States shall ensure that* ***national traceability and pharmacovigilance*** *requirements as well as the specific quality standards referred to in this paragraph are equivalent to those provided for at Community level in respect of advanced therapy medicinal products for which authorisation is required pursuant to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency – paragraph 2*

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# Exemption

✓ Marketing Authorisation

☒ Manufacture requires Authorisation

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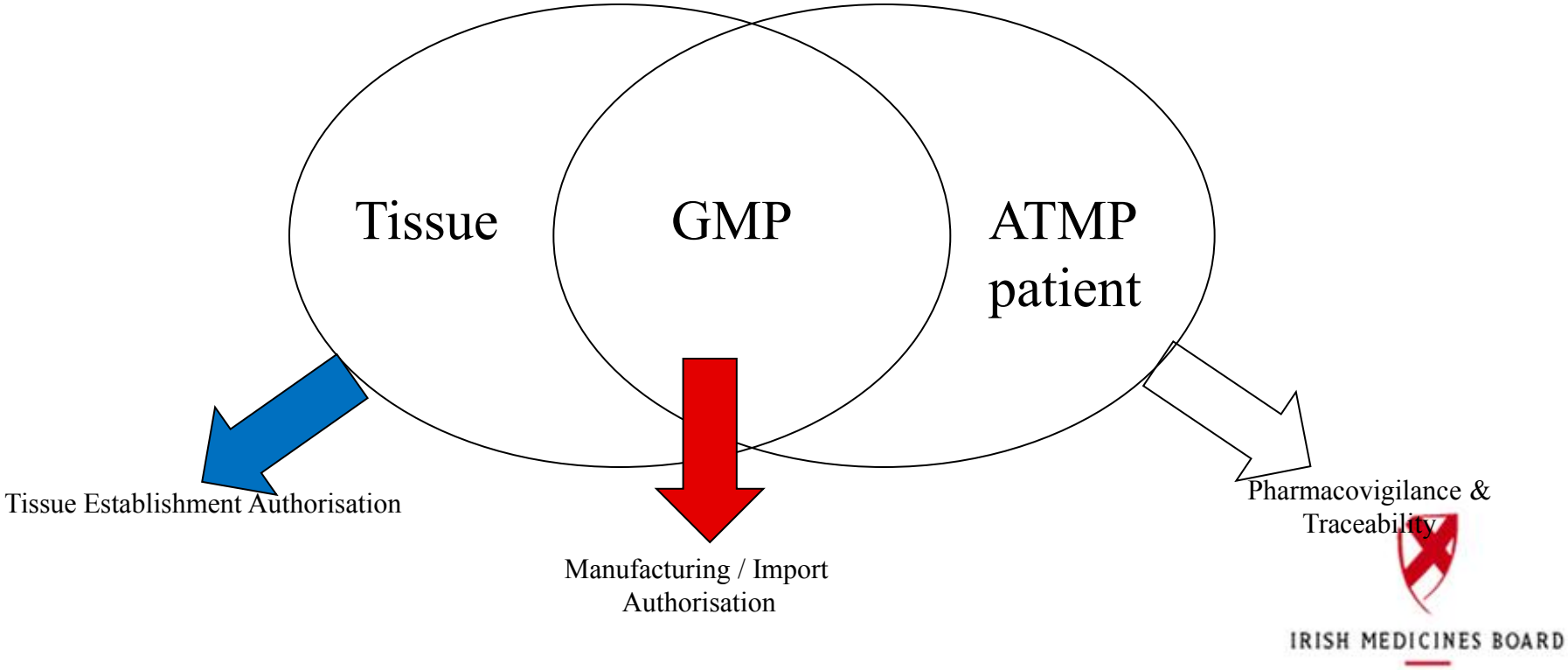
# How do I get authorised to manufacture a hospital exempt ATMP?

- Overlap of Tissues and Cells legislation and GMPs – 2 different pieces of legislation

