Paul-Ehrlich-Institut

SME-Workshop
„Focus on Scientific and Regulatory Advice“, 26 May 2011

>>www.pei.de

The Innovation Office at the Paul-Ehrlich-Institut

Bettina Ziegele, M.A., Head Innovation Office

Bundesinstitut für Impfstoffe
und biomedizinische Arzneimittel

Overview

- Framework
- Legal Basis
- Kinds of Advice and Focus
- Services
- Statistics
- Future Projects
- Challenges

Implementation of the Innovation Office

- February 2009 – August 2009:
  Setting of formal requirements together with the German Federal Ministry of Health
- August 2009 – October 2009:
  Preparations for implementing the Innovation Office
- Start of work November 2009:
  Press release, presentation at the website of the PEI
- December 2009:
  Opening workshop at the PEI

Regulation (EC) No. 1394/2007 (30 Dec. 2008)
A uniform regulatory framework for ATMP in the EU

- A marketing authorisation is required for industrially produced ATMP.
- Those ATMP having legally been on the national market by 30 December 2008 need a marketing authorisation after a transition period:
  - gene and cell therapy products starting 30 December 2011
  - TEPs starting 30 December 2012
- Marketing authorisation is provided via the centralised procedure co-ordinated by the European Medicines Agency (EMA).
- A full dossier (Directive 2009/120/EC incl. Annex I, Part IV) will be reviewed by experts in the
  - Committee for Advanced Therapies (CAT; PEI membership).
- An opinion (MA yes or no) by the CAT has to be agreed by the
  - Committee for Human Medicines (CHMP; PEI membership).
- MA is granted by the European Commission.

Legal Provision and Starting Point

- Regulation (EC) No. 1394/2007 ➡
  Need for central marketing authorisation by end of 2012 at the latest
- Article 28 of the Regulation ➡
  National Regulation „Hospital exemption“
- National Implementation in Germany ➡
  Section 4 b (sub-section 3) of the German Medicinal Products Act

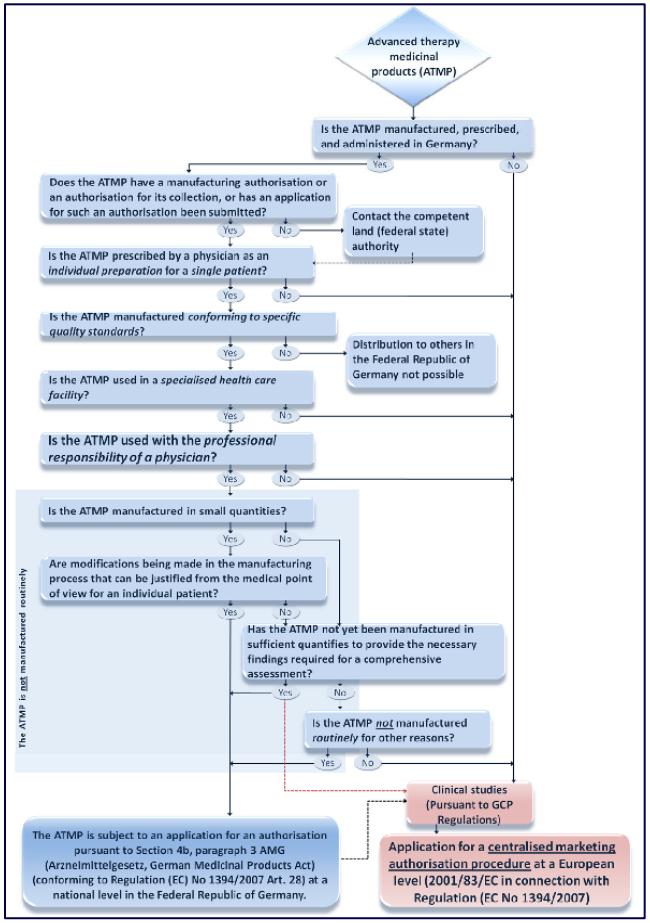
Regulation on a National Level

- Section 4 b AMG introduced in July 2009
  Non-routinely prepared ATMP having characteristics as in Section 4 b (1) require an authorisation by the PEI.
  Continued use if marketed and used on 23 July 2009:
  - application to PEI by 01 August 2010 for gene and cell therapy products
  - application to PEI by 01 January 2011 for TEP.

  A decision should be taken within 5 months (clock-stop for answering questions on possible grounds for non-acceptance).

- Use of ATMP not having a marketing authorisation: Section 40 ff AMG
  - Clinical trial authorisation by PEI and positive appraisal by ethics committee.

Decision Tree for Section 4b AMG (German Medicinal Products Act)



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Tasks of the Innovation Office

Co-ordination of national advice, regulatory and scientific with focus on ATMP

Preparing and providing (up-dated) information on ATMP

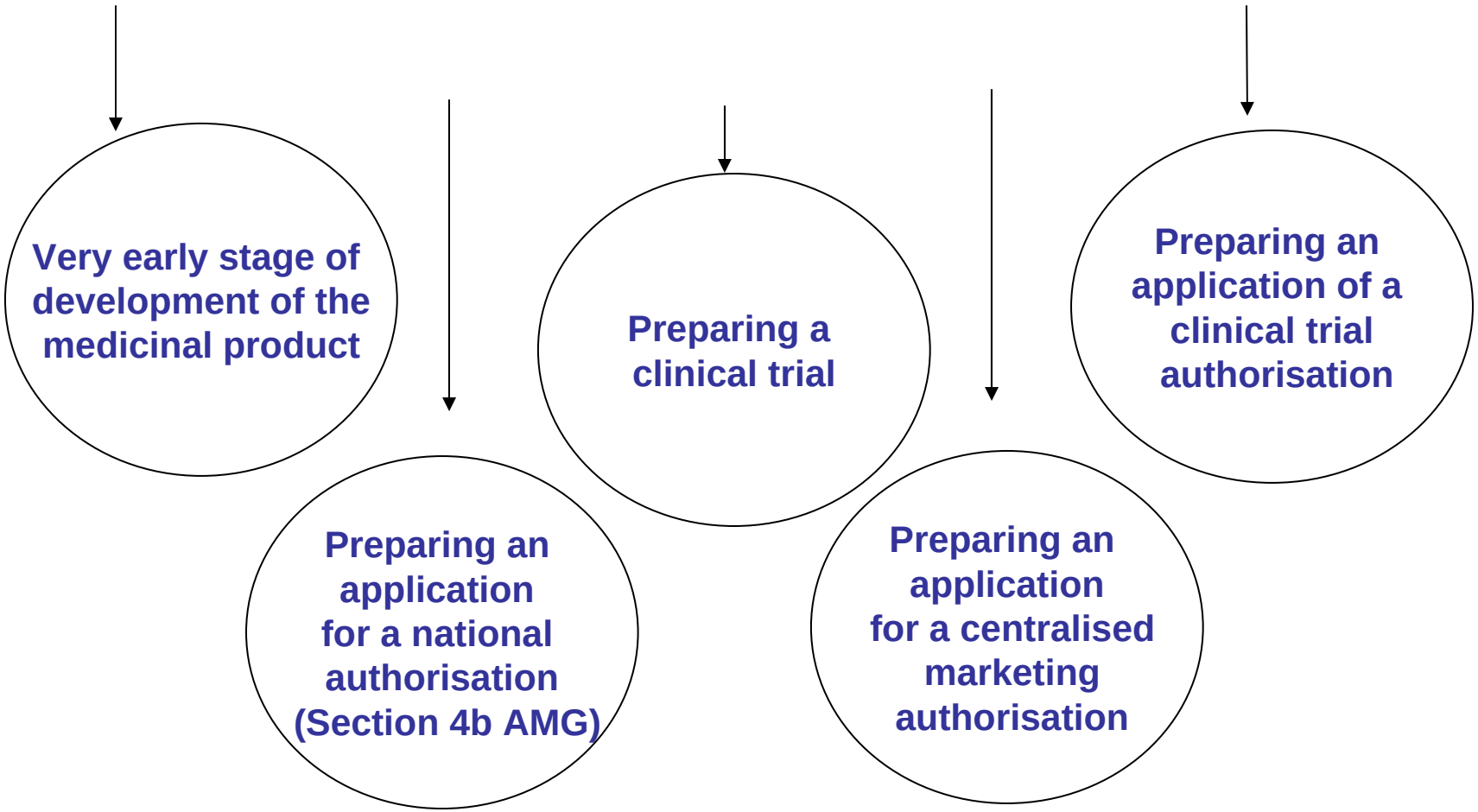
Regulatory Advice

FAQs - regulatory

- What are the regulatory requirements?
- What is a possible/best practice procedure – national/European;

  „hospital exemption“/clinical trial?
- When to ask for (national) scientific advice?
- How to apply for certification/classification with the EMA?

