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Process - Where are we Now? Lessons Learned and Identifying Blocks

Regulatory view

Jan Müller-Berghaus

The views presented here are my own and do not necessarily reflect the views of the Paul-Ehrlich-Institut, the EMA or its committees and working parties.

Regulator	HTA	Coverage
Does the product do more good than harm for patients with defined indications in this jurisdiction?	HTA seeks to support decisions on whether an intervention offers useful, appropriate and affordable benefits for patients in a particular healthcare System	Will the product offer useful, appropriate (and affordable) benefits for some or all eligible patients in this healthcare system?

Modified from: Int J Technol Assess Health Care 2011;27:253–260

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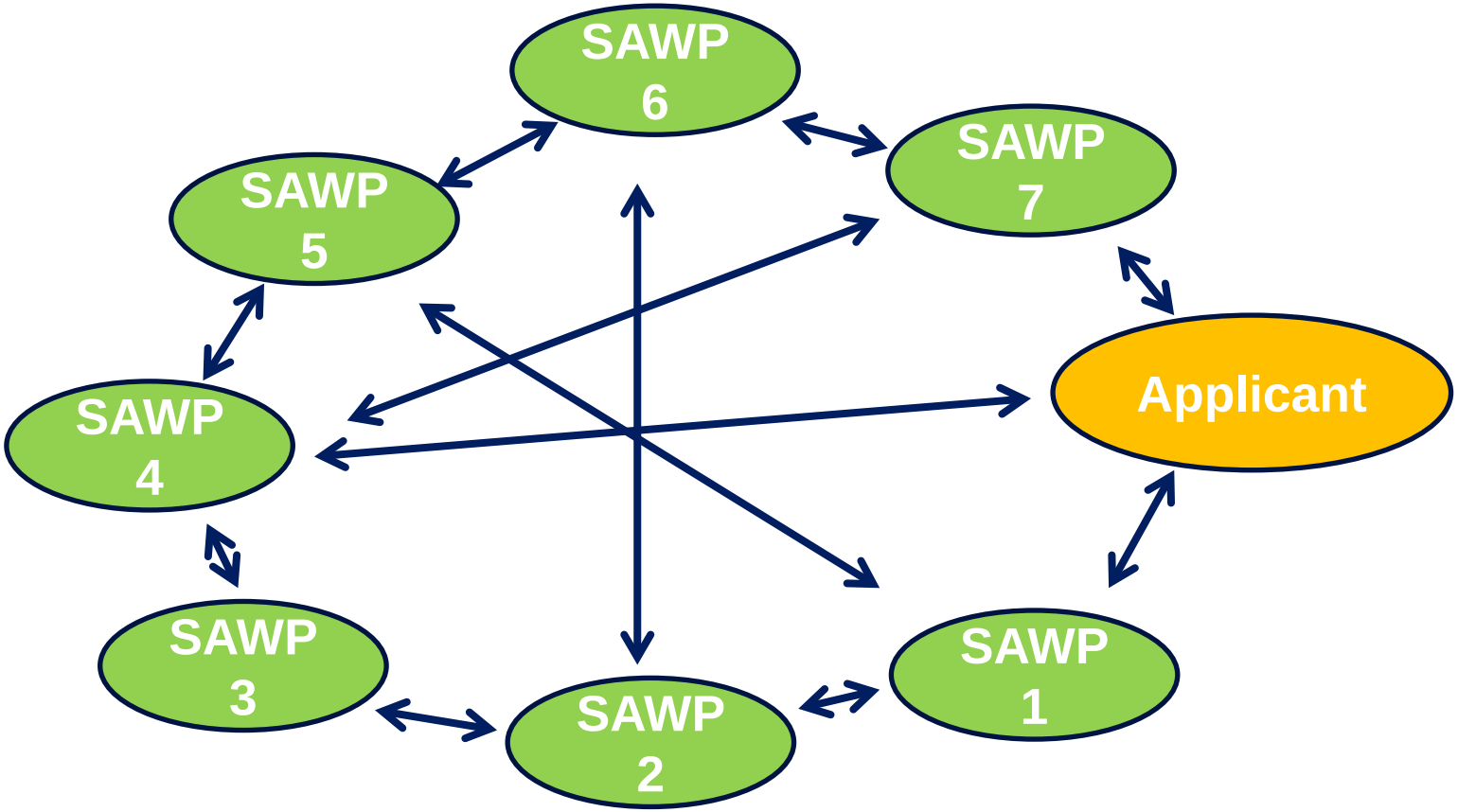
Regulatory advice



