EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Update from the Agency's SME Office

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Update from SME office

Scientific and Regulatory Advice:

Why? When? Where from? How?

- Profile of SMEs registered with EMA
- Recent experience with scientific advice
- SMEs in the centralised procedure
- Closing remarks

Experience with SMEs to date….

512 companies assigned SME status currently

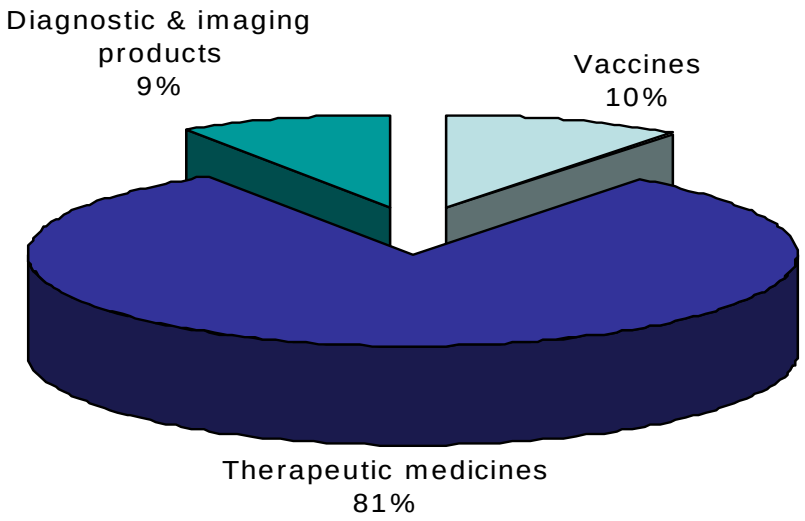
From 26 countries across EEA

40% micro, 34% small, 26% medium

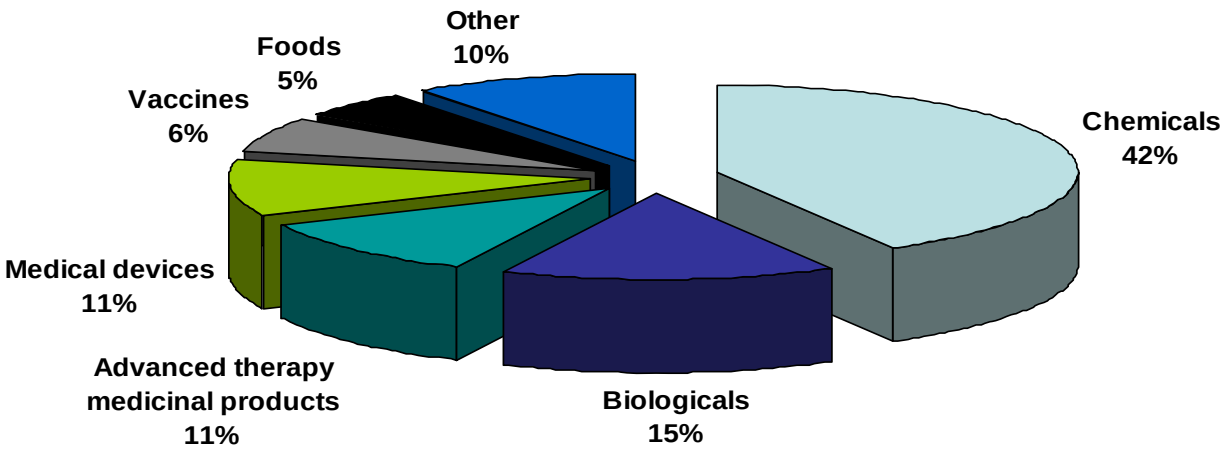
Majority human, 32 vet, 34 human/vet & 66 consultants

