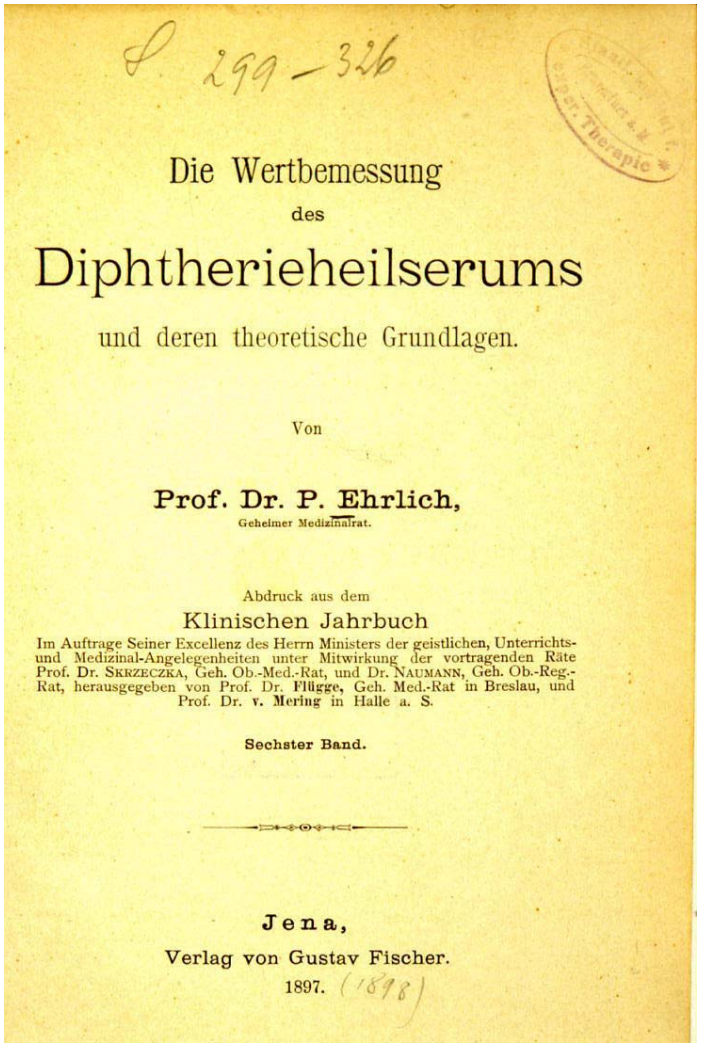
The Paul Ehrlich Institute - Centre of Excellence for Vaccines, Blood Products and Emerging Therapies

Johannes Löwer
and co-workers

8th DGRA Annual Congress
Bonn, 9 and 10 May 2006

www.pei.de **PEI**

Paul Ehrlich 1896



S. 299–326

Die Wertbemessung

des

Diphtherieheilserums

und deren theoretische Grundlagen.

Von

Prof. Dr. P. Ehrlich,

Geheimer Medizinalrat.

Abdruck aus dem

Klinischen Jahrbuch

Im Auftrage Seiner Excellenz des Herrn Ministers der geistlichen, Unterrichts- und Medizinal-Angelegenheiten unter Mitwirkung der vortragenden Räte Prof. Dr. Skrzeczka, Geh. Ob.-Med.-Rat, und Dr. Naumann, Geh. Ob.-Reg.-Rat, herausgegeben von Prof. Dr. **Flügge**, Geh. Med.-Rat in Breslau, und Prof. Dr. **v. Mering** in Halle a. S.

Sechster Band.

Jena,

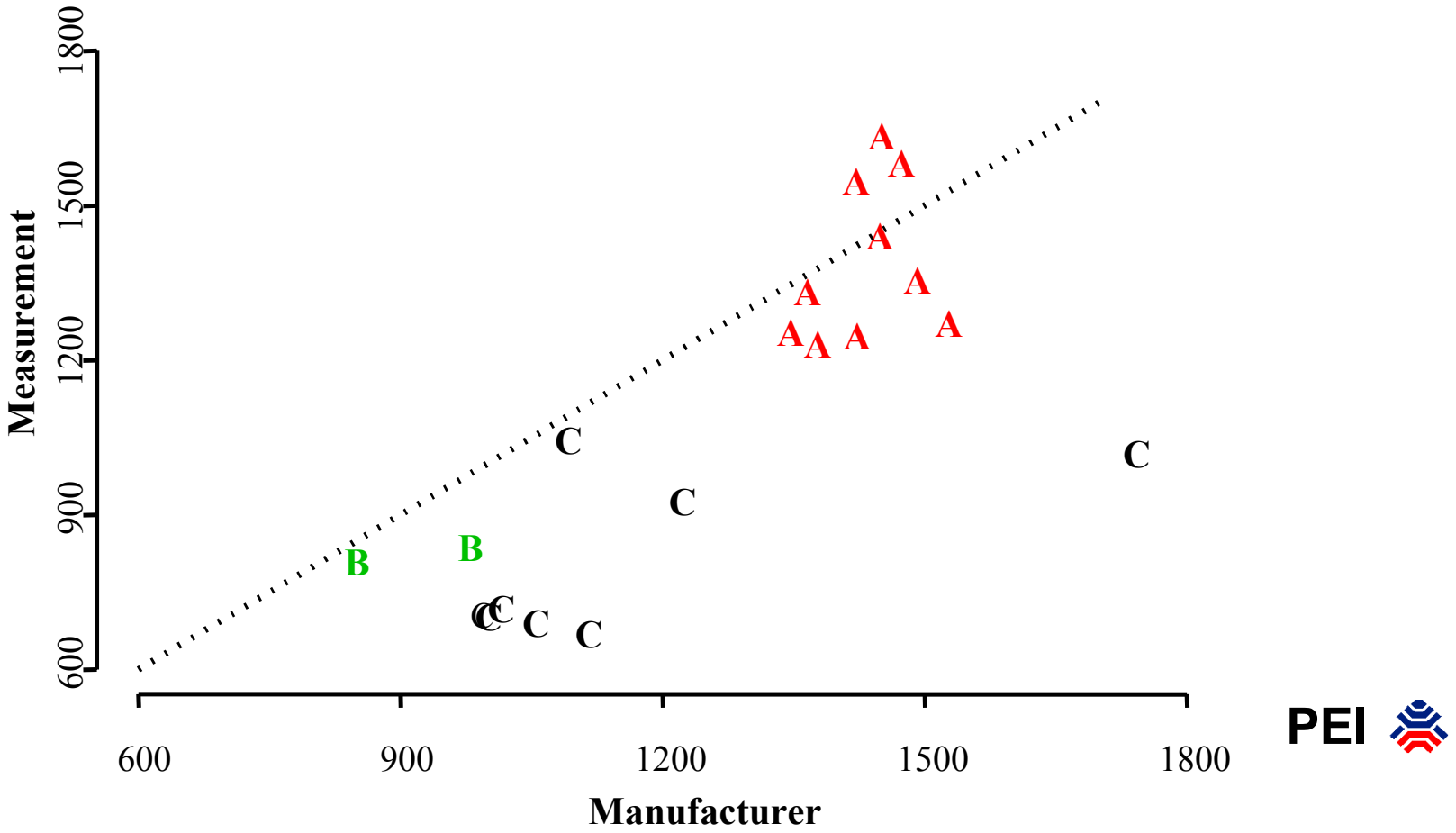
Verlag von Gustav Fischer.

