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
Die Wertbemessung
des Diphtherieheilserums
und deren theoretische Grundlagen.

Von

Prof. Dr. P. Ehrlich,
Geburtsdatum unbekannt.

Abdruck aus dem Klinischen Jahrbuch
Im Auftrage Seiner Excellenz des Herrn Ministers der geistlichen, Unterrichts-
und Medizinal-Angelegenheiten einer Mitwirkung der vongezogenen Klinisch-
Prof. Dr. Sauerbruch, geb. Med.-Hut., und Dr. Naudin, geb. Med.-Reg.-
Hut., herausgegeben von Prof. Dr. Pfeiffer, Leb. Med.-Hut. in Halle, und
Prof. Dr. F. Werling in Halle a. S.

Jena,
Verlag von Gustav Fischer.
1895 (1895)
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: 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
- Advice to government
- 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
Institutsleitung
Präsident und Professor
Hr. Prof. Dr. Löwer
Vizepräsident und Professor
Hr. Prof. Dr. Cichutek

Referat L1
Leitungsassistenten, Sprechendienst
Fr. Plumbaum

Referat L2
Grundsatzfragen, Zentrale Steuerung
Hr. Wiegelmann

Referat L3
Presse, Öffentlichkeitsarbeit
Fr. Dr. Stöcker

Referat L4
Qualitätsmanagement
Fr. Dr. v. Wangenheim

Referat L5
Europäische Verfahren
Fr. Dr. Schröder

Abteilung 1
Bakteriologie
Hr. Dr. Haase

Abteilung 2
Virologie
Hr. PD Dr. Sutter

Abteilung 3
Immunologie
Hr. Dr. Kalinke

Abteilung 4
Veterinärmedizin
Hr. Dr. Moos

Abteilung 5
Allergologie
Hr. Prof. Dr. Vieths

Abteilung 6
Medizinische Biotechnologie
Hr. Prof. Dr. Cichutek

Abteilung 7
Hämatologie/Transfusionsmedizin
Hr. Prof. Dr. Seitz

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
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• Appointment of the expert team
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- Evaluation
- Review by the PEI Peer Review Group
  (Manfred Haase’s idea!)
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”
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
• Finalization of the assessment report
• Support to the CHMP member (Manfred Haase)
European Procedures for Products in PEI‘s Remit
(until 31 December 2005)
Distribution of (Co-)rapporteurships [Hum]
European Procedures for Products in PEI‘s Remit
(until 31 December 2005)
Distribution of (Co-)rapporteurships [Vet]
European Procedures for Products in PEI‘s Remit
(until 31 December 2005)
Distribution of RMSs with Germany involved [Hum]
European Procedures for Products in PEI’s Remit
(uptil 31 December 2005)
Distribution of RMSs with Germany involved [Vet]
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Scientific Advice [Hum] for Biological Products Co-ordination by PEI (in Percent)
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TGN 1412: αCD28 mAb

Area of contact

Antigen-presenting cell

T cell

Antigen

MHC

T cell receptor

CD28

Signal 1
No activation

Activation

Antigen-presenting cell

CD28

B7

Signal 1
Signal 2
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
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

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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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
Research Grants in 2003

- DFG: 7
- BMGS: 4
- BMBF: 4
- EU: 9
- DLR: 2
- Others: 5

Sum: 31

Total amount: 2,081,786 €
Research Grants in 2004

DFG: 8
BMGS: 5
BMBF: 4
EU: 9
DLR: 2
Others: 6

Sum: 34
Total amount: 2,248,927 €
Journal Impact Factors of PEI Publications

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Thanks to all PEI employees