Public register of companies launched in 2010

Product pipeline – medicinal product categories

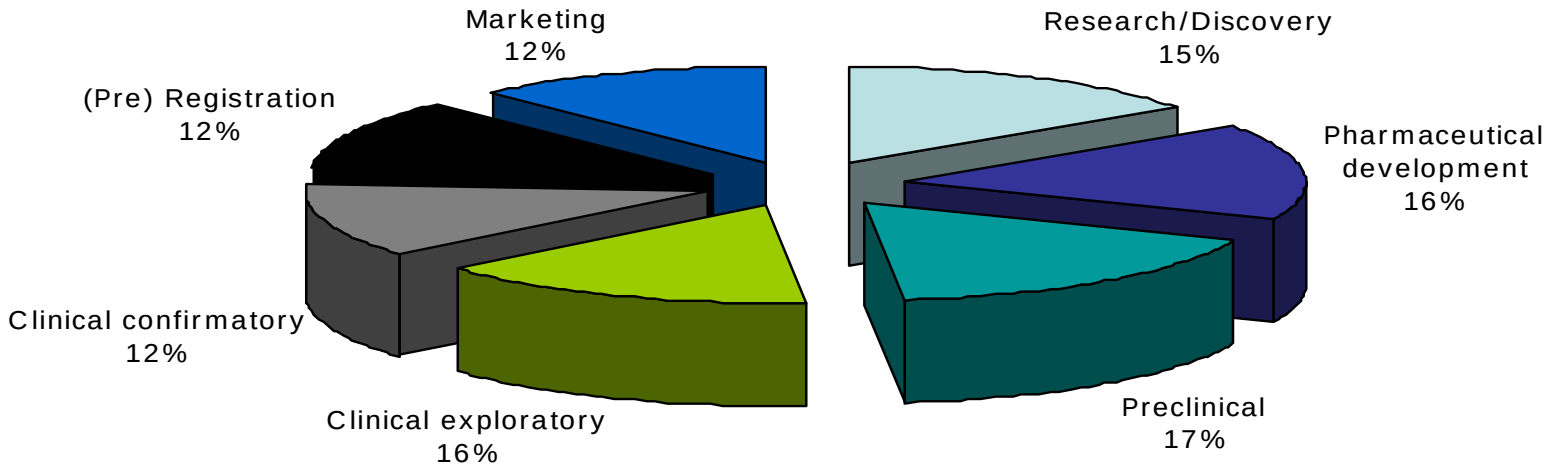


Product pipeline – substance/product categories



Categories relate to distinct products in the pipelines or 'combined' substances/products

Product pipeline – product development stages



Support to SMEs

Regulatory assistance:

> 260 SMEs received direct regulatory assistance

Scientific advice (SA):

