



DRA Doktoranden Tag 2010:

Advanced therapy medicinal products

Chances and challenges in a new
regulatory environment



Legal definition of ATMPs

Europe:

Legal framework: Regulation (EC) No 1394/2007 (*lex specialis*)

- amendment to:
- Directive 2001/83/EC
 - Regulation (EC) No 726/2004

Scope: To regulate ATMPs which are intended to be placed on the market in memberstates



Regulation (EC) No 1394/2007

- Only applies to ATMPs that are either prepared industrially or manufactured by a method involving an industrial process
- ATMPs are subject to the centralised authorization procedure (EC) No 726/2004



Who is responsible?

Committee for Advanced Therapies (**CAT**)

Primary task: the evaluation of ATMP marketing authorisation applications for the CHMP

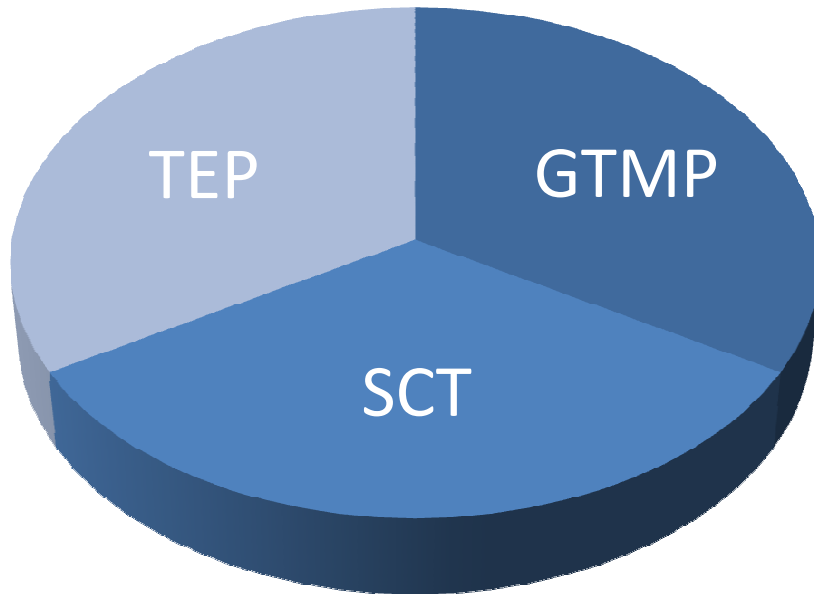


prepare a
draft opinion

final approval



Definition of ATMPs



GTMP = Gene therapy
medicinal products

SCT = Somatic cell therapy

TEP = Tissue engineered
products



Definition of ATMPs

- Gene therapy medicinal products ¹
 - Adenovirus and lentivirus are the only viruses for gene transfer (VGFEC) combinant nucleic acid used in or administered to human beings
 - treatment of secondary lymphoedema associated with the treatment of breast cancer
 - The primary effect is directly related to the recombinant nucleic acid sequence
 - Do not include vaccines

¹ According to part VI of Annex 1 to 2001/83/EC



Definition of ATMPs

- Somatic cell therapy medicinal products ¹
 - Contain therapeutic products composed of autologous tumor cells which have been manipulated in order to alter properties relevant for their clinical purpose
treatment of colon cancer
 - Cells do not fulfill the same function in the recipient as they do in the donor
 - Are intended for use in or are administered to human beings

¹ According to part VI of Annex 1 to 2001/83/EC



Definition of ATMPs

○ Tissue engineered products ¹

- ~~Expanding or restoring or replacing human cells, tissues or organs~~
- Shall be considered engineered if cells/tissues regeneration of urethral sphincter muscle in patients with urinary incontinence have been **substantially** manipulated in order to alter properties relevant for their clinical purpose (regeneration, repair, replacement)
- Cells do not fulfill the same function in the recipient as they do in the donor

¹ According to chapter 1 of (EC) No 1394/2007



Definition of ATMPs

Manipulations that are not considered substantial are listed in Annex I to regulation (EC) No. 1394/2007