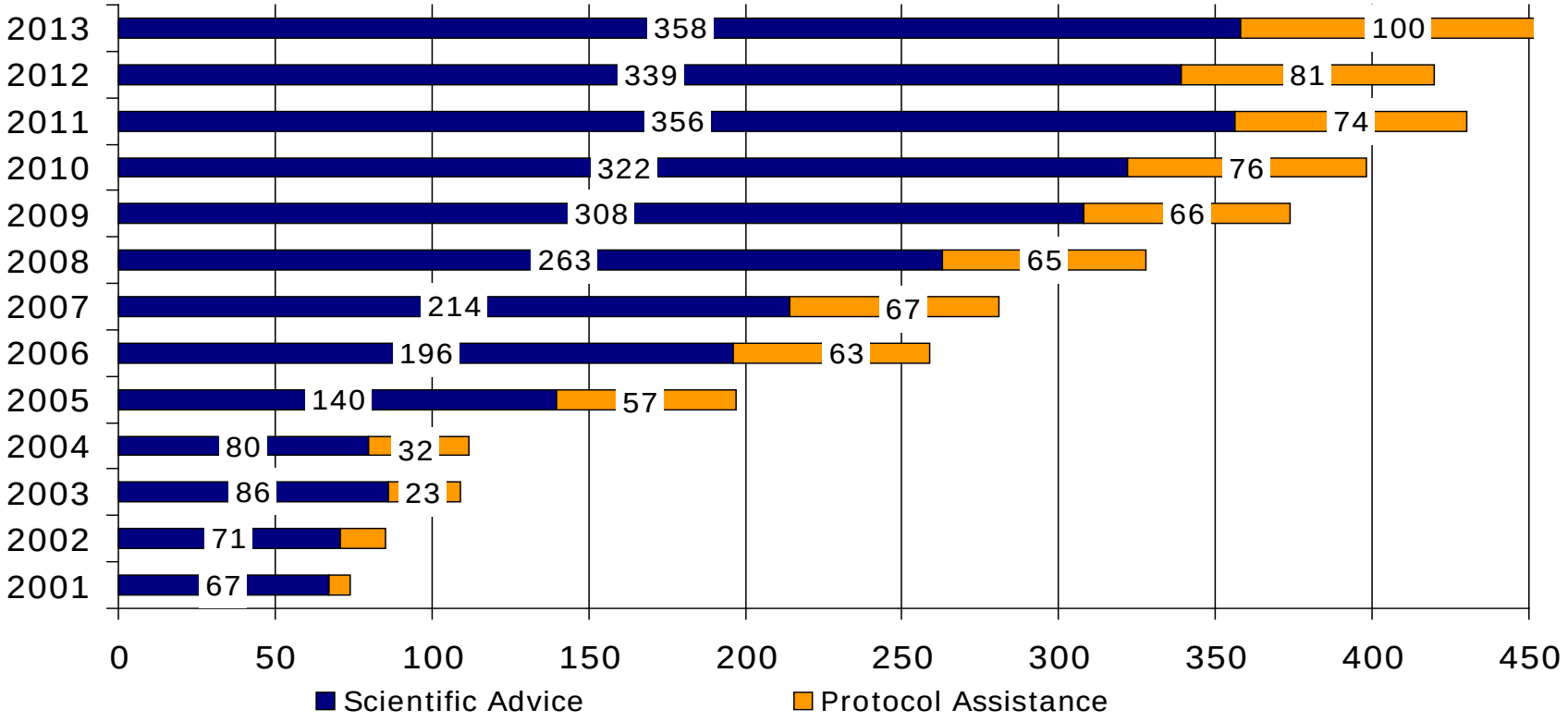
Regulatory advice

Sebastian Munster, AD 1570