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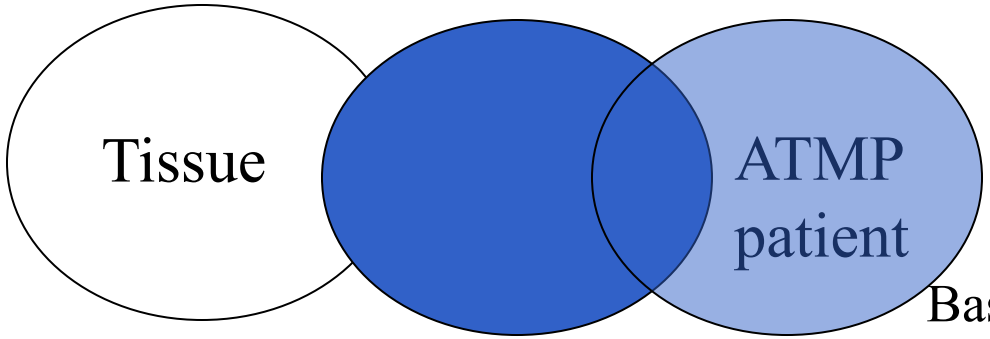
- Overlap of Tissues and Cells legislation and GMPs




Tissue Establishment Authorisation

- Donation
- Procurement
- Testing of donor

Basic Processing to present tissues/ Cells to manufacturer

- Purification of cells
- Cryopreservation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# Tissues and Cells Legislation

- **“Donation"** means donating human tissues or cells intended for human applications;
  - Voluntary Unpaid
  - Information provision to donor
  - Consent
- **“Testing”** of donors
  - Range of infectious diseases
  - Other when required

- **“Procurement**" means a process by which tissue or cells are made available;
  - Donor evaluation & selection criteria
  - Trained staff
  - Procedures in place for procurement
  - Facilities, Material, Equipment
  - Procurement Report
  - Labelling
  - SAE/R associated with procurement

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# Tissue Establishment Authorisation in Ireland

- Application form on our website
  http://www.imb.ie/EN/Publications/Publications/Application-for-Authorisation-of-a-Tissue-Establishment-Document-1-.aspx?page=1
- Following validation, inspection coordinated
- If successful, tissue establishment authorisation issued
- Seems to be not so straight forward

**9-12 months**

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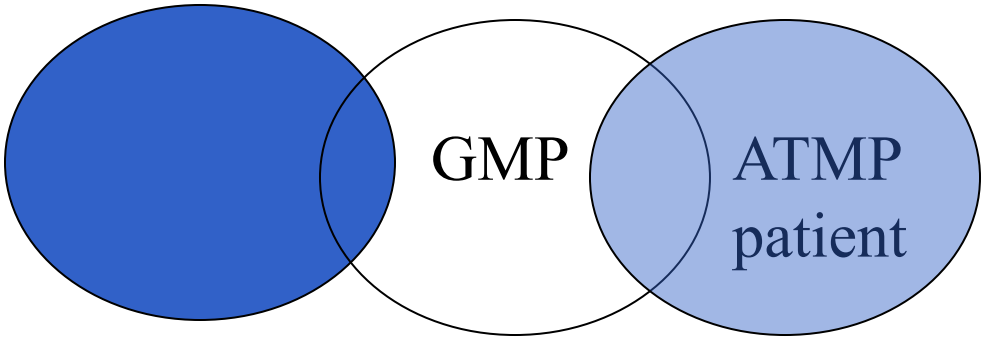
# How do I get authorised to manufacture a hospital exempt ATMP?

- Overlap of Tissues and Cells legislation and GMPs




Manufacturing / Import Authorisation

- Manufacture / Processing
- Pharmacovigilance
- Traceability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# “The GMP’s”

- EudraLex - Volume 4 Good manufacturing practice (GMP) Guidelines http://ec.europa.eu/health/documents/eudralex/vol-4/index_en.htm
- **Part 1** – 9 Chapters
- **Part 2** - Basic Requirements for Active Substances used as Starting Materials
- **Part 3** – GMP related documents
- **Annexes** – 19 in total

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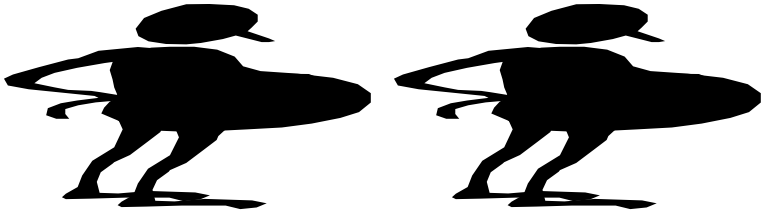
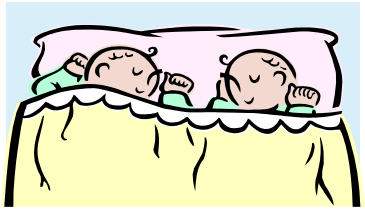
# Manufacturing Authorisation Application in Ireland