Stages for National Scientific Advice



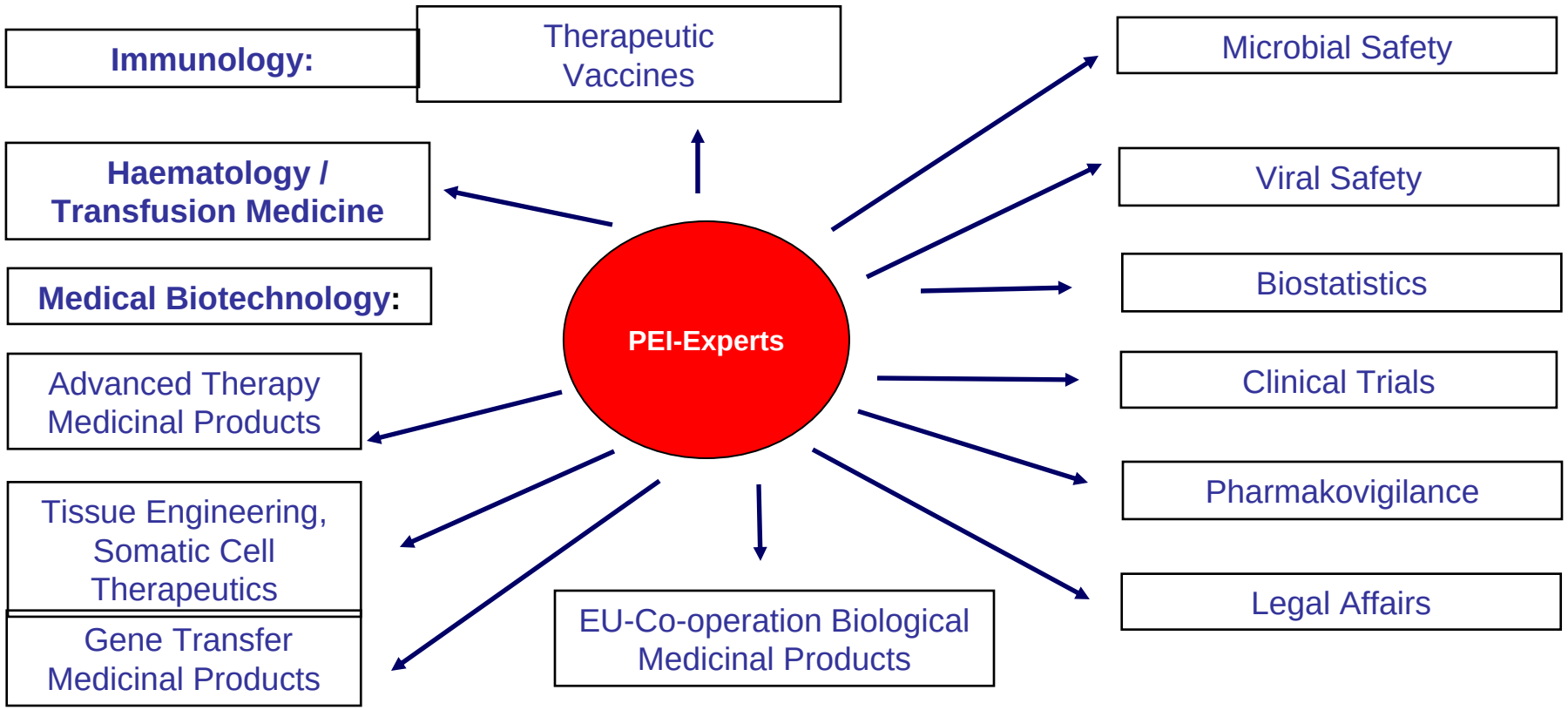
FAQs - scientific

- Provide advice on:
  - Identification of a risk-based approach
  - Development of medicinal product and proof of concept/first in man
  - Concept designs of clinical trials / definition of relevant endpoints

Points of Discussion and Requirements

Quality	Non-Clinic	Clinic
• Characterisation of the cell type • Final control • In-process-control	• Proof of Principle • Discussion of a clinically relevant animal model • Validation of data • Implementation of studies on the basis of GXP	• Proof of safety of the medicinal product (first proofs of efficacy) • Proof of concept • Discussion of primary und secondary endpoints

Areas of Advice and Expertise



Summary

Target Groups	Focus: Group of ATMP	Developmental Stages
• Academic institutions (e.g. clinical research groups)	• Gene Therapy Medicinal Products 1)	• In preparation for:
• Small and medium sized enterprises (SME)	• Somatic Cell Therapy Medicinal Products 2)	• Non-clinical studies
	• Tissue Engineered Products 3)	• Application of a clinical trial
		• National authorization
		• Centralised marketing authorisation

1) e.g. genetically modified cells as therapeutic vaccines

2) e.g. autologous haematopoietic bone marrow stem cells for the treatment of myocardial infarction

3) e.g. autologous chondrocyte-transplants for the treatment of cartilage defects

National Advice for ATMP by the Innovation Office of the PEI

Addressees: Academia (clinical research groups) and companies focused on ATMP

Provision of advice on general regulatory issues

- MAA, European
- Section 4b AMG*): national

Co-ordination of scientific advice:

Scientific advice with regard to the requirements of the quality of ATMP

Scientific advice with regard to preclinical development of ATMP

Scientific advice with regard to applications for clinical trials of ATMP

Supportive process-related advice on the basis of first data throughout the development of the ATMP

First application-oriented development and / or application

non-clinical studies

clinical trials

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*) Arzneimittelgesetz = German Medicinal Products Act

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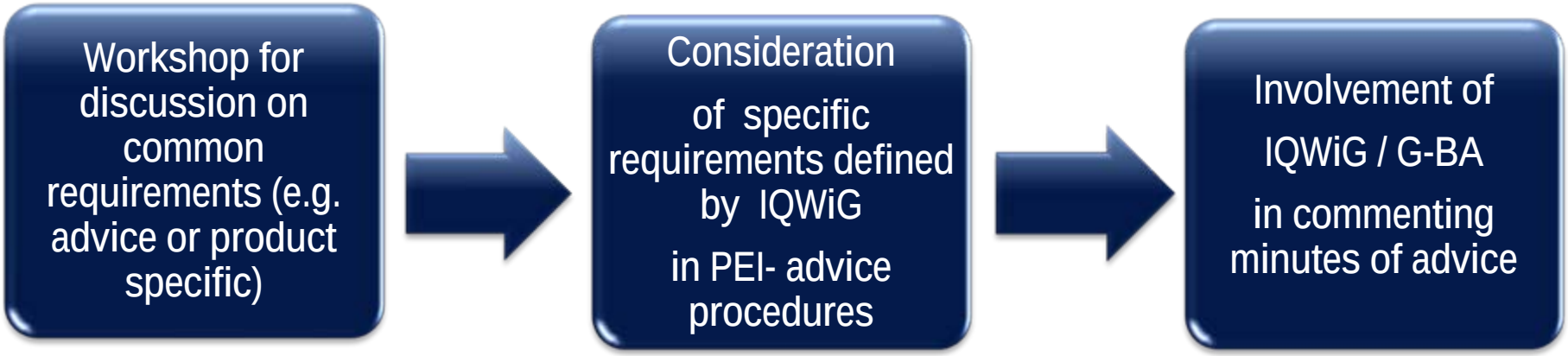
Innovationsbüro

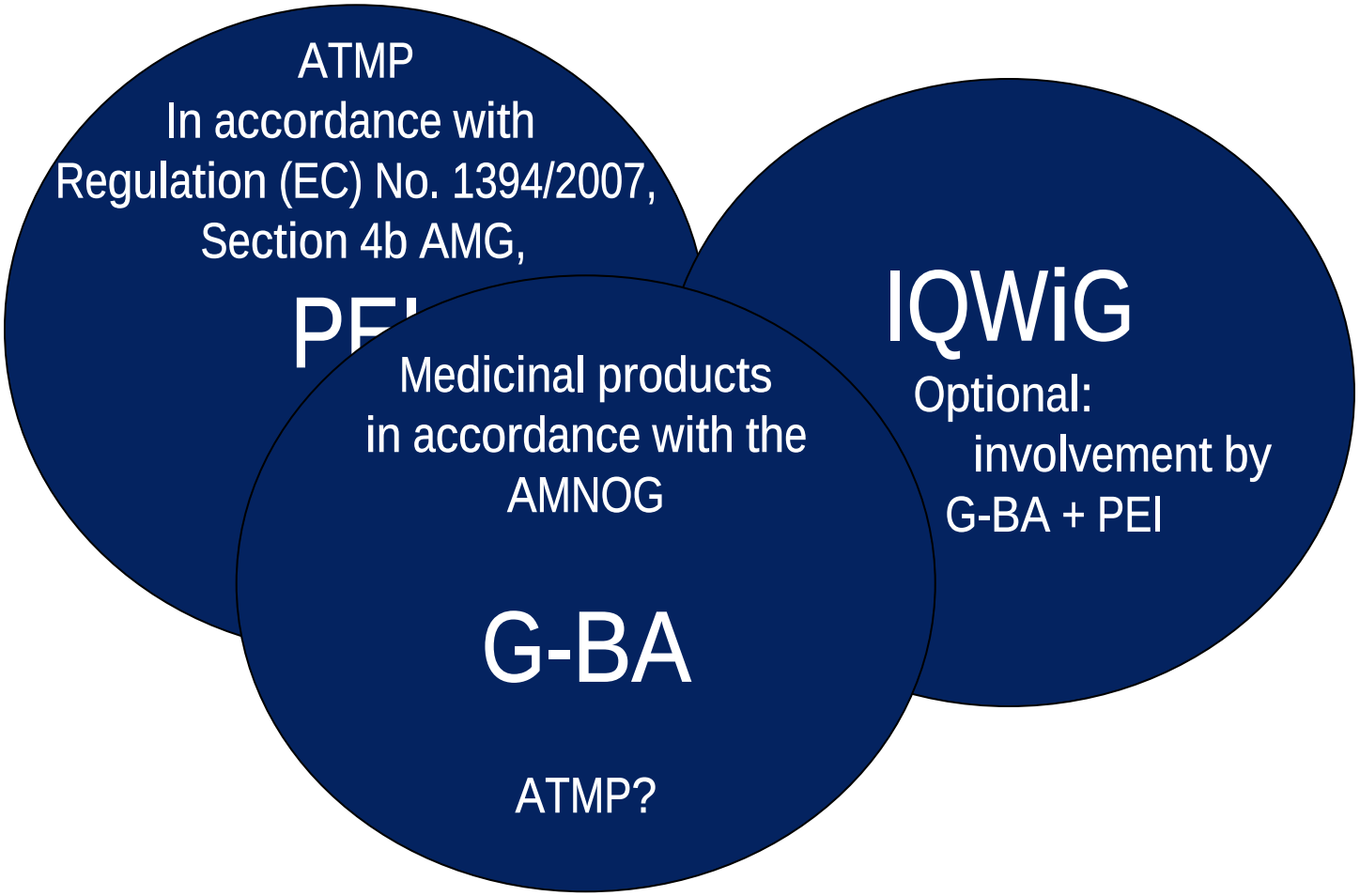
Optional joint and/or resp. parallel advice together with G-BA*/IQWiG**/PEI