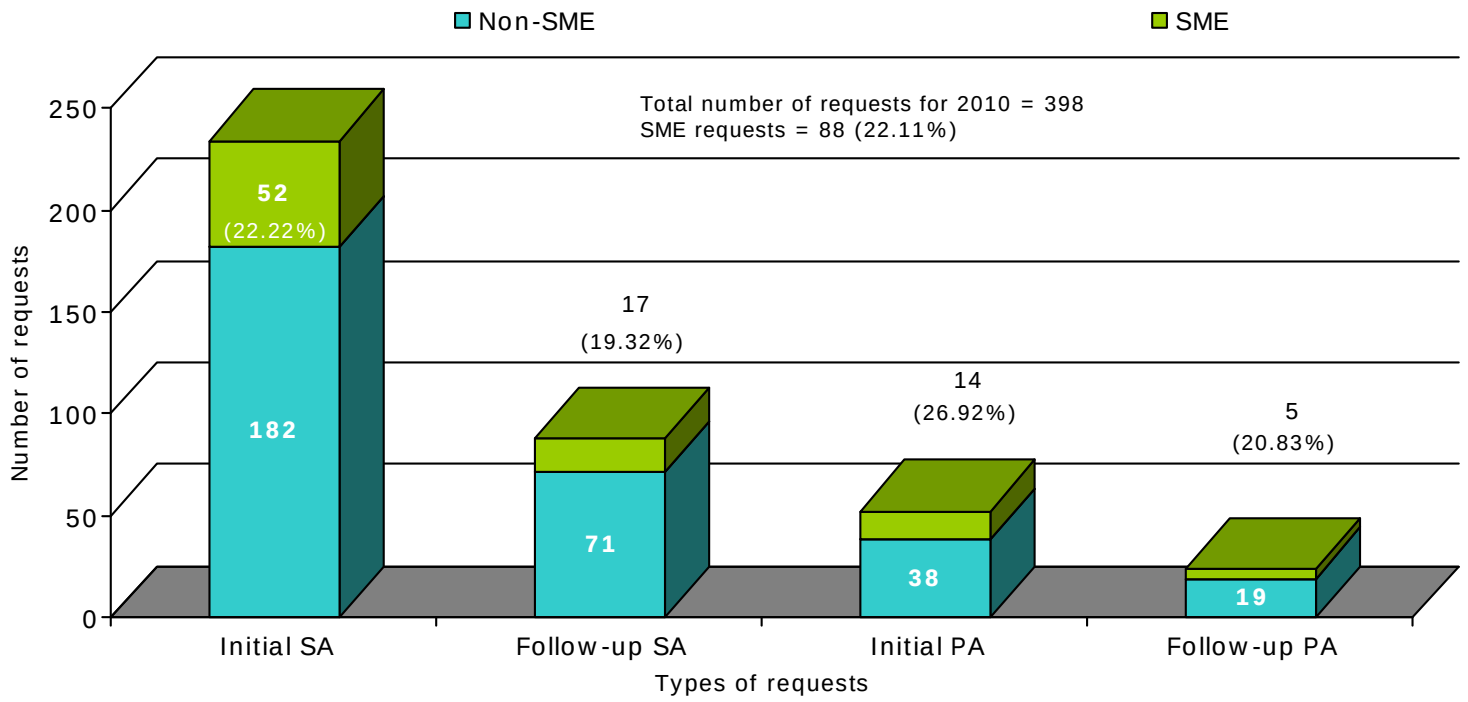
>300 SME's in scientific advice

Applications for marketing authorisation (MAA)

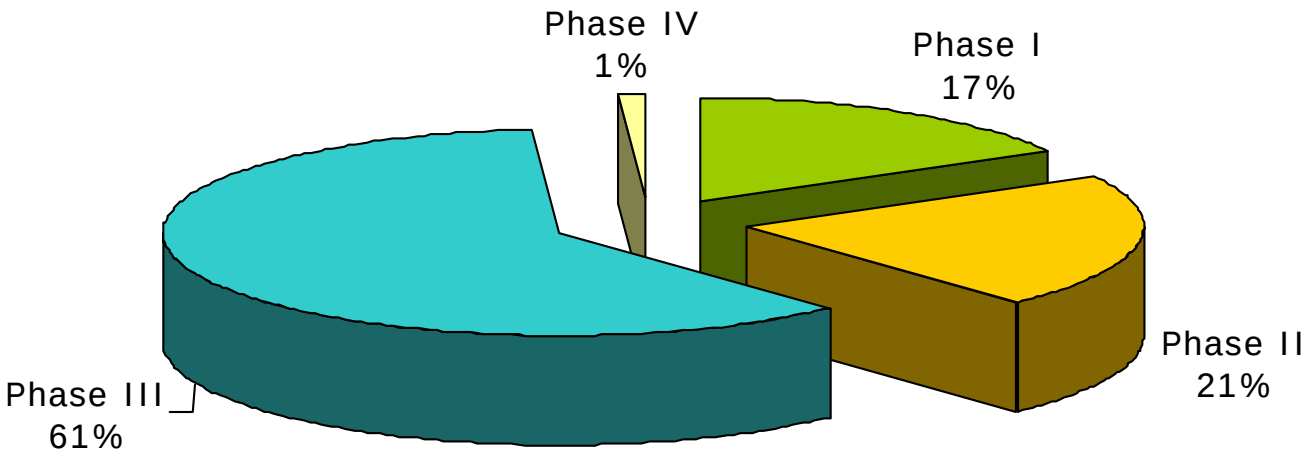
61 submitted MAAs (human & vet medicines)