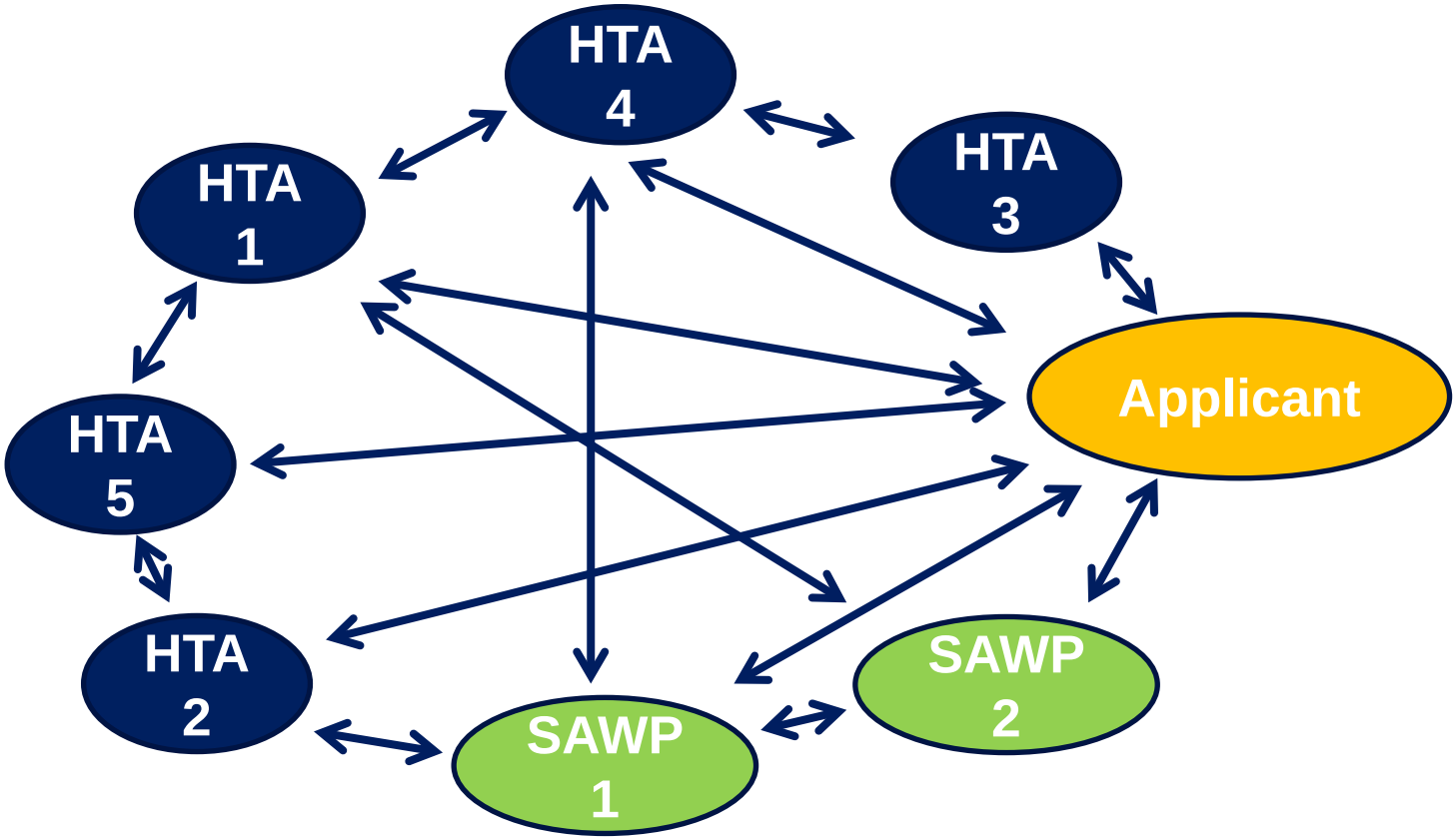
Characteristics of CHMP scientific advice