1897. (1898)

PEI

Potency of Anti-D Immunoglobulin

Correlation between PEI's and Manufacturer's Results



History

1896 Institute for Serum Research and Serum Examination, Berlin-Steglitz

1899 Royal Institute for Experimental Therapy, Frankfurt/Main

1947 Paul-Ehrlich-Institut - State Institute for Experimental Therapy, Frankfurt/Main

1972 Paul-Ehrlich-Institut, Federal Agency for Sera and Vaccines, Frankfurt/Main

1990 Paul-Ehrlich-Institut, Federal Agency for Sera and Vaccines, Langen/Hessen

PEI

PEI: Areas of Responsibility

- Vaccines (human, veterinary)
- Sera, immunoglobulins, monoclonal antibodies
- Allergens (diagnostic, therapeutic)
- Blood products (plasma derived, recombinant)
- Blood components for transfusion
- Gene transfer products
- Cell therapy products (somatic, xenogeneic)
- Tissues
- (Engineered tissues)

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PEI: Duties

- Official batch release
- Authorisation of medicinal products
- Scientific advice
- Pharmakovigilance
- Expert support for inspections
- Permission of clinical studies
- Experimental research
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Sequence of the Evaluation of an Application

- Appointment of the rapporteur by the CHMP
- Appointment of the leading unit at the PEI

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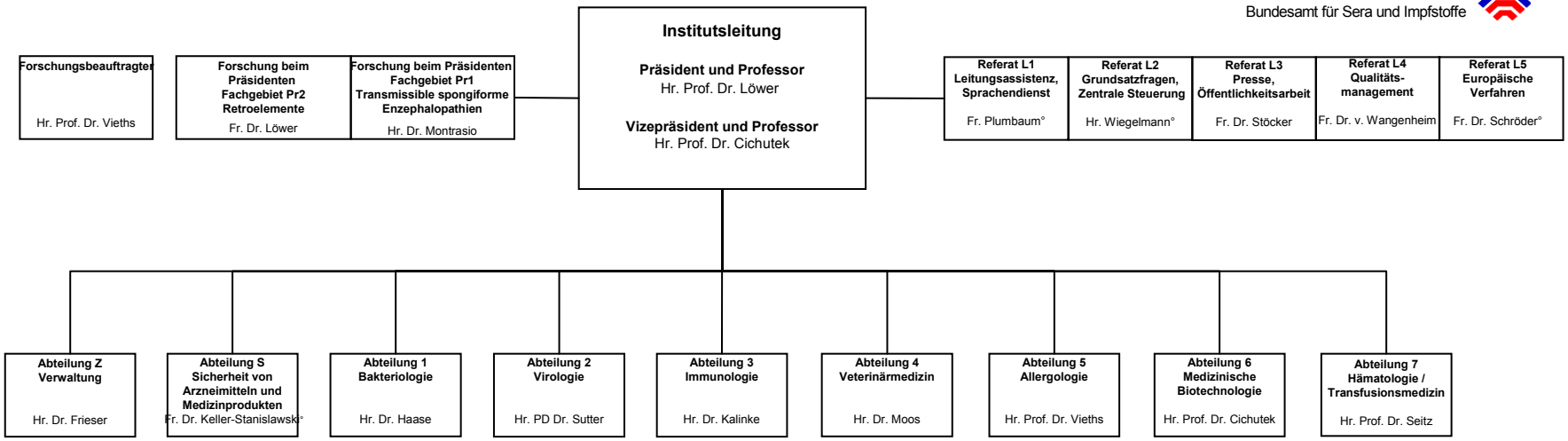
Paul-Ehrlich-Institut
Bundesamt für Sera und Impfstoffe



Div. 1 Bacteriology
Div. 2 Virology
Div. 3 Immunology
Div. 4 Veterinary medicine
Div. 5 Allergology
Div. 6 Medicinal Biotechnology
Div. 7 Hematology/Transfusion medicine

Div. S Safety of medicinal products and medical devices

Div. Z Administration

PEI

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- Appointment of the expert team