Provision of translations for 21 SMEs

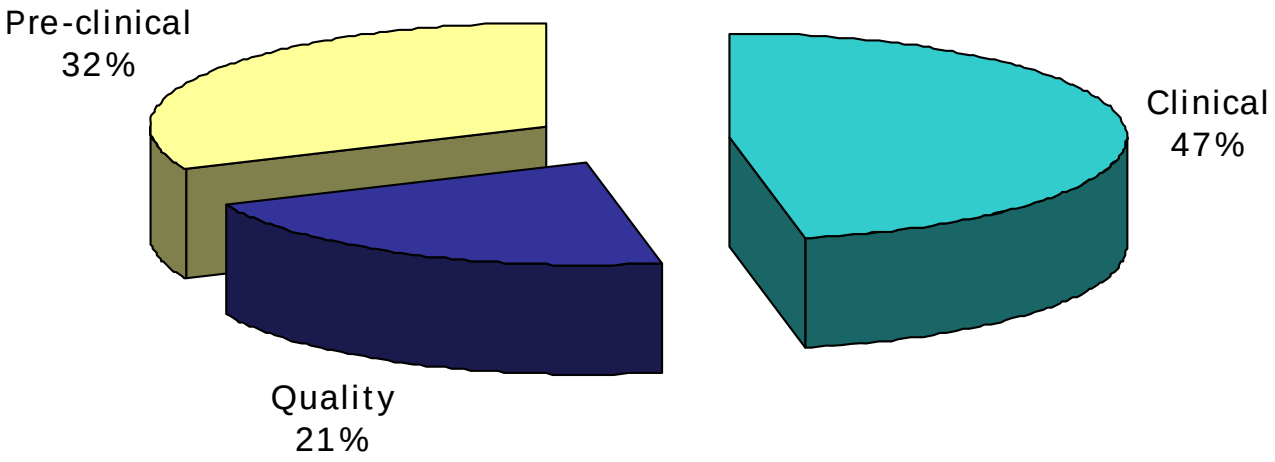
Scientific advice/Protocol assistance in 2010



Scientific Advice 2006-2010 SMEs



Scientific Advice 2006-2010 SMEs



2010 Multidisciplinary requests:
Quality+Preclinical+Clinical: 24%

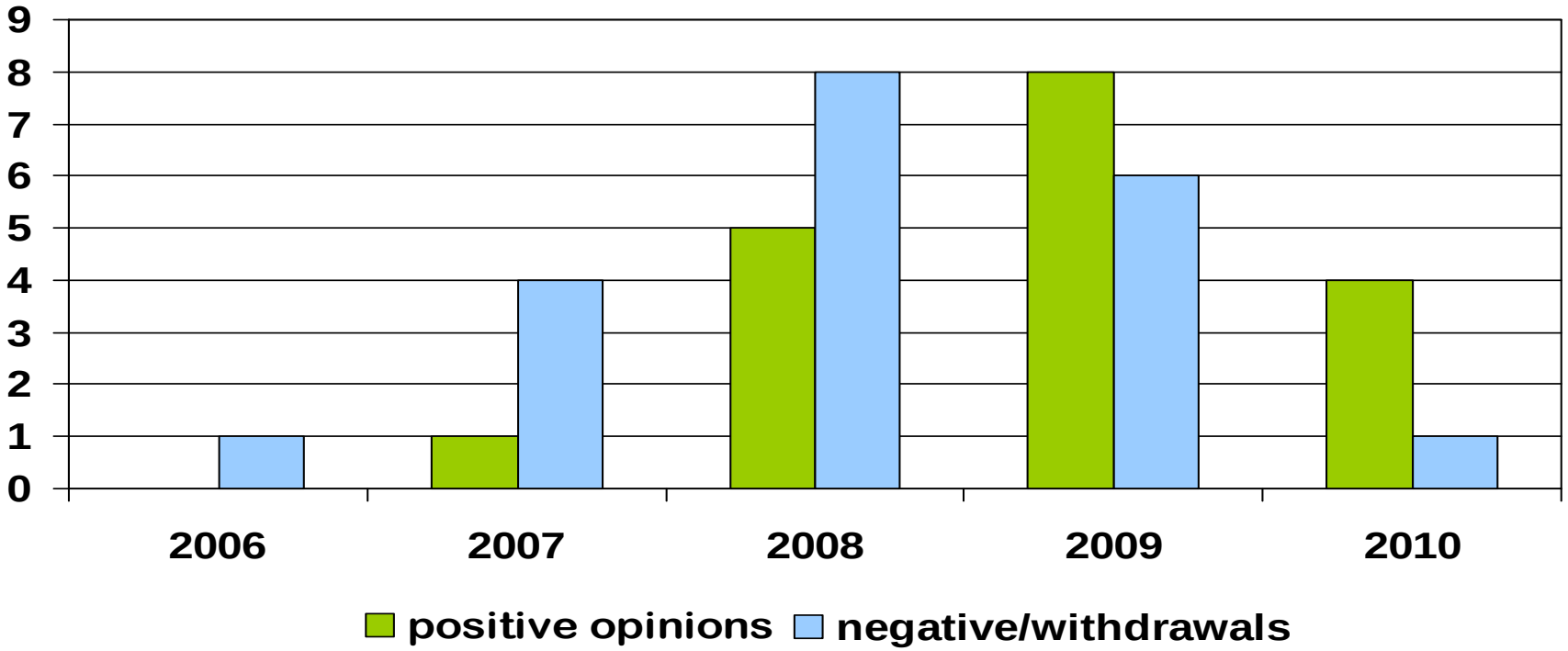
Status of SME Applications for Marketing Authorisation for Human Medicines