*Joint Federal Committee

** German Institute for Quality and Efficiency in Healthcare

Formal Frame



Demand on advice for scientific requirements of clinical trials (PEI)

Demand on advice for requirements of clincial trials with regard to (additional) health benefit (IQWiG)

Applicant

Advice on the basis of § 35a SGB (social code) V (G-BA)

Advice on ATMP
Basis?
(IQWiG und G-BA + PEI?)

Function of the Innovation Office

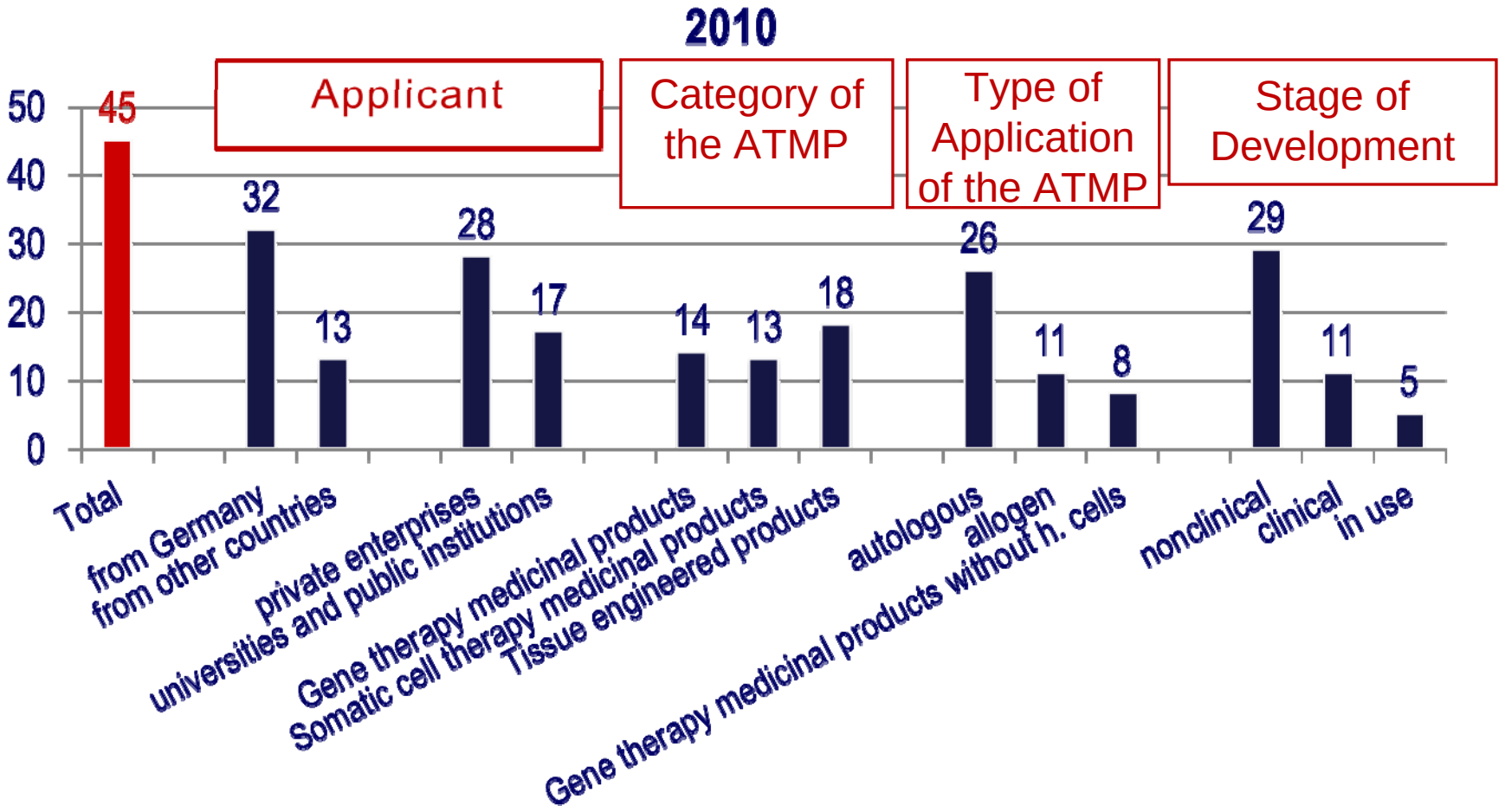
- Central contact point for requests for advice
- Co-ordination of advice across various expert areas
- Contact point for further information and queries on planned or completed advice
- „All-in-one service“:

  bridge to EMA, IQWiG and G-BA and as far as possible to clinical trial centres and non-clinical facilities

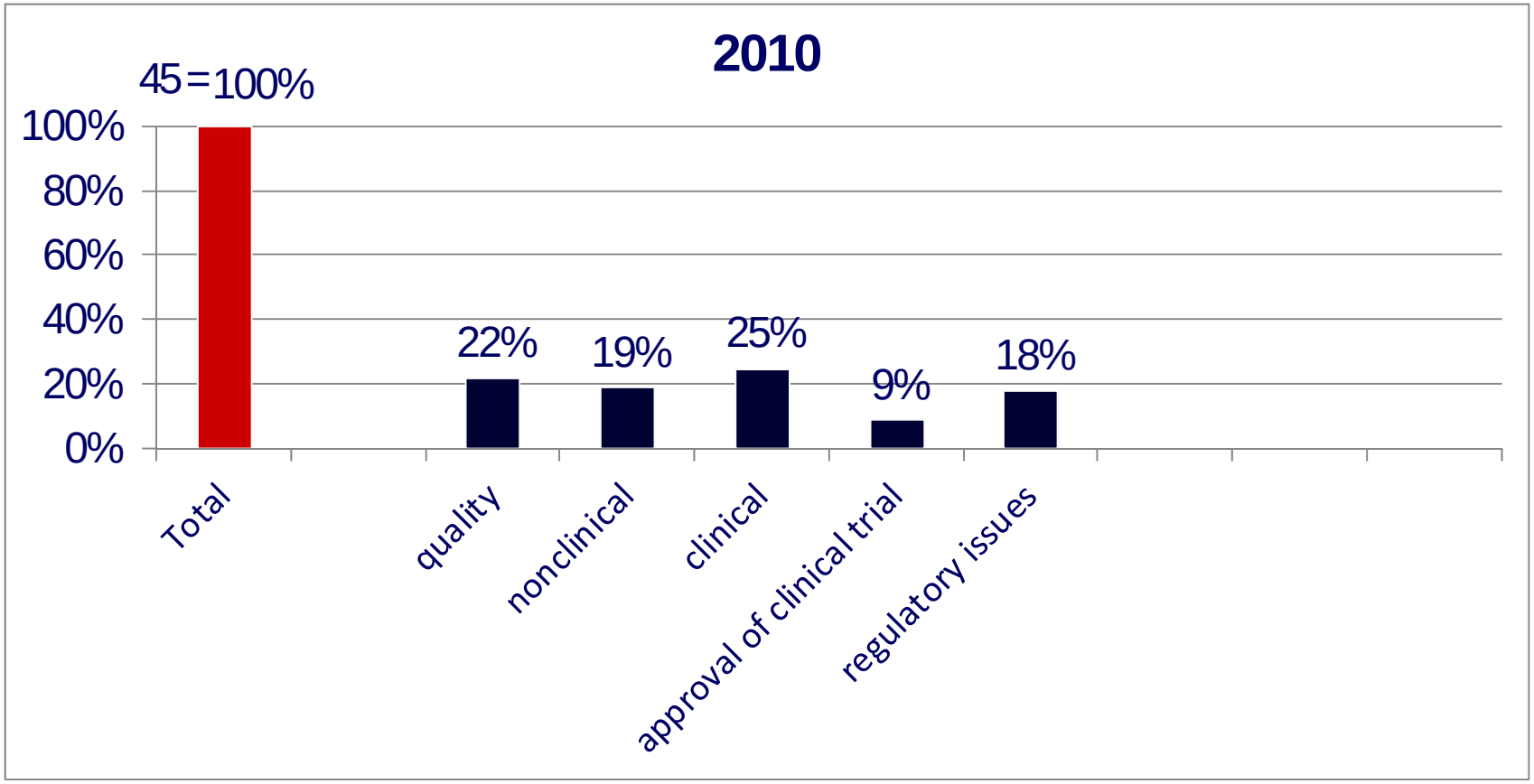
Service and Information

- General information on the website of the PEI
- Request form for national advice
- Booklet on ATMP as guide to applicants
- Guides for national applications for ATMP
- Register of useful guidelines and links
- Selection of FAQs