- Harmonised opinion applicable across EU with regard to MAA data on medicinal products
- Vast array of scientific questions
- Network of Experts
- Reasonable timeframe – 40 or 70 days
- Voluntary
- SME and Orphans fees / regulatory assistance
- Flexibility
- Experience

Scientific advice given by the Committee of Medicinal Products for Human (CHMP) on recommendation of the Scientific Advice Working Party (SAWP) *with forecast*

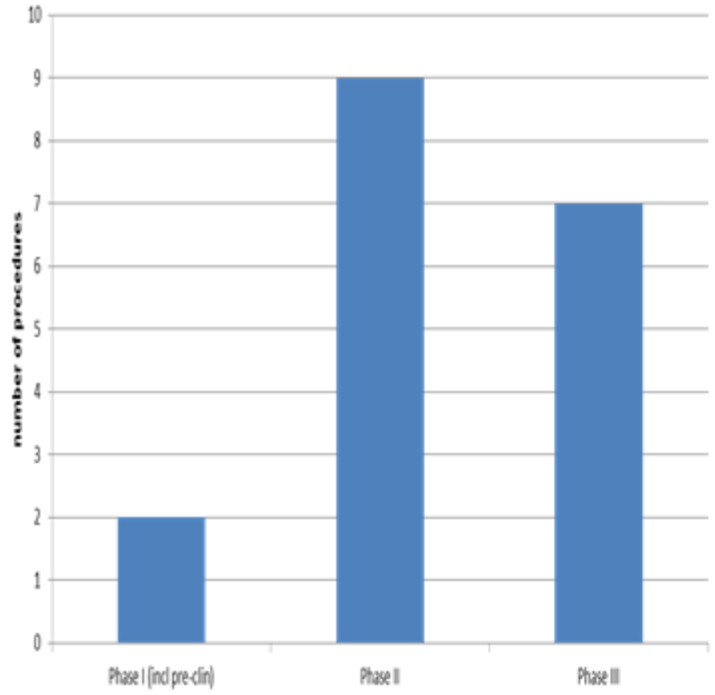


Parallel HTA-EMA advice

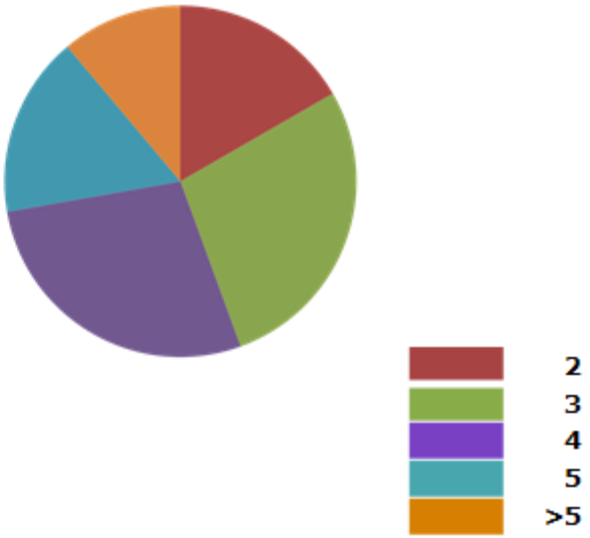


Current experience (18 of 19 analysed)

