# ESGCT/ICH Workshop on Viral Vector Shedding

- Introductory notes:

  What is vector shedding?

  Why is it important?

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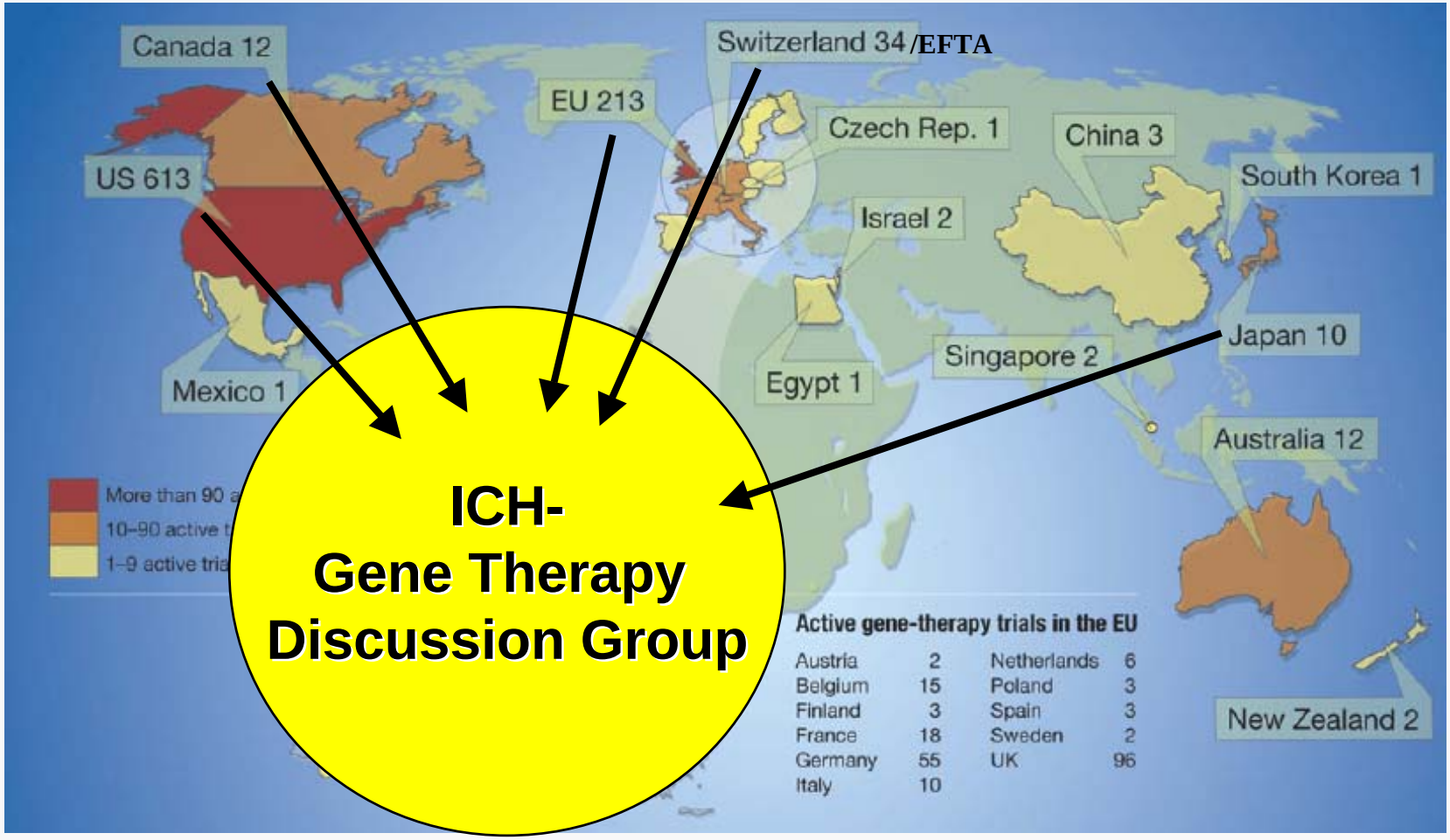
Rotterdam, 30 October 2007