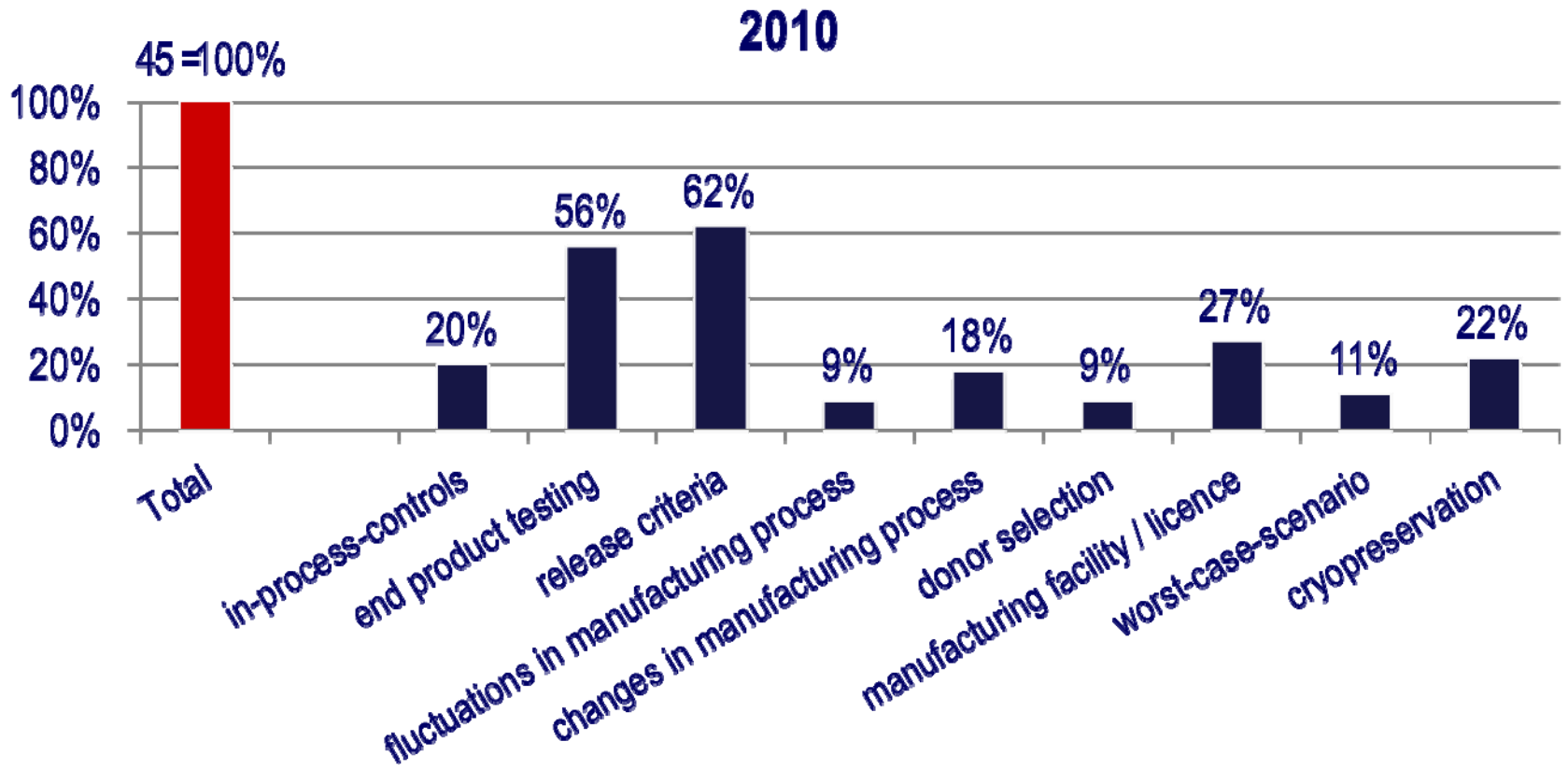
Some details on advice



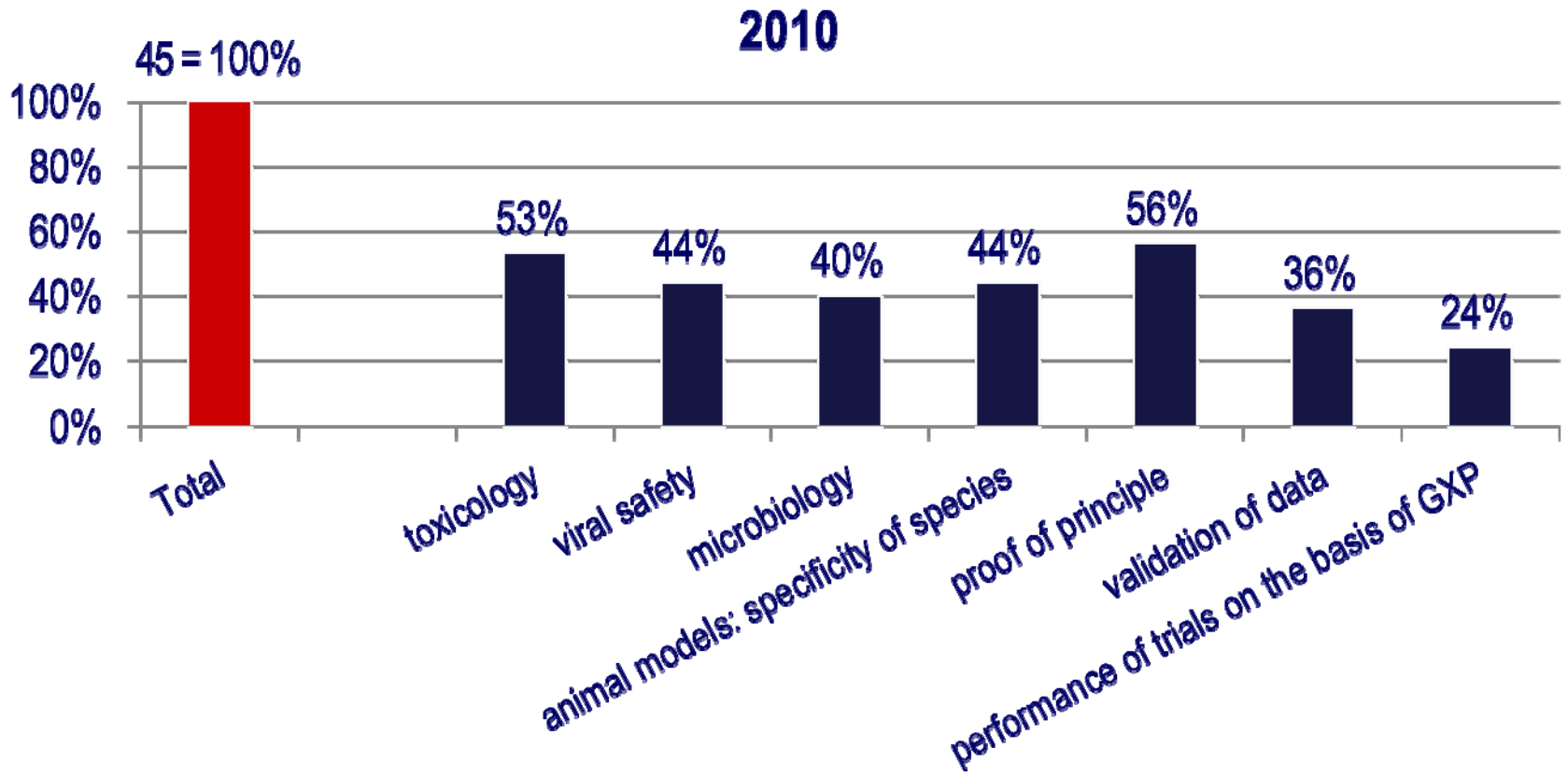
Main focuses of advice



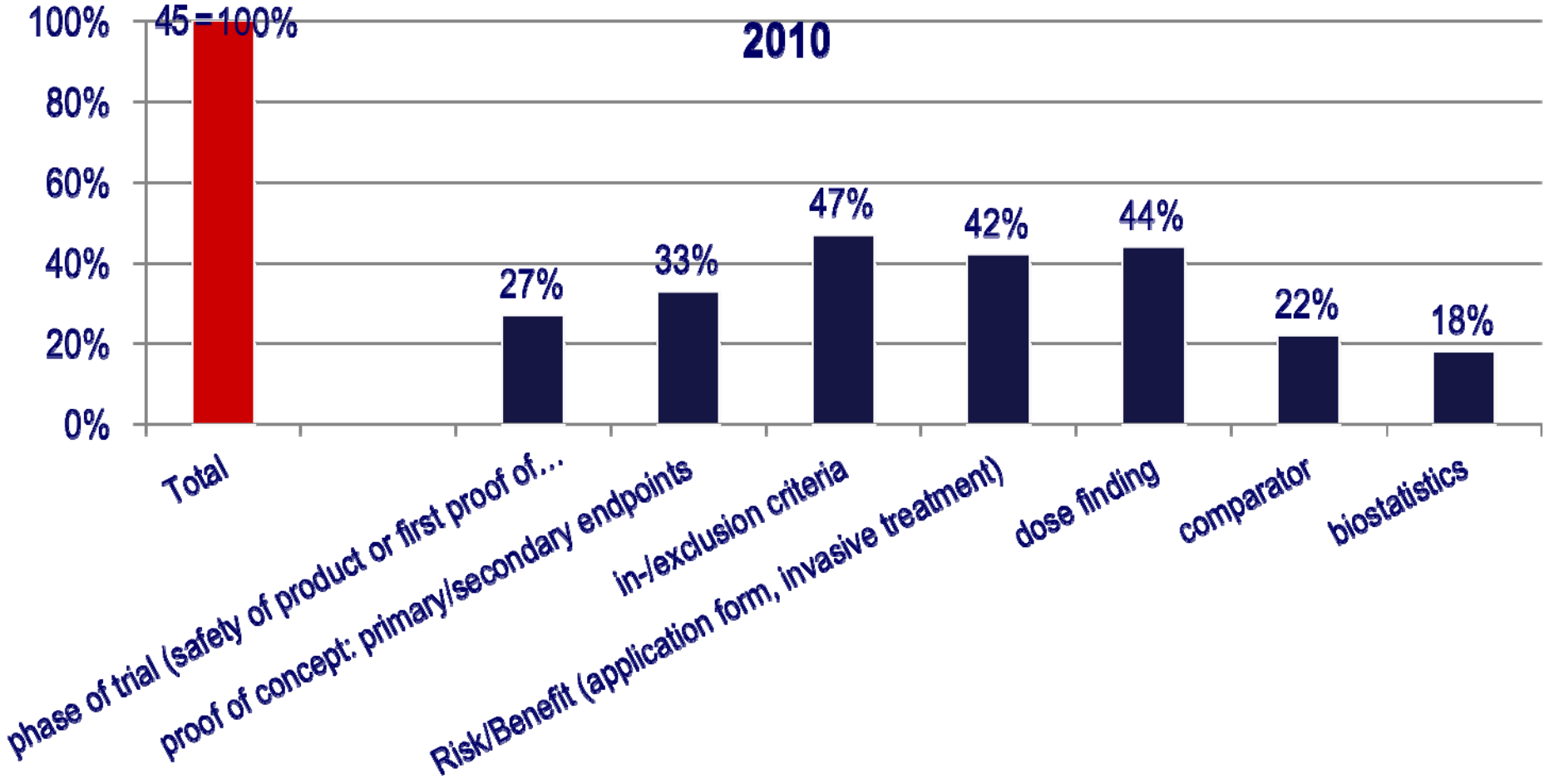
Details of advice: Quality



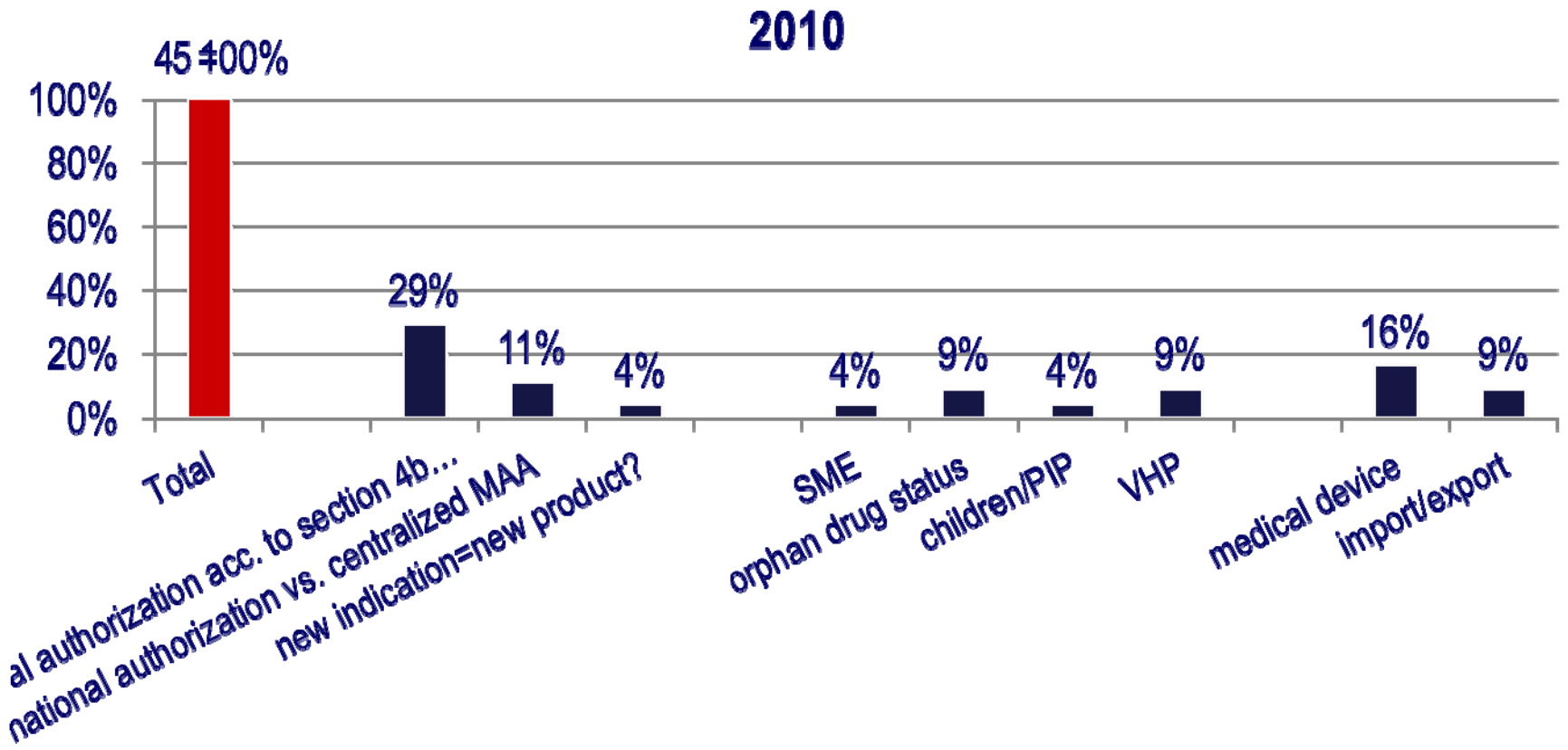
Details of advice: Non-clinic



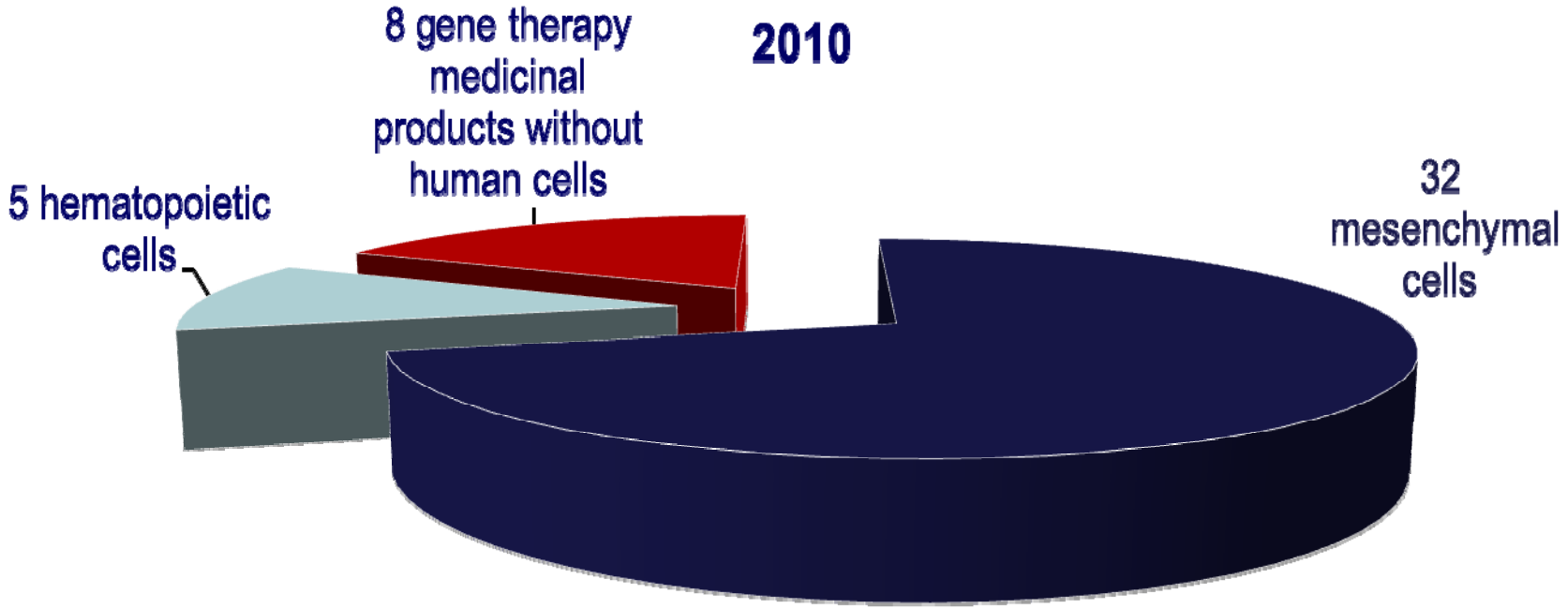
Details of advice: Clinic



Details of advice: Regulatory issues

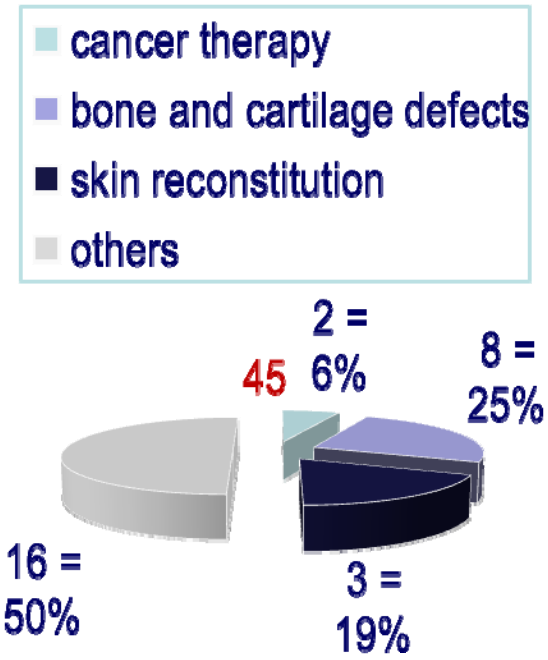


Advice with regard to product / type of cells

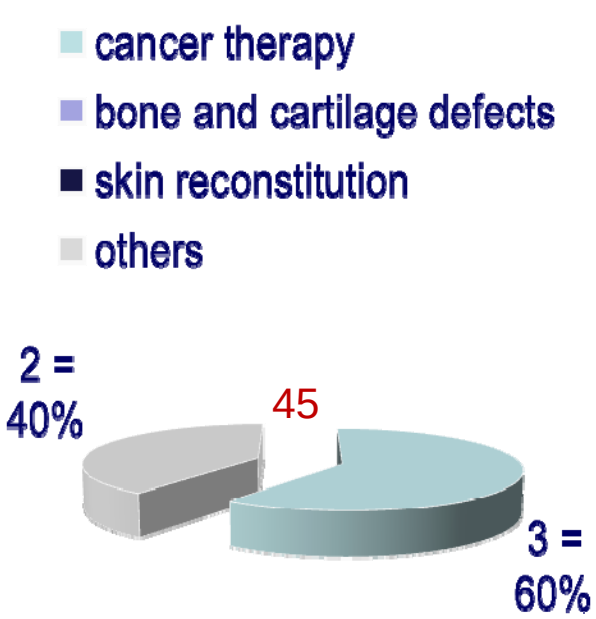


Advice:
Origin / Type of the cells with regard to indication

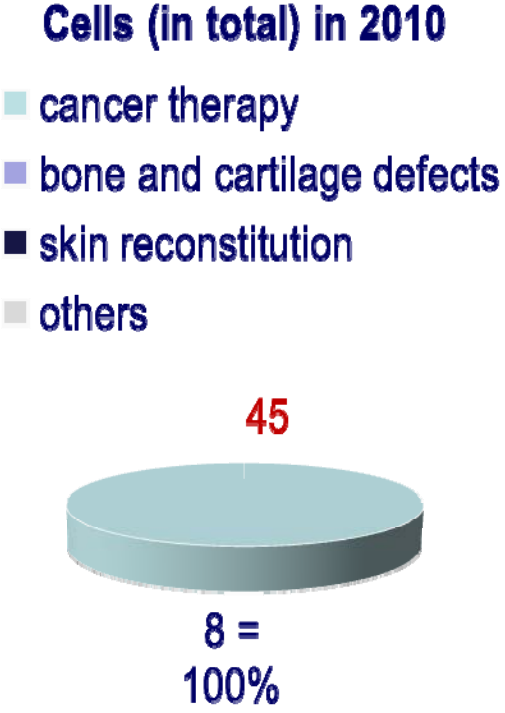