Status of development programme

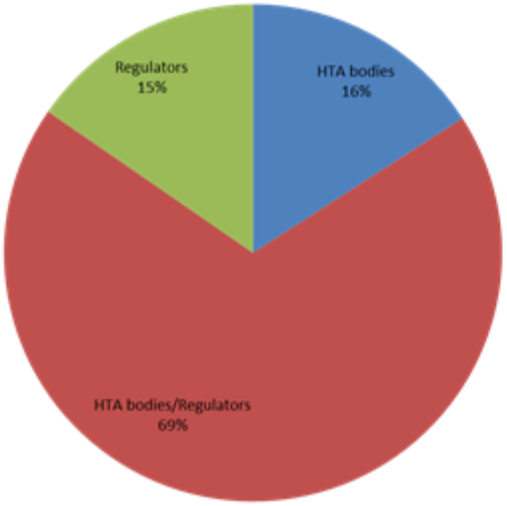


Number of HTA bodies involved

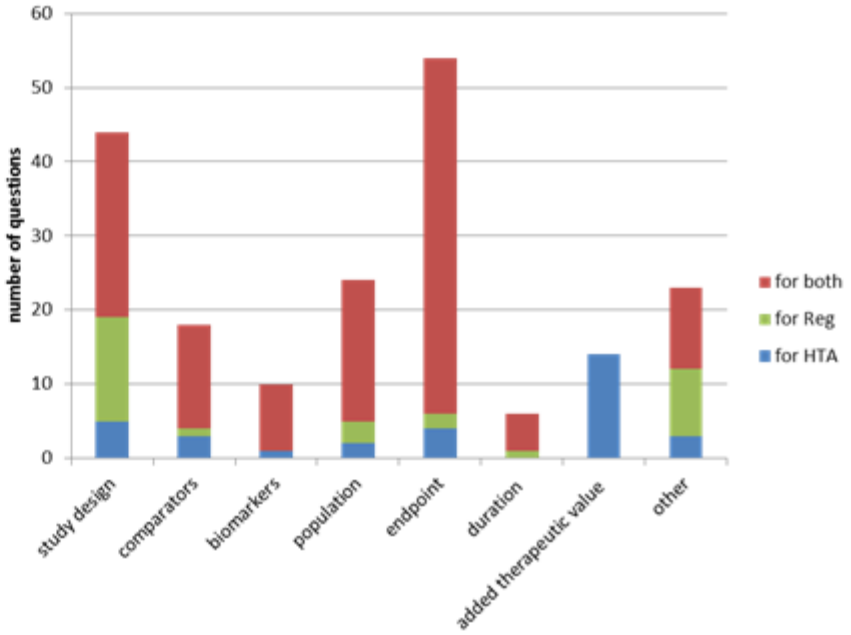


Questions asked by applicants (N=18)

Questions raised by the applicant



Topic areas



E.g. choice of comparator

- Exact indication statement of nationally licensed comparators may be important for HTA/payer
  - May even have impact on general thinking of regulators as regards unintended consequences of wordings
  - Need for bringing SmPC of approved products to current state of knowledge?

- Dose recommendations for active comparator may vary considerably across countries
  - Expectation that all parties reflect on the evidence and whether differences truly exist

- How can requirements for placebo and active control be aligned

E.g. population

- Homogenous population
  - „Cleaner results“
  - Decreased sample size, possibly less confounders

- But
  - Threat to external validity

- Common scenario of multiple lines of treatment:
  - E.g. RA: MTX, sulfasalazine, hydroxychloroquine, leflunomide, etanercept, adalimumab, infliximab, certolizumab, tocilizumab, rituximab, abatacept

- Feasiblity, e.g. orphan

E.g. endpoints

- Different views on many levels
  - Very important topic for discussion

- HTA ask for different endpoints and but seem less concerned about methodology and statistical considerations

- Regulators less well versed with PROs and QoL measures

Advantages of HTA EMA parallel scientific advice

- EMA/HTAs equal partners
- Interaction between HTAs
- Interaction between HTAs and regulators
  - listening to each others views, improves understanding
  - Closed session between EMA and HTAs before the face to face meeting to review respective positions and identify critical divergences
  - People get to know each other

- Flexible in choice of HTAs, EMA can facilitate contacts

Advantages of HTA EMA parallel scientific advice

- Uses experience administration/machinery of scientific advice
- Critical mass done/ no restriction in indications/eligibility
- External experts
- Comprehensive constructive discussions
- Written outcome
- Possible for Orphan and SME; populations limited/resources critical

- Personal reflection from a national perspective (DE)
  - Involvement of of regulators in HTA advice forseen in national legistation
  - National implementation sluggish
  - German HTA/payers are increasingly participating in EMA/HTA parallel procedure

Disadvantages of HTA EMA parallel scientific advice

- No harmonised, joint written advice
  - Not even a harmonised advice is guaranteed

- At present organisation more complicated, longer time required

- Whatever we see, we are looking at the same thing!

Ehrlich in seinem Arbeitszimmer