- Dr. M. Papaluca-Amati and Dr. O. Maki-Ikola,
  European Medicines Agency

- Prof. G. Dickson, ESGCT President,
  and the ESGCT Board

- Prof. G. Wagemaker, Rotterdam,
  and the local Organizing Committee of the
  XVth Annual Congress of the European Society of Gene and Cell Therapy (ESGCT)

- Dr. Odile Cohen-Haguenauer, Coordinator,
  and Clinigen Network of Excellence,
  a European Network for the Advancement of Clinical Gene Transfer and Therapy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EU 213
Czech Rep. 1
China 3
US 613
South Korea 1
Israel 2
Japan 10
Singapore 2
Egypt 1
Mexico 1
Australia 12
New Zealand 2
ICH-
Gene Therapy
Discussion Group
Active gene-therapy trials in the EU
Austria 2
Belgium 15
Finland 3
France 18
Germany 55
Italy 10
Netherlands 6
Poland 3
Spain 3
Sweden 2
UK 96

ICH INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE

25 October 2006

**ICH Considerations**

**General Principles to Address the Risk of Inadvertent Germline Integration of Gene Therapy Vectors**

- **Update from the ICH Regions**
- **Issues**
- **Harmonisation of technical requirements**

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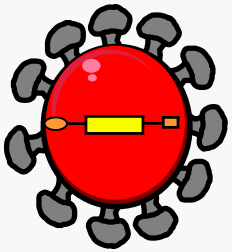
- Dr. S. Simek, CBER-FDA, Prof. K. Cichutek and the ICH Gene Therapy Discussion Group (EU, US-FDA, MHLW/JPM, Health Canada, EFTA)

| |
|---|
| **Professor Dr Klaus Cichutek**<br>Vice President<br>Paul-Ehrlich-Institute<br>Langen |
| **Dr Outi Maki Ikola instead of Dr Marisa Papaluca Amati**<br>Scientific secretary of Gene Therapy Working Party (GTWP)<br>Safety and Efficacy of Medicines<br>European Medicines Agency – EMEA<br>Canary Wharf, London E14 4HB |
| **Dr Sharon Longhurst**<br>Medicines and Healthcare products Regulatory Agency<br>London |
| **Dr Richard Pilsudski**<br>Directeur Scientifique et Affaires Réglementaires AstraZeneca 1, Place Renault<br>Rueil-Malmaison |

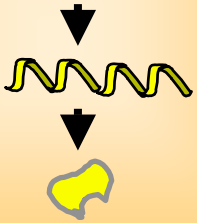
# What is Gene Therapy?

viral or non-viral vector/ DNA



transgene/ vector

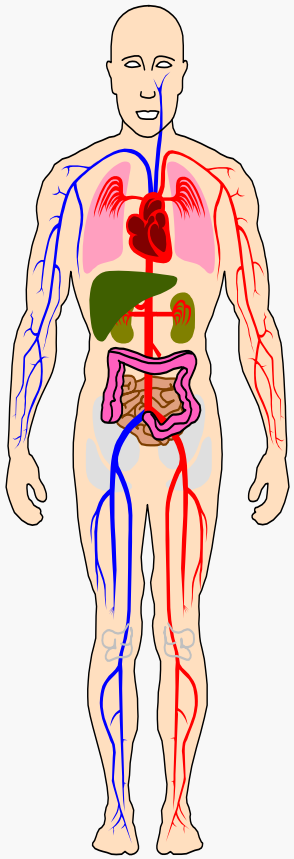
gene product



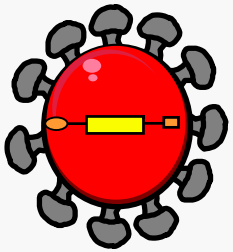
therapeutic

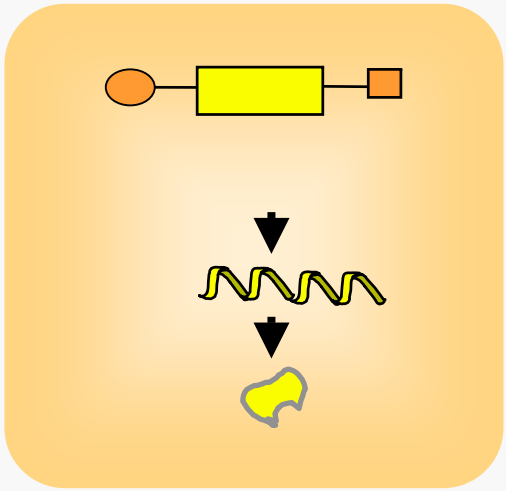
(preventive)