- cutting
- grinding
- shaping
- centrifugation
- sterilization
- irradiation
- soaking in antibiotic or antimicrobial solutions
- cell separation, concentration or purification
- filtering
- lyophilization
- freezing
- cryopreservation
- vitrification



Stagnation in drug development vs. escalation of development costs

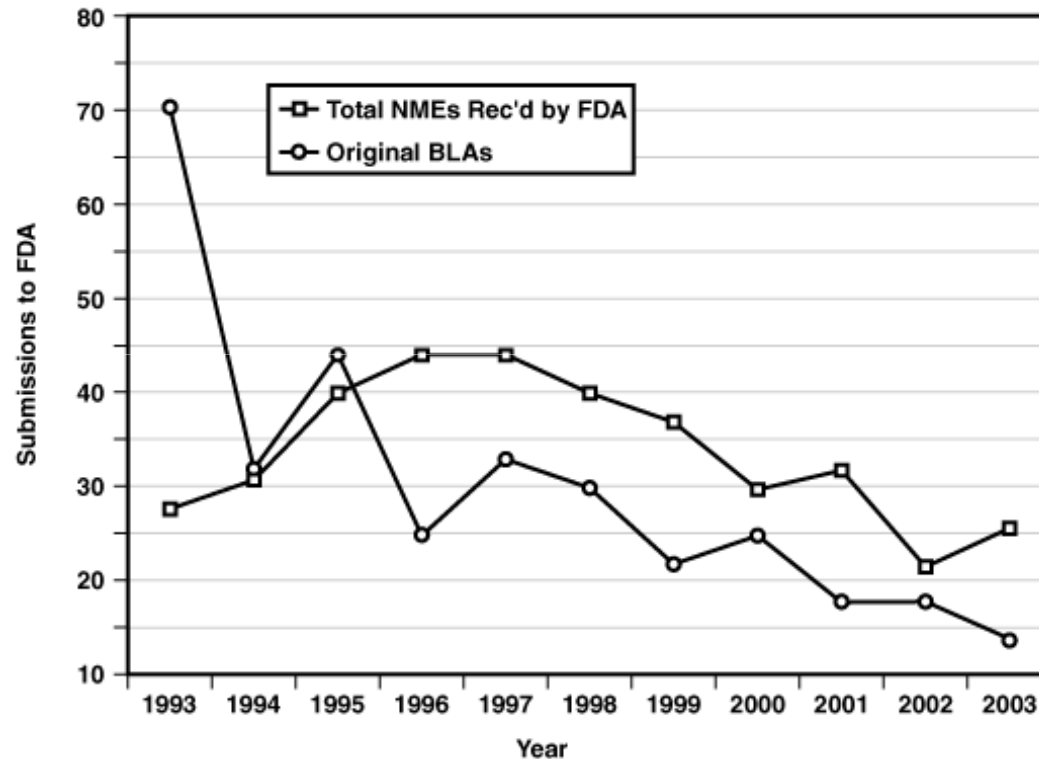


Figure 1: Submissions of new molecular entity (NME) and biologics license applications (BLAs) to FDA over a ten year period.



What's new?