Mesenchymal Cells (in total) in 2010



Hematopoietic cells (in total) in 2010



Gene Therapy Medicinal Products without H. Cells (in total) in 2010

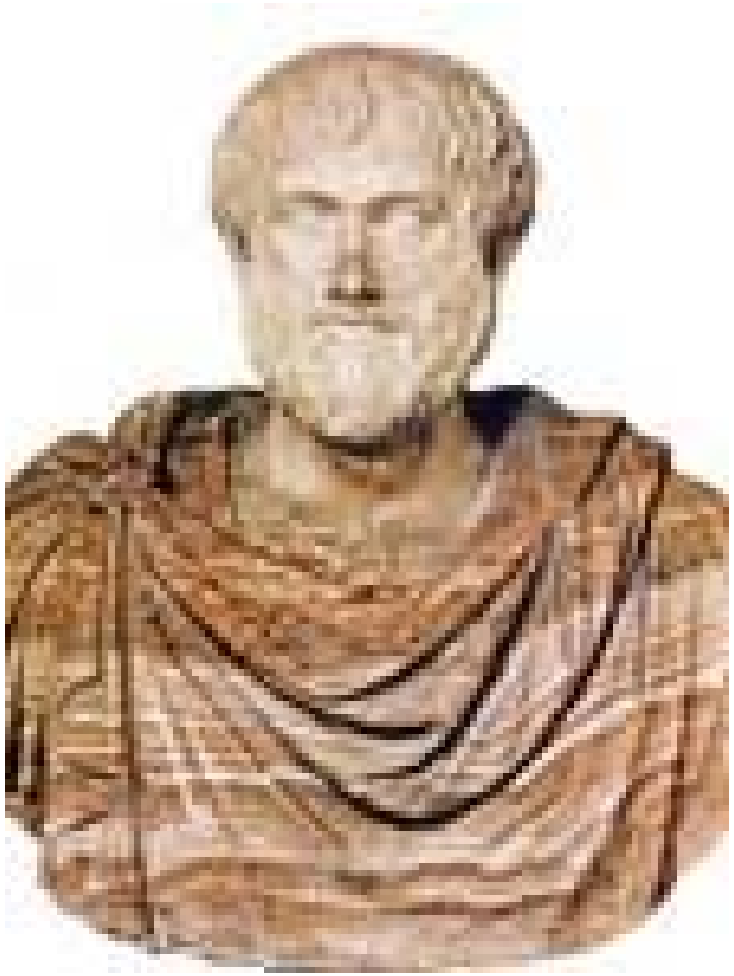


Future Projects

- Communication with and feedback from stakeholders
- Organisation of target group-specific workshops
- Organisation of ATMP group-specific workshops
- Special workshops on important topics, e.g. special development, bottlenecks
- Production and publication of regular printed and/or electronic newsletters, providing overviews of current scientific issues, developments and trends

Challenges

- Risk-based approach
- From VHP to HP