PEI

Paul-Ehrlich-Institut
Bundesamt für Sera und Impfstoffe

Forschungsbeauftragter
Hr. Prof. Dr. Vieths

Forschung beim Präsidenten Fachgebiet Pr2 Retroelemente
Fr. Dr. Löwer

Forschung beim Präsidenten Fachgebiet Pr1 Transmissible spongiforme Enzephalopathien
Hr. Dr. Montrasio

Institutsleitung

Präsident und Professor
Hr. Prof. Dr. Löwer

Vizepräsident und Professor
Hr. Prof. Dr. Cichutek

Referat L1 Leitungsassistenz, Sprachendienst
Fr. Plumbaum°

Referat L2 Grundsatzfragen, Zentrale Steuerung
Hr. Wiegelmann°

Referat L3 Presse, Öffentlichkeitsarbeit
Fr. Dr. Stöcker

Referat L4 Qualitäts-management
Fr. Dr. v. Wangenheim

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Fr. Dr. Schröder°

Prüflabor für IVD PEI-IVD
Fr. Dr. S. Nick

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Referat Z4 Technik Hr. Pieschner-v. Meltzer	**Referat S4 Rechtsangelegenheiten** Fr. Ruoff°	**Fachgebiet 1/4 Biostatistik** Hr. Dr. Volkers	**Fachgebiet 2/4 Molekulare Pathologie** Hr. Dr. Nübling	**Fachgebiet 3/4 Tumorimpfstoffe, Zellbank, Medien** Hr. Frieling	**Fachgebiet ZT Zentrale Tierhaltung** Hr. Dr. Plesker	**Fachgebiet 5/4 Entwicklung und Standardisierung** Hr. Dr. Scheurer*	**Fachgebiet 6/4 Xenogene Zelltherapeutika** Hr. PD Dr. Tönjes	**Fachgebiet 7/4 Transfusionsmedizin** Fr. Dr. Heiden
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Referat Z6 Arbeitsschutz, Genehmigungen Fr. Dr. Pfitzner*								

External expert

Personalrat Vorsitzende	**Gleichstellungs-beauftragte**	**Schwerbehinderten-vertrauensfrau**	**Jugend- und Auszubildenden-vertretung**
Fr. Gravelius	Fr. Dr. Krämer	Fr. Grote	Fr. Zitzmann

*mit der Wahrnehmung der Geschäfte beauftragt
° für die Wahrnehmung der Geschäfte vorgesehen
——— Dienst- und Fachaufsicht
- - - - Dienstaufsicht

Wissenschaftliche Nachwuchsgruppen
(NG) Sprecher: N.N.

NG1 Neue Impfstoffstrategien	**NG2 Bioinformatik**	**NG3 Zelldifferenzierung**	**NG4**	**NG5**
N.N.	N.N.	N.N.	N.N.	N.N.

Sequence of the Evaluation of an Application

- Appointment of the rapporteur by the CHMP
- Appointment of the leading unit at the PEI
- Appointment of the expert team
- Evaluation
- Review by the PEI Peer Review Group (Manfred Haase's idea!)

PEI

Good Regulatory Practice (GRP) in the PEI Peer Review Group

Members:

- Experienced scientists not involved in the evaluation of the product in question

Aim:

- To widen the scientific basis of the decisions made by the assessors
- To assist in the decision on critical issues
- To provide access to the “regulatory memory”

Involvement:

- Obligatory in centralised and decentralised procedures and in the co-ordination of “Scientific Advice”

PEI

Sequence of the Evaluation of an Application

- Appointment of the rapporteur by the CHMP
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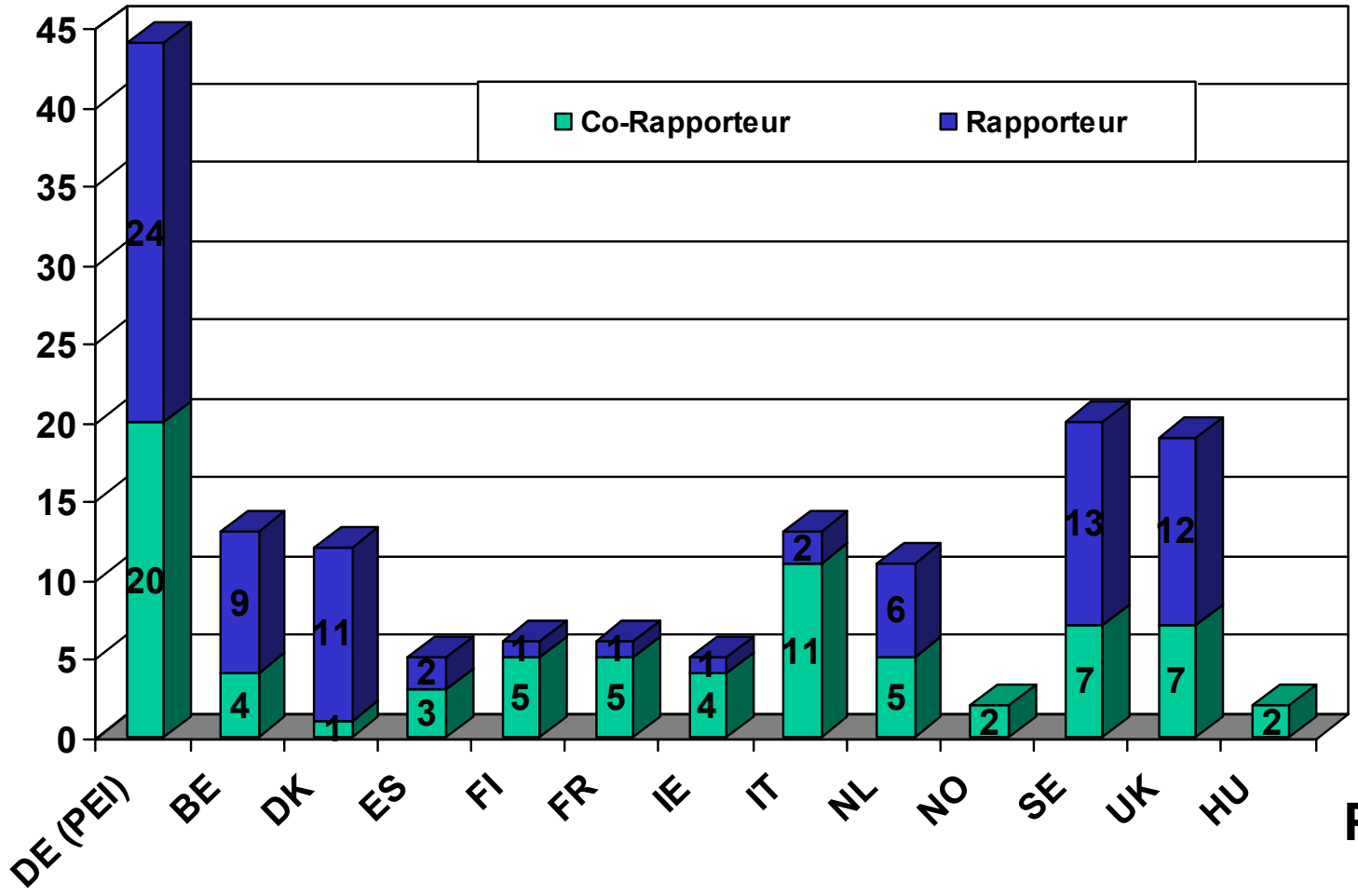
- Finalization of the assessment report
- Support to the CHMP member (Manfred Haase)