Classification



Supporting SMEs at early
development stages



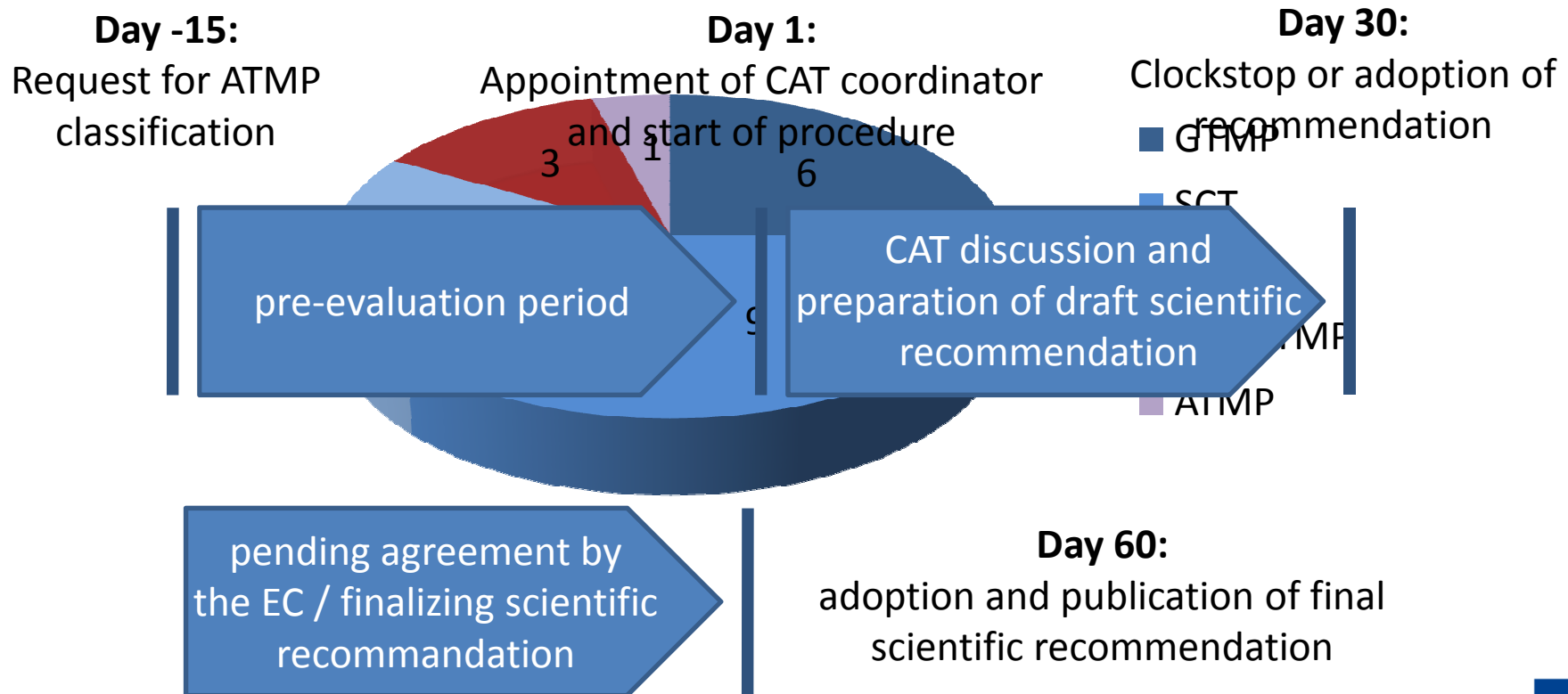
Certification¹

¹Available for SMEs only (as defined in 2003/361/EC)



Classification procedure

Is my IMP an ATMP or something else?





Certification

- Provide a solid foundation for SMEs in terms of evaluating the early development stages
- May provide an incentive for bigger companies to buy or support the further development of new ATMPs
- Certification may relate to either:
 - Quality data only (module 3 Part 1 and Part 4 of Annex 1 to 2001/83/EC)
 - Quality and non-clinical data (module 4 Part 1 of Annex 1 to 2001/83/EC)



Certification

COMMISSION REGULATION (EC) No 668/2009

Quality data only

- information related to the starting and raw materials
- manufacturing process of the active substance
- characterization and control of the active substance, limited to the data necessary to adequately describe the active substance
- description and composition of the finished product