in vivo diagnostic



# What is Shedding?



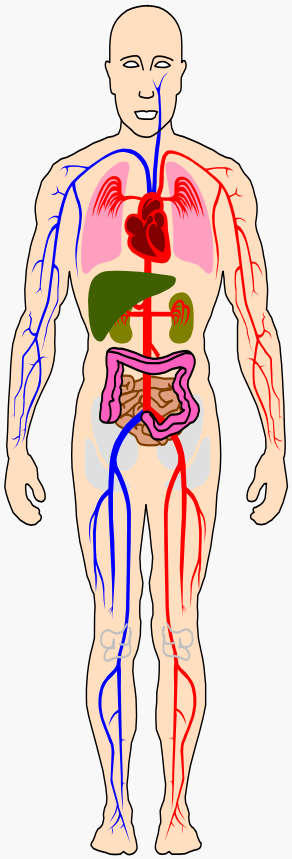


product in gene therapy:
- vector
or
- cell

therapeutic

(preventive)

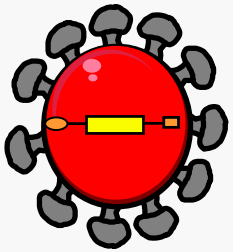
in vivo diagnostic

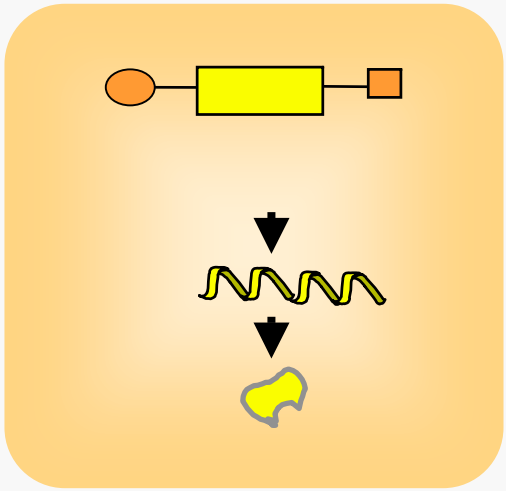


shedding

release of product from subject/patient to whom the product has been administered

# What may be shed in gene therapy?





product in gene therapy:
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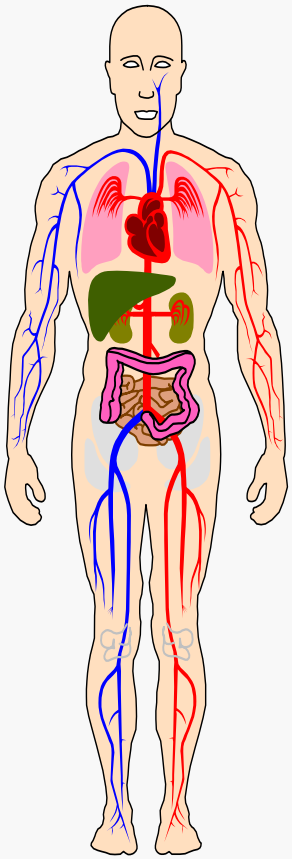
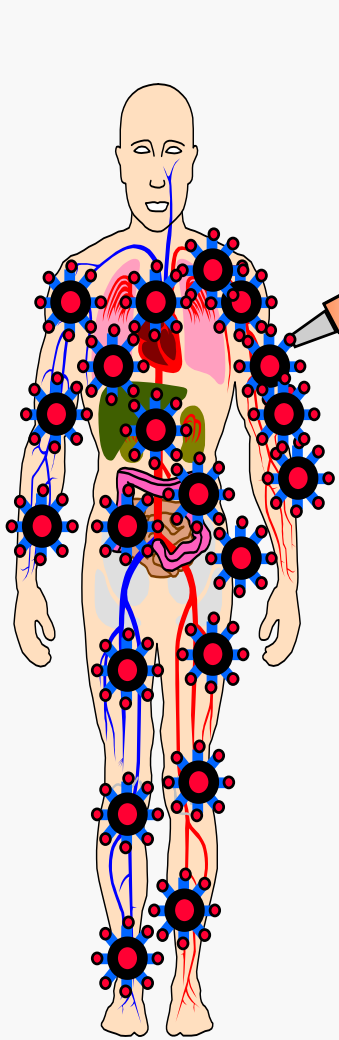


shedding

release of product from subject/patient to whom the product has been administered:

- viral or non-viral vector particle/ micro-organism
- vector nucleic acid
- genetically modified cell
- virus derived from/ mobilising/ recombined with vector

# In-vivo gene transfer using vectors



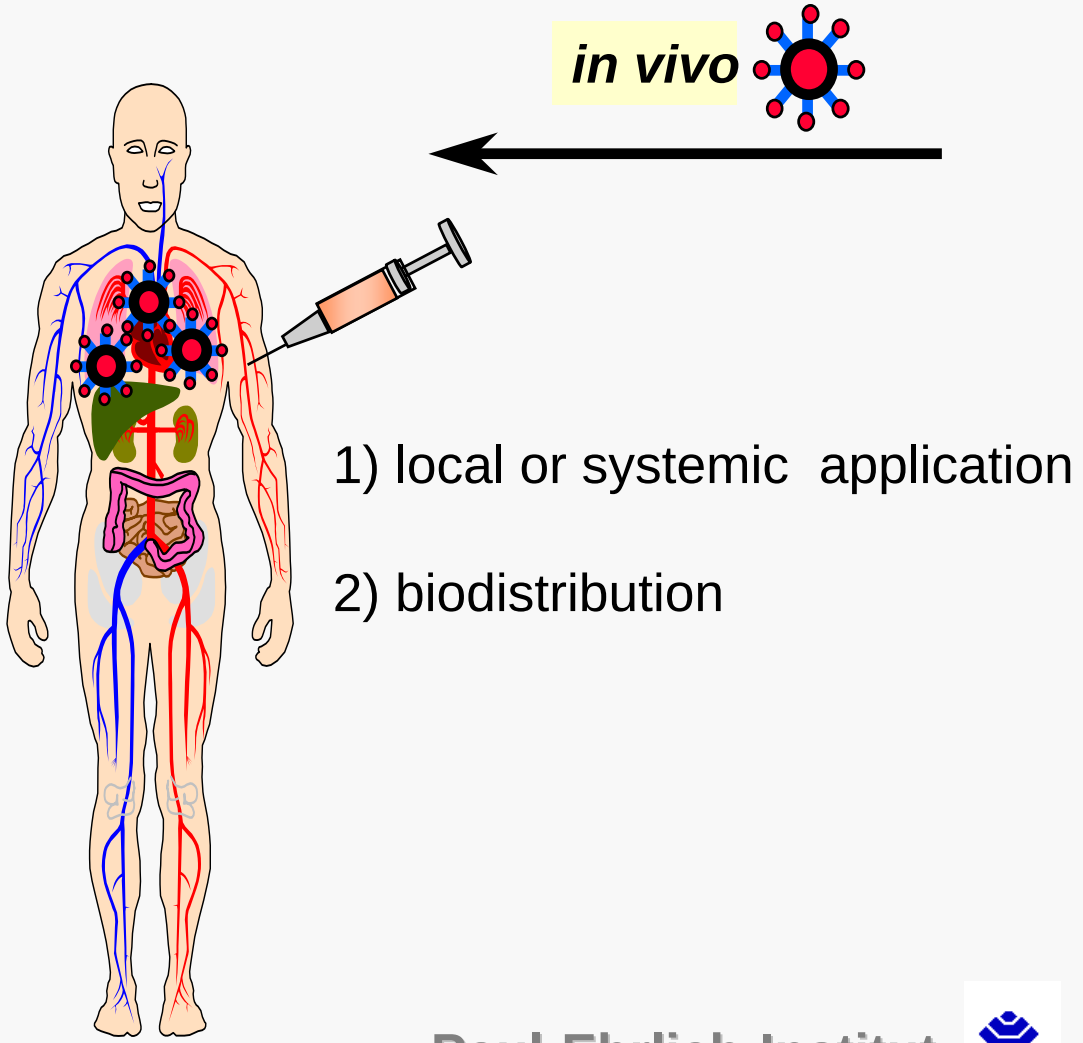
*in vivo*

1) local or systemic application

2) biodistribution

# In-vivo gene transfer using vectors

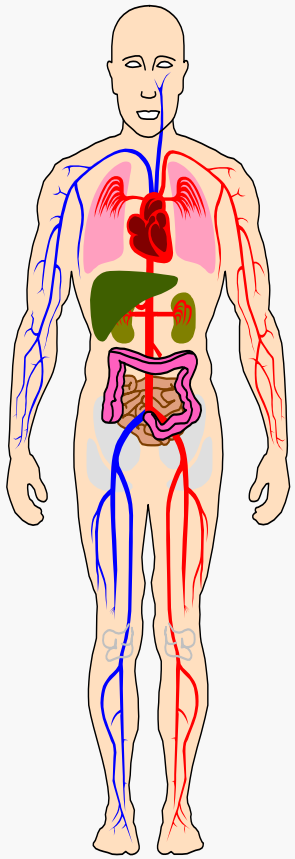
- biodistribution into bodily fluids including excreta
- infectious or non-infectious agent
- transmission to third parties: humans, animals
- recombination with other agents: viruses, micro-organisms, TSE agents
- spread in humans




1) local or systemic application

2) biodistribution

# Which shed products/organisms pose a risk?



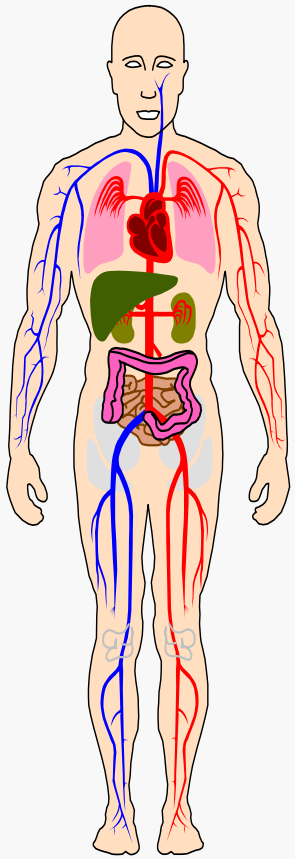
shedding

release of product from subject/patient to whom the product has been administered:

- viral /non-viral vector particle/m.-org.
- vector nucleic acid
- genetically modified cell
- virus/micro-organism derived from/ mobilising/ recombined with vector

- infection of other human beings or animals:
- risk to individual: adverse effects
- risk to public: new pathogenic organism

# What may be the result of shedding?



shedding

release of product from subject/patient to whom the product has been administered

- transmission to other human beings
- transmission to animals
- transmission (from reservoirs) to micro-organisms, viruses, TSE-agents, plants

# Definition of shedding in gene therapy

- Shedding in the field of gene therapy

  may be defined as

  - dissemination and/or transmission of
  - gene therapy product or product-related vector or infectious agent
  - from bodily fluids and excreta of the treated subject or patient
  - to humans other than the patient.

# Considerations with respect to shedding in gene therapy

- What is shed?
- How  and whereto is something shed?
- Does shedding lead to dissemination/transmission?
- What are the consequences of dissemination/transmission?
- How can the risk of shedding be assessed
  - in non-clinical studies,
  - in clinical studies
  - in post-marketing studies?
- What kind of measures can be recommended to
  - assess shedding and/or
  - to reduce harmful consequences of shedding?

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European Medicines Agency (EMEA)

European Society of Gene and Cell Therapy (ESGCT)

European Network of Excellence in Gene Therapy

# EMEA/ICH WORKSHOP ON VIRAL/VECTOR SHEDDING

Tuesday **30 October 2007 (11.00-18.30)**

in conjunction with:

The XVth Annual Congress of the European Society of Gene and Cell Therapy

27-30 October 2007 Rotterdam, The Netherlands

CHMP GTWP

Paul-Ehrlich-Institut

Federal Agency for Sera and Vaccines

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Rotterdam, 30 October 2007