PEI

European Procedures for Products in PEI‘s Remit

(until 31 December 2005)

Distribution of (Co-)rapporteurships [Hum]

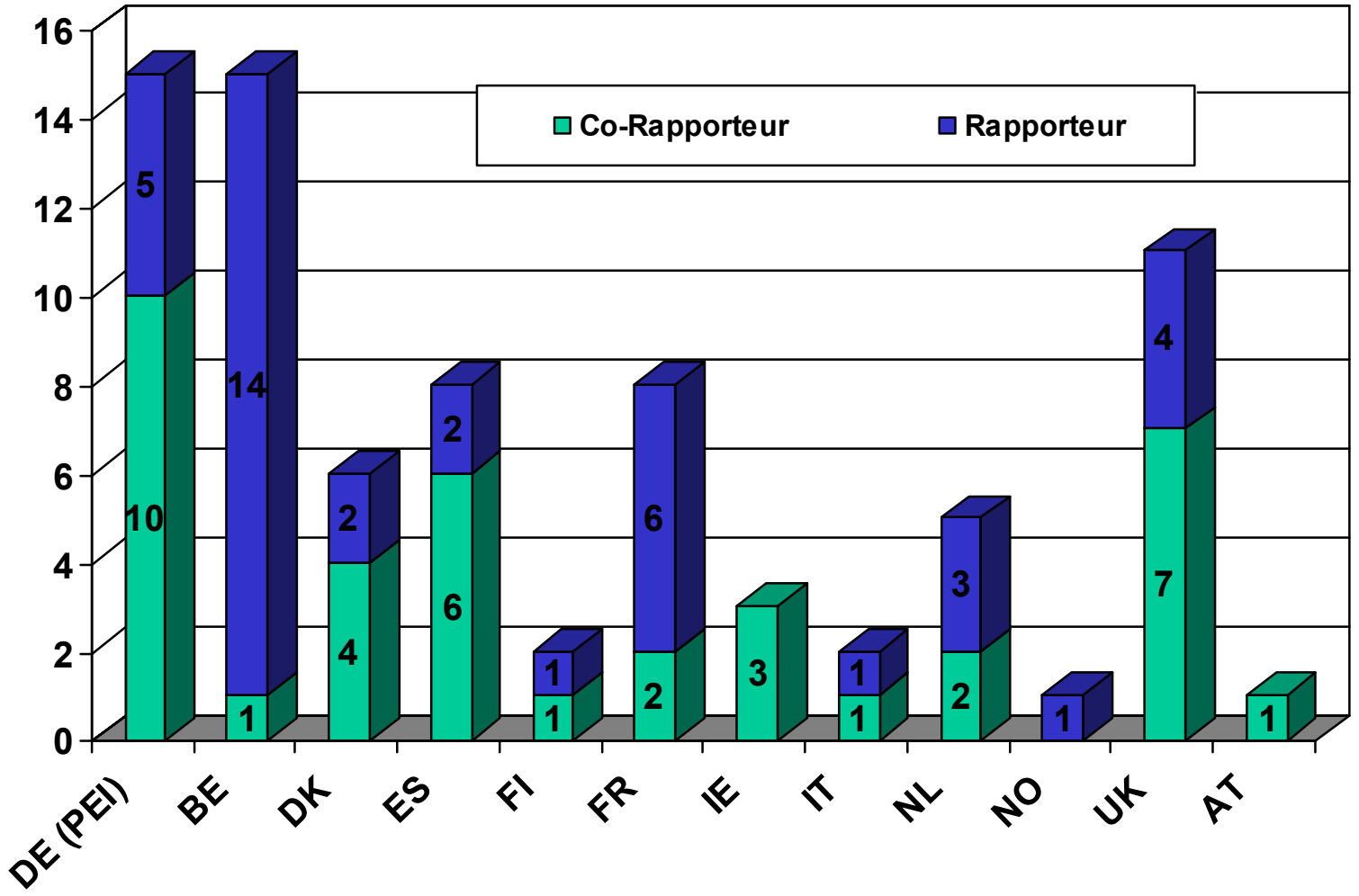


PEI

European Procedures for Products in PEI‘s Remit

(until 31 December 2005)