- Application form on our website

  http://www.imb.ie/EN/Publications/Publications/Application-for-a-Manufacturers-Authorisation-.aspx?page=1&tags=48
- Following validation, inspection coordinated
- If successful authorisation issued (90 day timeframe)
- Seems to be not so straight forward





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# Inspection in Ireland

- Usually a number of meetings are held prior to inspection.
- Inspection coordinated when site ready
- Combined team of tissue / gmp inspectors
- Possible to bring assessor expertise

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# Advice

- We need these products on our market
- We are happy to facilitate meetings with applicants regarding facilities / equipments /

**Its good to talk!!!**

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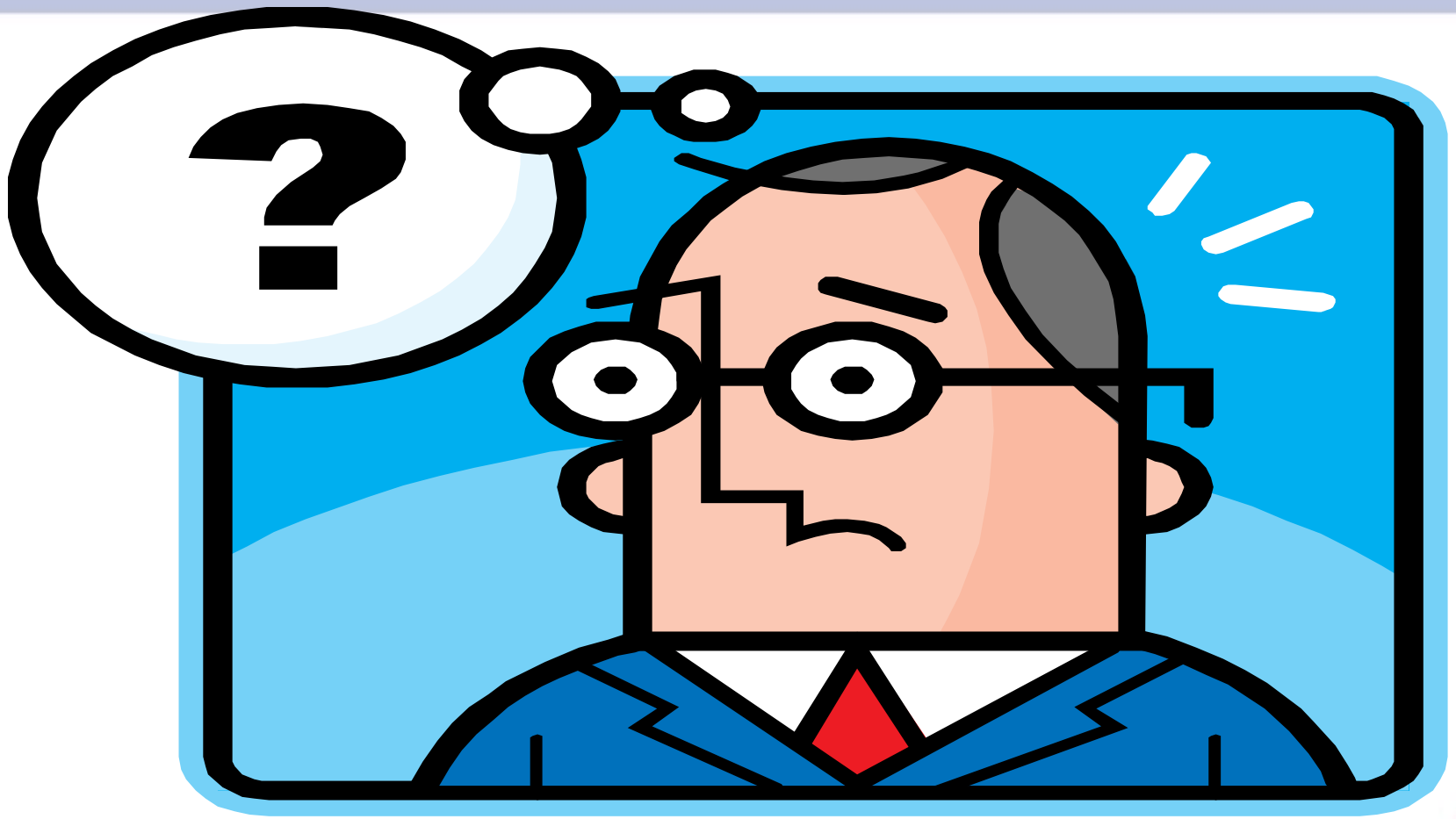
# QUESTIONS



patrick.costello@imb.ie

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