Certification

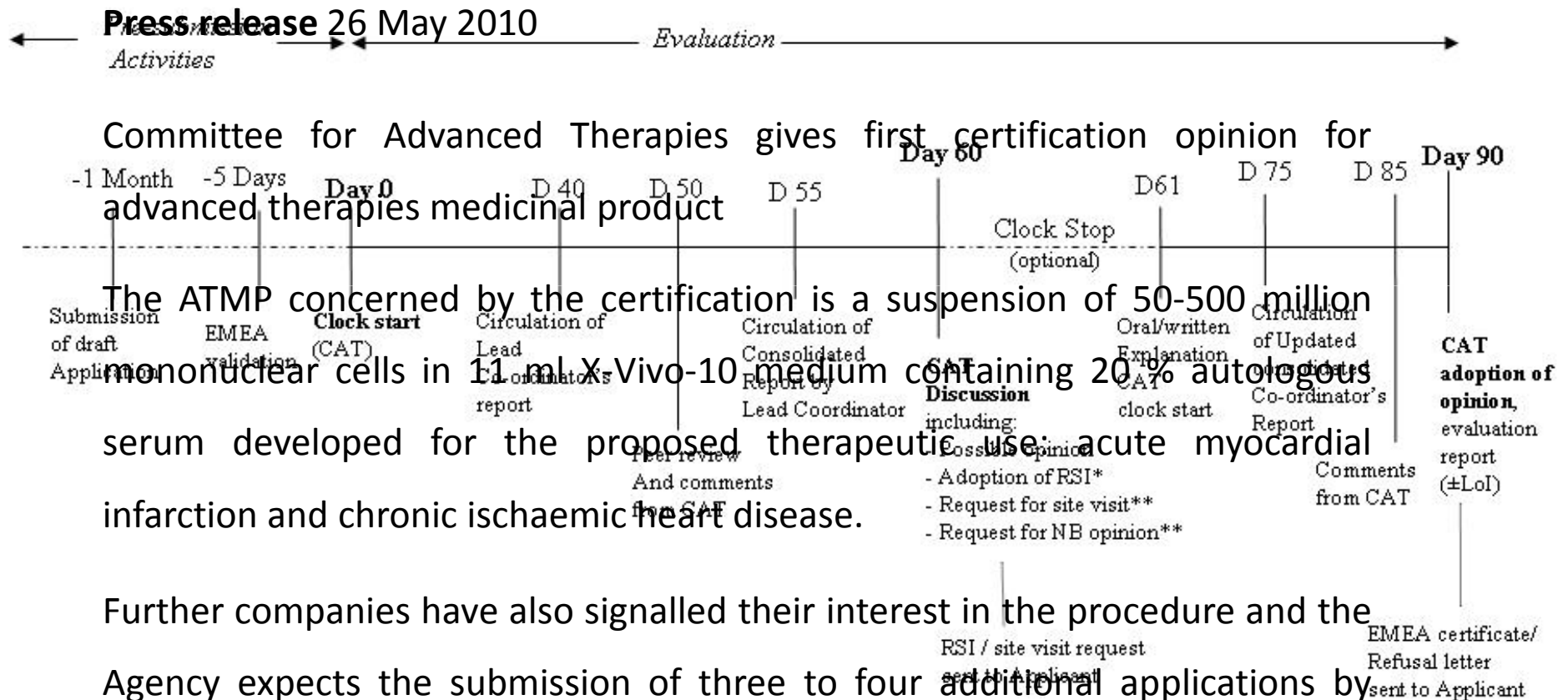
COMMISSION REGULATION (EC) No 668/2009

Quality and non-clinical data

- primary pharmacodynamic data supporting the rationale for the proposed therapeutic use
- pharmacokinetics bio-distribution data, if relevant to corroborate the primary pharmacodynamics data
- at least one toxicity study



Certification procedure



*The clock stop will be 30 or 60 days

**In case of site visit/consultation of NB clock stop is until site visit report/NB opinion is made available



Challenges

- Problems inherent to ATMPs
 - Definition and control of cell based product (see biologicals / biosimilars)
 - Need for novel animal models in order to demonstrate basic PK / PD principles
 - Phase 1 in clinical trails may not be applicable for some ATMPs (see anti-tumor therapeutics)
 - long term follow up will probably be needed in order determine the efficacy of most ATMPs
 - A new set of safety measures should be considered in order to provide patient safety in clinical trails (see TGN)



Thanks!

Thank you
for your attention