Distribution of (Co-)rapporteurships [Vet]



PEI

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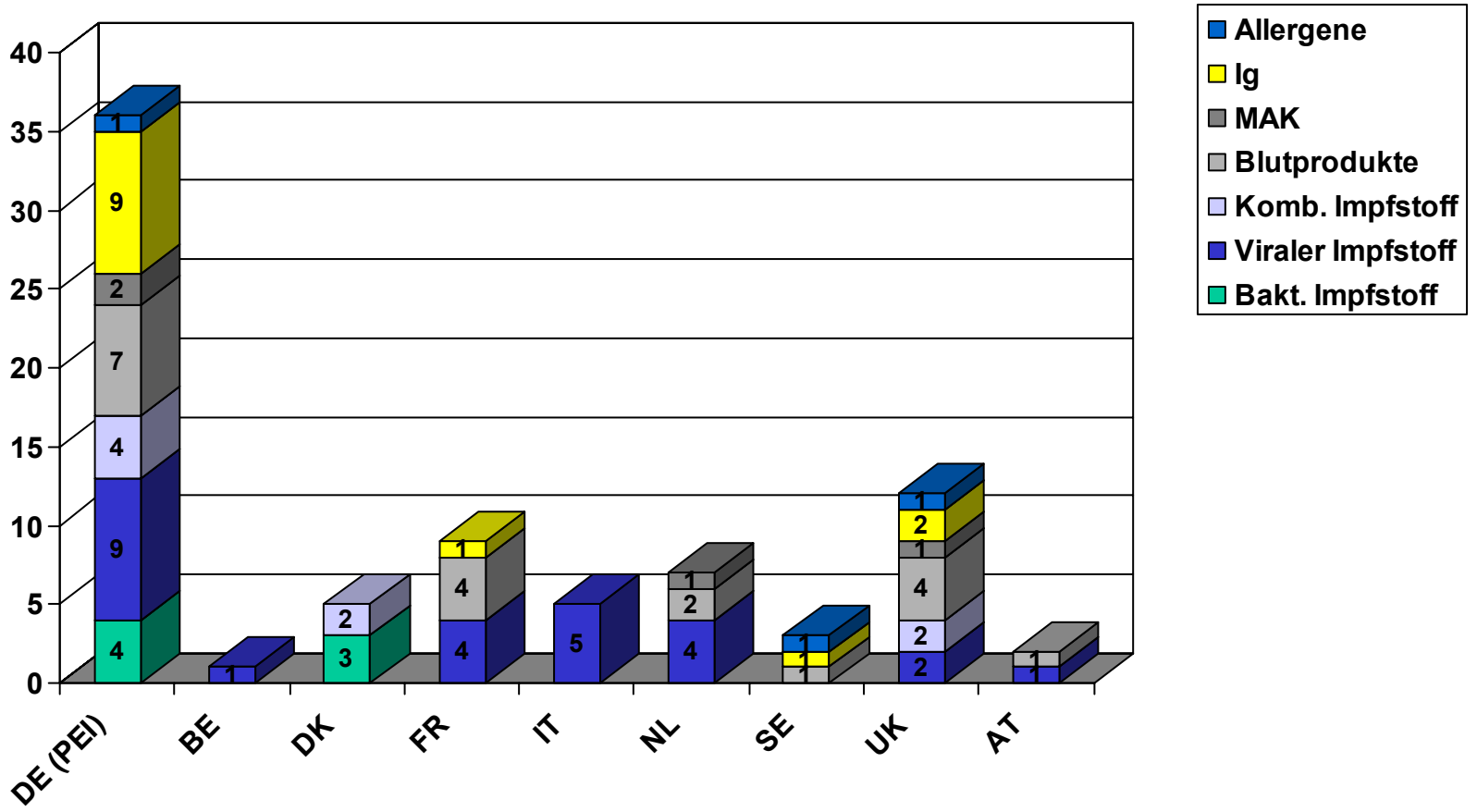
(until 31 December 2005)

Distribution of RMSs with Germany involved [Hum]