- Networks and inclusion of HTAs
- Harmonisation of reimbursement
- Joint advice
- Parallel advice



Der Anfang ist die Hälfte des Ganzen

Aristoteles

Passion is the only orator who can always convince us.

Contact

- Dr. Lotte Dahl — Tel. 06103/77-2131
- Athalia Müller, B.Sc. — Tel. 06103/77-1038
- Bettina Ziegele, M.A., Head — Tel: 06103/77-1012

E-mail: innovation@pei.de

For further information, please click on the following link.:

http://www.pei.de/cln_092/nn_154420/DE/infos/pu/innovationsbuero/innovationsbuero-inhalt.html?__nnn=true

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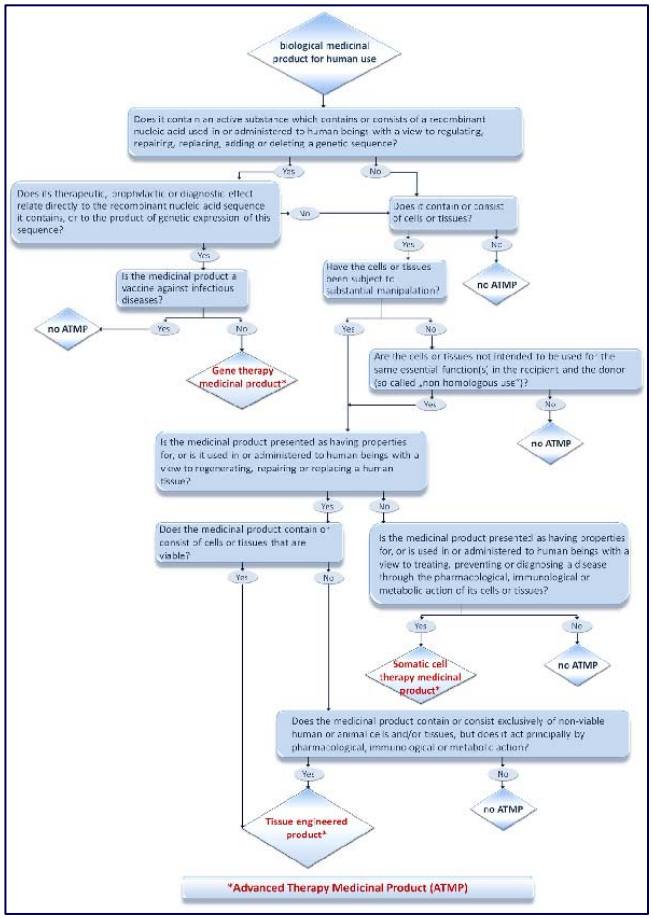
Thank you!