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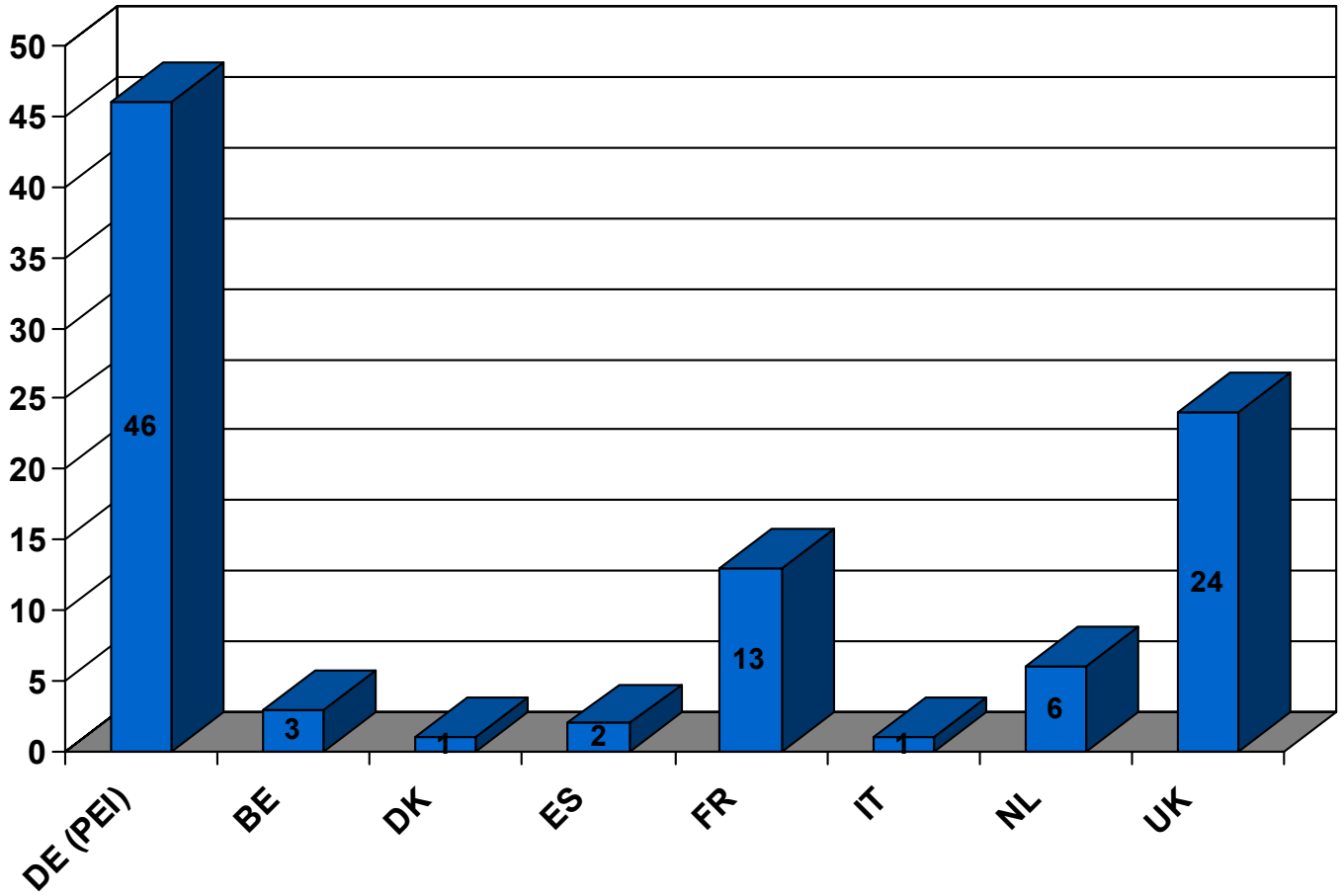

PEI

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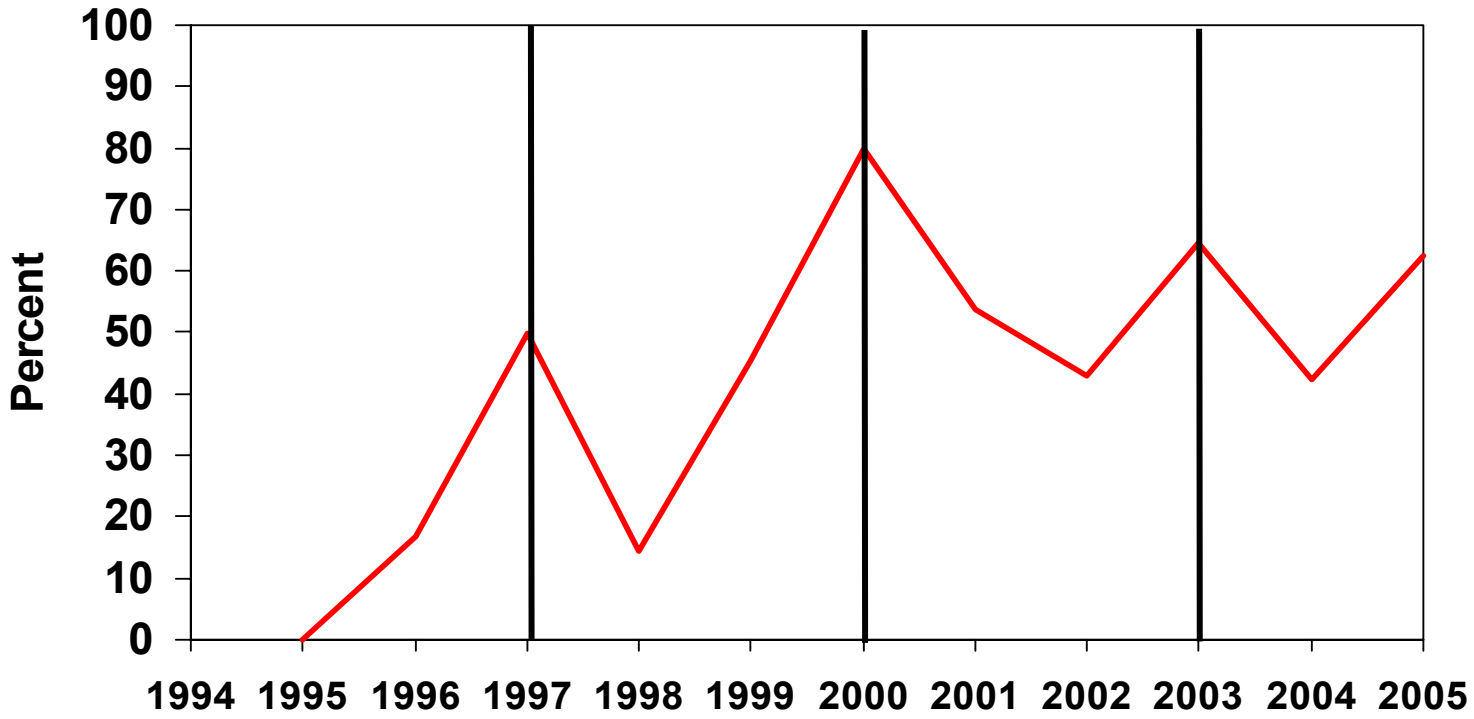
Scientific Advice [Hum] for Biological Products Co-ordination by PEI (in Percent)



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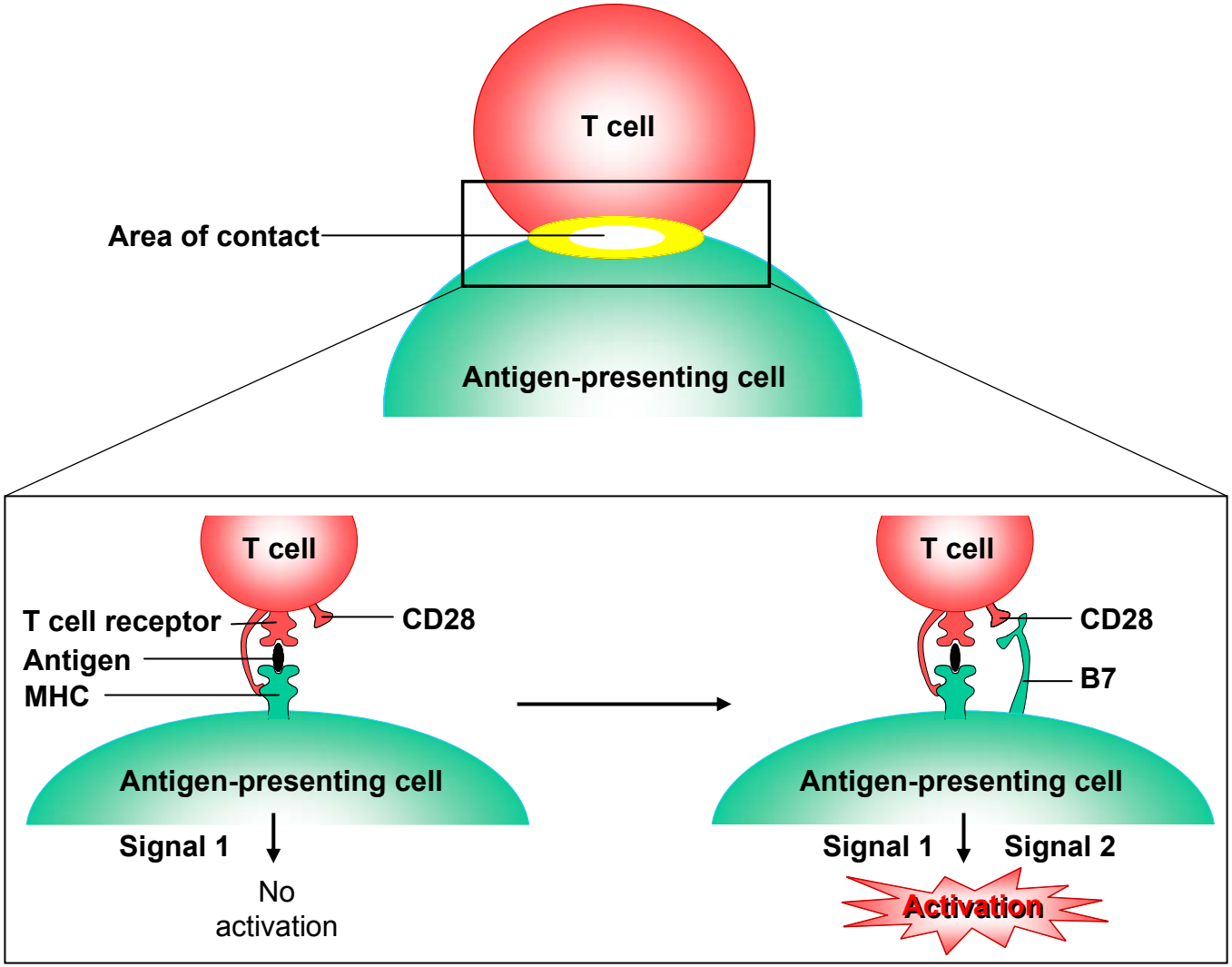
PEI

TGN 1412: αCD28 mAb



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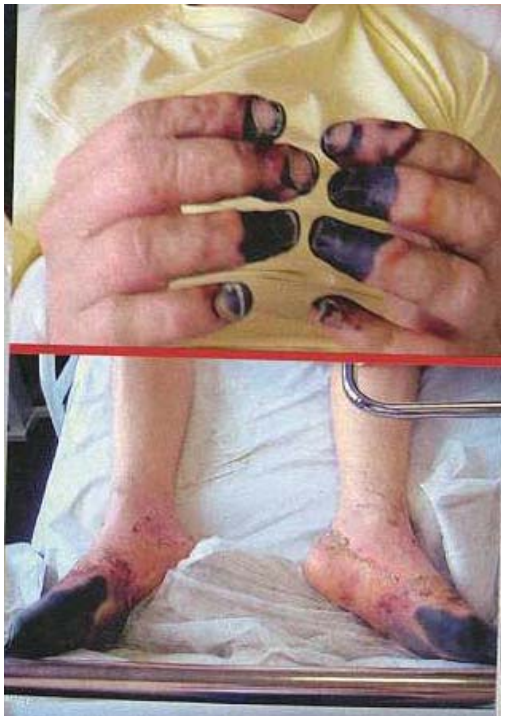
TGN 1412: Adverse Events

- Treatment of 8 volunteers (6 verum, 2 placebo) during two hours
- Adverse events (cytokine release syndrome) occurred 40 to 90 min after administration



stern no. 17, 20.04.2006

PEI

TGN 1412: Consequences

Introduction of a phase 0 for some mAbs (low dose, single volunteers, interval of 1 or 2 days)