Bundesinstitut für Impfstoffe
und biomedizinische Arzneimittel

Decision Tree for ATMP



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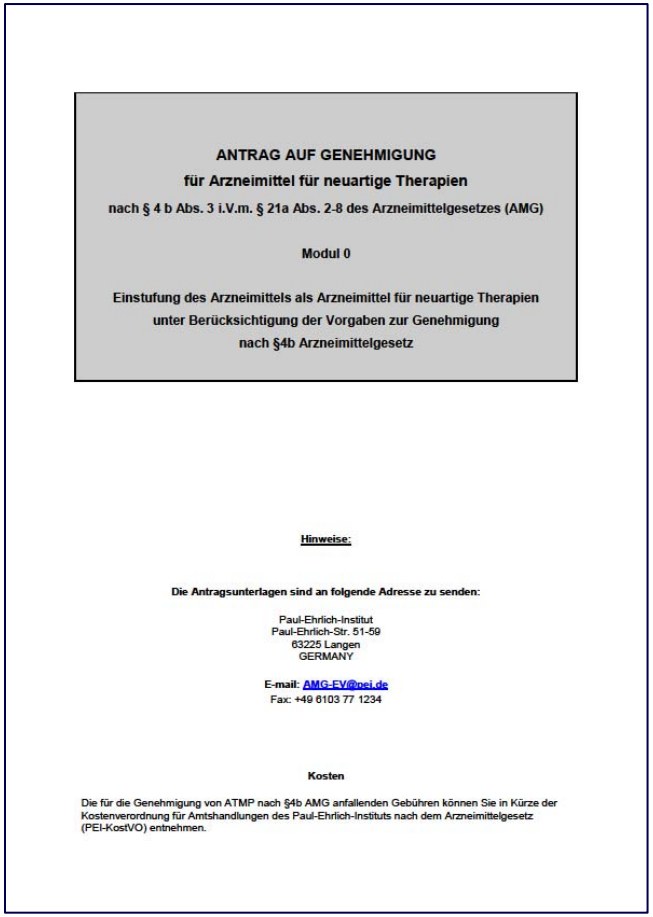
Guide for Application: Module 0



ANTRAG AUF GENEHMIGUNG
für Arzneimittel für neuartige Therapien
nach § 4 b Abs. 3 i.V.m. § 21a Abs. 2-8 des Arzneimittelgesetzes (AMG)

Modul 0

Einstufung des Arzneimittels als Arzneimittel für neuartige Therapien
unter Berücksichtigung der Vorgaben zur Genehmigung
nach §4b Arzneimittelgesetz

Hinweise:

Die Antragsunterlagen sind an folgende Adresse zu senden:

Paul-Ehrlich-Institut
Paul-Ehrlich-Str. 51-59
63225 Langen
GERMANY

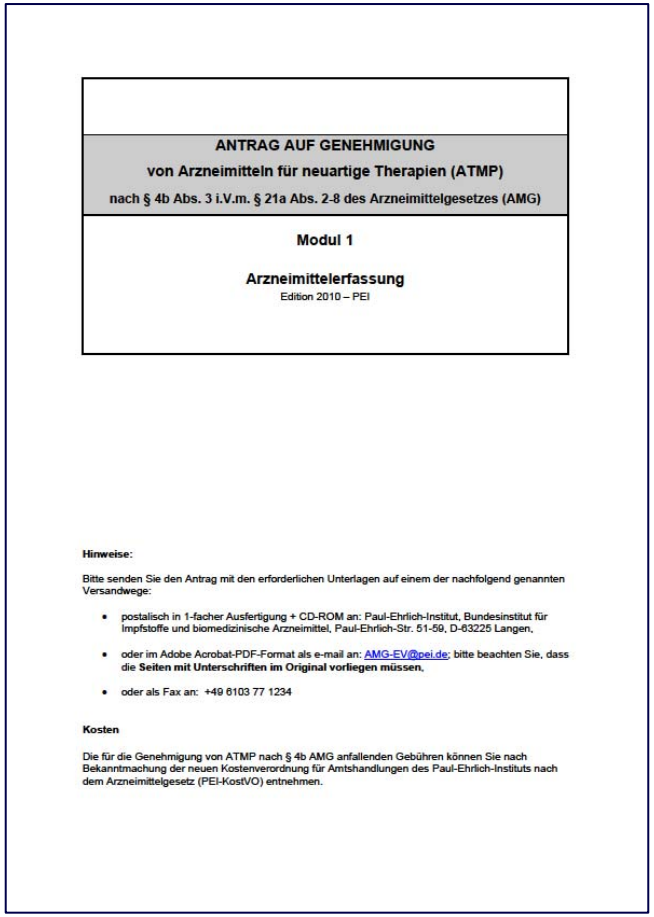
E-mail: AMG-EV@pei.de
Fax: +49 6103 77 1234

Kosten

Die für die Genehmigung von ATMP nach §4b AMG anfallenden Gebühren können Sie in Kürze der Kostenverordnung für Amtshandlungen des Paul-Ehrlich-Instituts nach dem Arzneimittelgesetz (PEI-KostVO) entnehmen.

http://www.pei.de/cln_170/nn_1946116/SharedDocs/Downloads/pu/innovationsbuero/modul-0-formulare,templateId=raw,property=publicationFile.pdf/modul-0-formulare.pdf

Guide for Application: Module 1



ANTRAG AUF GENEHMIGUNG
von Arzneimitteln für neuartige Therapien (ATMP)
nach § 4b Abs. 3 i.V.m. § 21a Abs. 2-8 des Arzneimittelgesetzes (AMG)

Modul 1

Arzneimittelerfassung
Edition 2010 – PEI

Hinweise:

Bitte senden Sie den Antrag mit den erforderlichen Unterlagen auf einem der nachfolgend genannten Versandwege:

- postalisch in 1-facher Ausfertigung + CD-ROM an: Paul-Ehrlich-Institut, Bundesinstitut für Impfstoffe und biomedizinische Arzneimittel, Paul-Ehrlich-Str. 51-59, D-63225 Langen,
- oder im Adobe Acrobat-PDF-Format als e-mail an: AMG-EV@pei.de; bitte beachten Sie, dass die **Seiten mit Unterschriften im Original vorliegen müssen**,
- oder als Fax an: +49 6103 77 1234

Kosten

Die für die Genehmigung von ATMP nach § 4b AMG anfallenden Gebühren können Sie nach Bekanntmachung der neuen Kostenverordnung für Amtshandlungen des Paul-Ehrlich-Instituts nach dem Arzneimittelgesetz (PEI-KostVO) entnehmen.

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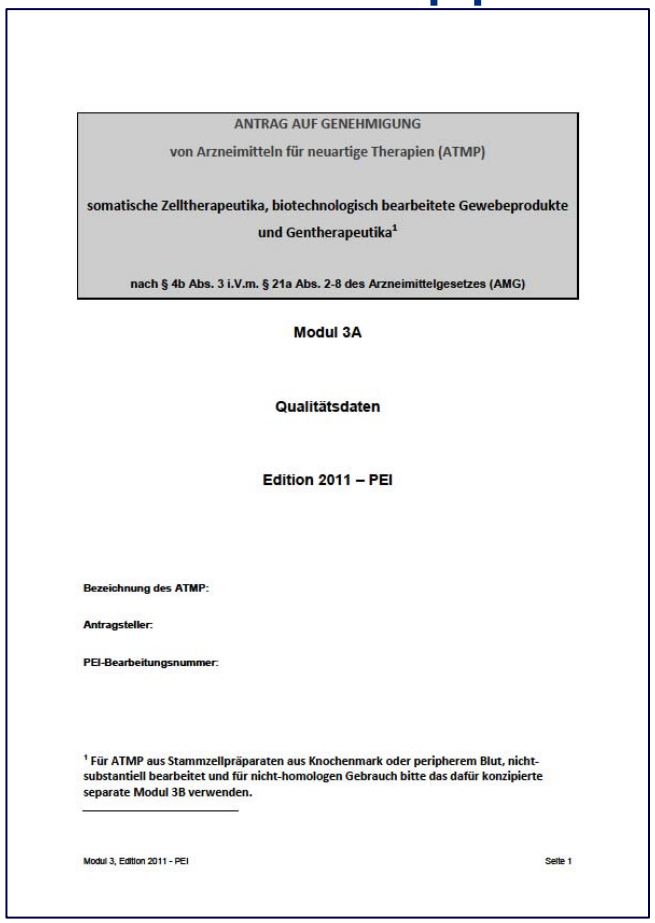
Guide for Application: Modules 3A + 3B



ANTRAG AUF GENEHMIGUNG

von Arzneimitteln für neuartige Therapien (ATMP)

somatische Zelltherapeutika, biotechnologisch bearbeitete Gewebeprodukte und Gentherapeutika[1]

nach § 4b Abs. 3 i.V.m. § 21a Abs. 2-8 des Arzneimittelgesetzes (AMG)

Modul 3A

Qualitätsdaten

Edition 2011 – PEI

Bezeichnung des ATMP:

Antragsteller:

PEI-Bearbeitungsnummer:

[1] Für ATMP aus Stammzellpräparaten aus Knochenmark oder peripherem Blut, nicht-substantiell bearbeitet und für nicht-homologen Gebrauch bitte das dafür konzipierte separate Modul 3B verwenden.