- Criterion 1
  The mAb employs a new mechanism of action.
  - mAbs interfering with 'master switches' of the immune system, such as CD28 or CTLA-4
  - mAbs that act as inducers and/or modulators of pleiotropic cytokines (e.g. IFN-γ, IFN-α, IL-10)
- Criterion 2
  The mAb addresses a target that lacks appropriate animal models.
  - binding (sub)epitopes that are present only in humans
  - mAbs for which no surrogate model exists
  - mAbs interfering with signaling pathways that show human-specific properties
- Criterion 3
  The mAb comprises a new type of engineered structural format
  - engineered Fc parts
  - divalent antibodies and other new constructs

Schneider; C., Kalinke, U., Löwer, J. Nature Biotechnology, May 2006

PEI

TGN 1412: Consequences

Development of pre-clinical *in vitro* and *in vivo* tests with a higher predictive value

- *In vitro*
  - Cytokine release of human PMBC stimulated in vitro
  - Stimulation of T cell subsets as measured by FACS
- *In vivo*
  - Comparison of the response in non-human primates and in irradiated mice reconstituted with the human adaptive immune system

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PEI

Major Research Areas

- Safety of Biological and Biotechnology Medicines
- New Test Methods
- Pathogenesis of Prion Diseases and Viral Infections
- Viral Gene Transfer and Cell Therapy
- Immunobiology of Allergens

PEI

Research Grants in 2003

DFG:	7
BMGS:	4
BMBF:	4
EU:	9
DLR:	2
Others:	5
Sum:	31
Total amount:	2.081.786 €

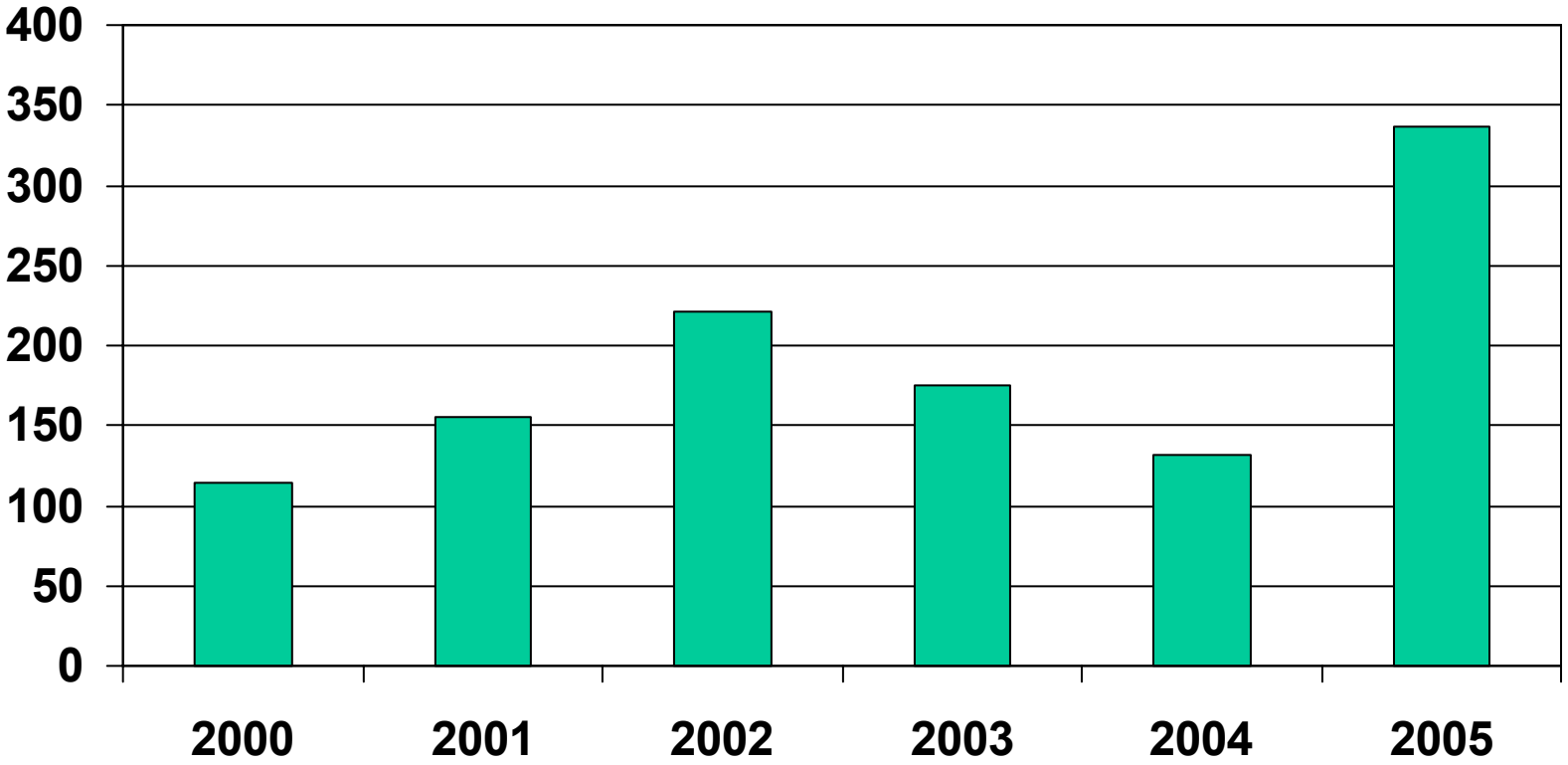
PEI

Research Grants in 2004

DFG:	8
BMGS:	5
BMBF:	4
EU:	9
DLR:	2
Others:	6
Sum:	34
Total amount:	2.248.927 €

PEI

Journal Impact Factors of PEI Publications



PEI

PEI

Thanks to all
PEI employees

PEI