Modul 3, Edition 2011 - PEI Seite 1

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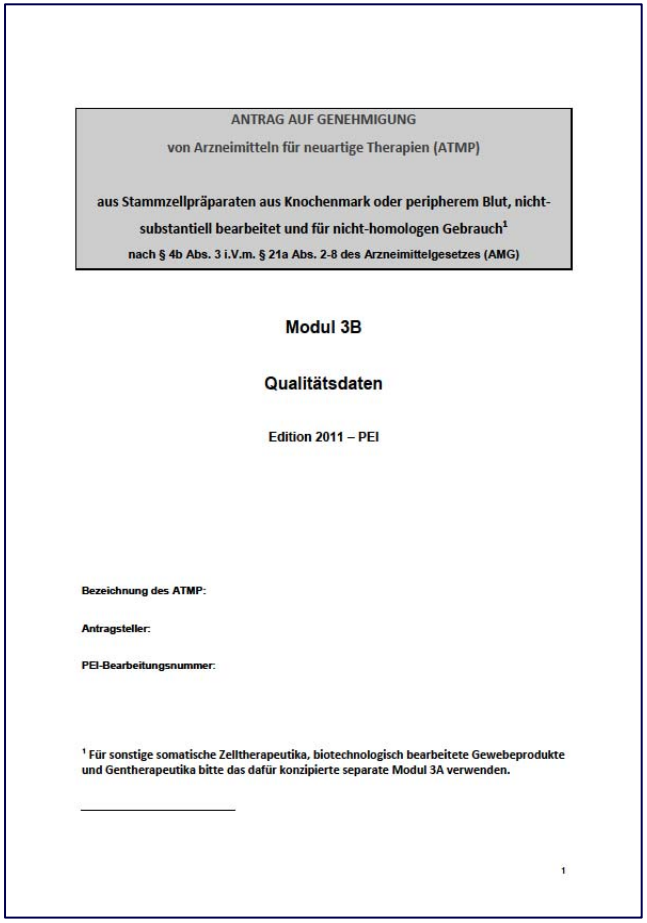


ANTRAG AUF GENEHMIGUNG

von Arzneimitteln für neuartige Therapien (ATMP)

aus Stammzellpräparaten aus Knochenmark oder peripherem Blut, nicht-substantiell bearbeitet und für nicht-homologen Gebrauch[1]

nach § 4b Abs. 3 i.V.m. § 21a Abs. 2-8 des Arzneimittelgesetzes (AMG)

Modul 3B

Qualitätsdaten

Edition 2011 – PEI

Bezeichnung des ATMP:

Antragsteller:

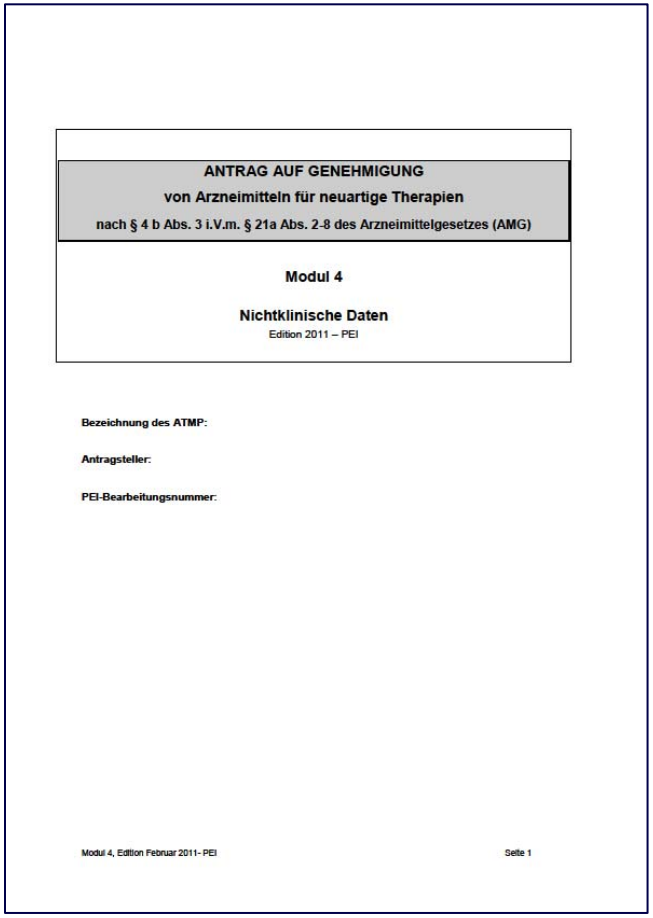
PEI-Bearbeitungsnummer:

[1] Für sonstige somatische Zelltherapeutika, biotechnologisch bearbeitete Gewebeprodukte und Gentherapeutika bitte das dafür konzipierte separate Modul 3A verwenden.

1

http://www.pei.de/cln_170/nn_1946116/SharedDocs/Downloads/pu/innovationsbuero/modul-3b-qualitaetsdaten,templateId=raw,property=publicationFile.doc/modul-3b-qualitaetsdaten.doc

Guide for Application: Module 4



ANTRAG AUF GENEHMIGUNG
von Arzneimitteln für neuartige Therapien
nach § 4 b Abs. 3 i.V.m. § 21a Abs. 2-8 des Arzneimittelgesetzes (AMG)

Modul 4

Nichtklinische Daten
Edition 2011 – PEI

Bezeichnung des ATMP:

Antragsteller:

PEI-Bearbeitungsnummer:

Modul 4, Edition Februar 2011- PEI Seite 1

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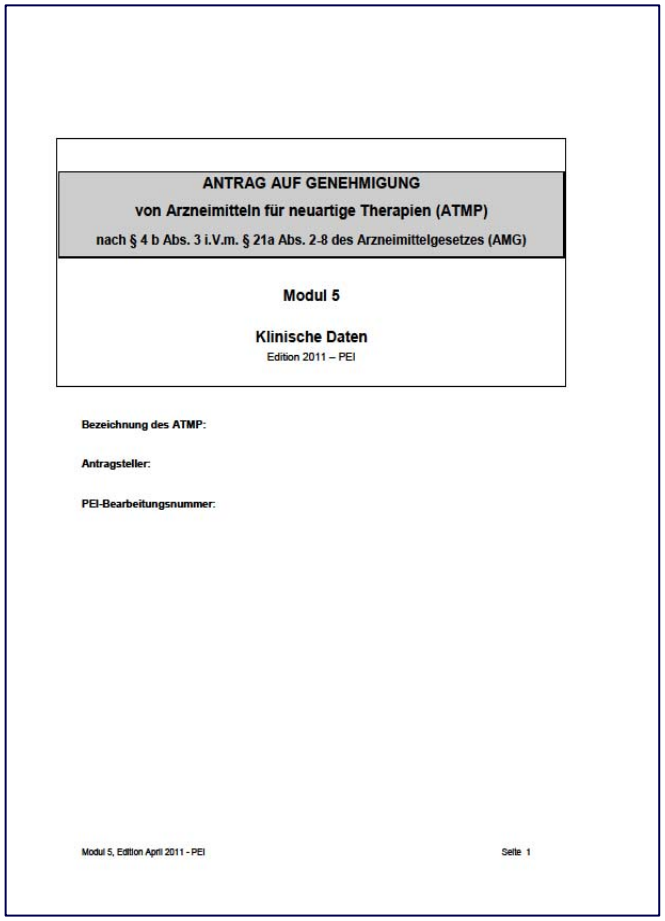
Guide for Application: Module 5



ANTRAG AUF GENEHMIGUNG
von Arzneimitteln für neuartige Therapien (ATMP)
nach § 4 b Abs. 3 i.V.m. § 21a Abs. 2-8 des Arzneimittelgesetzes (AMG)

Modul 5

Klinische Daten
Edition 2011 – PEI

Bezeichnung des ATMP:

Antragsteller:

PEI-Bearbeitungsnummer:

Modul 5, Edition April 2011 - PEI Seite 1

http://www.pei.de/cln_170/nn_1946116/SharedDocs/Downloads/pu/innovationsbuero/modul-5-klinische_20daten,templateId=raw,property=publicationFile.pdf/modul-5-klinische%20daten.pdf