	2006	2007	2008	2009	2010	Total
No. of applications submitted	10	11	12	4	13	50
Positive	-	1	5	8	4	18
Negative	-	1	2	-	-	3
Withdrawals	1	3	6	6	1	17

Dec 2005- Dec 2010

MAA outcomes over time for SMEs

For medicines for human use

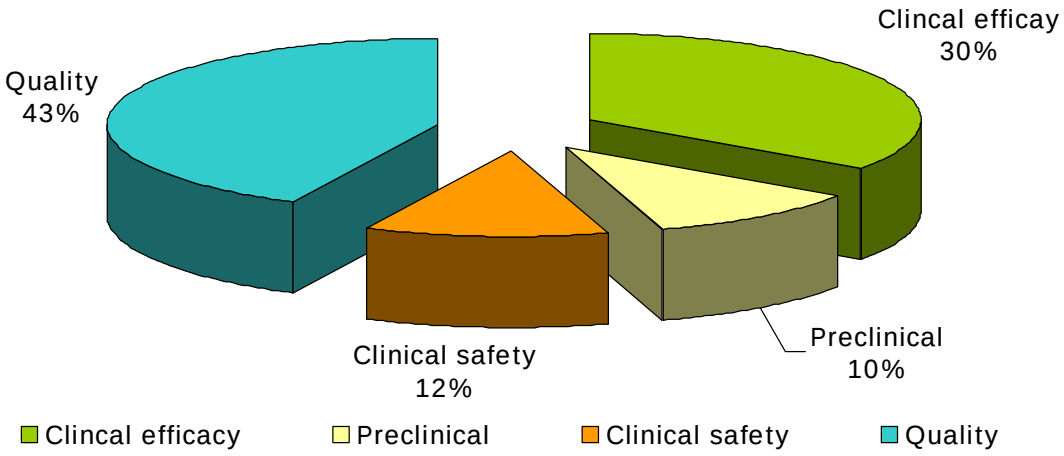


Overall success rate for SMEs 47% vs 75% for all companies

Questions raised & response time

Average number of major objections:

- 4 for positive MAAs (from 0 to 10)
- 10 for negative/withdrawn MAAs (from 1 to 34)



Response time on average: 7 months

Most frequent major objections in SME applications with negative outcomes

-Quality

-Non-clinical

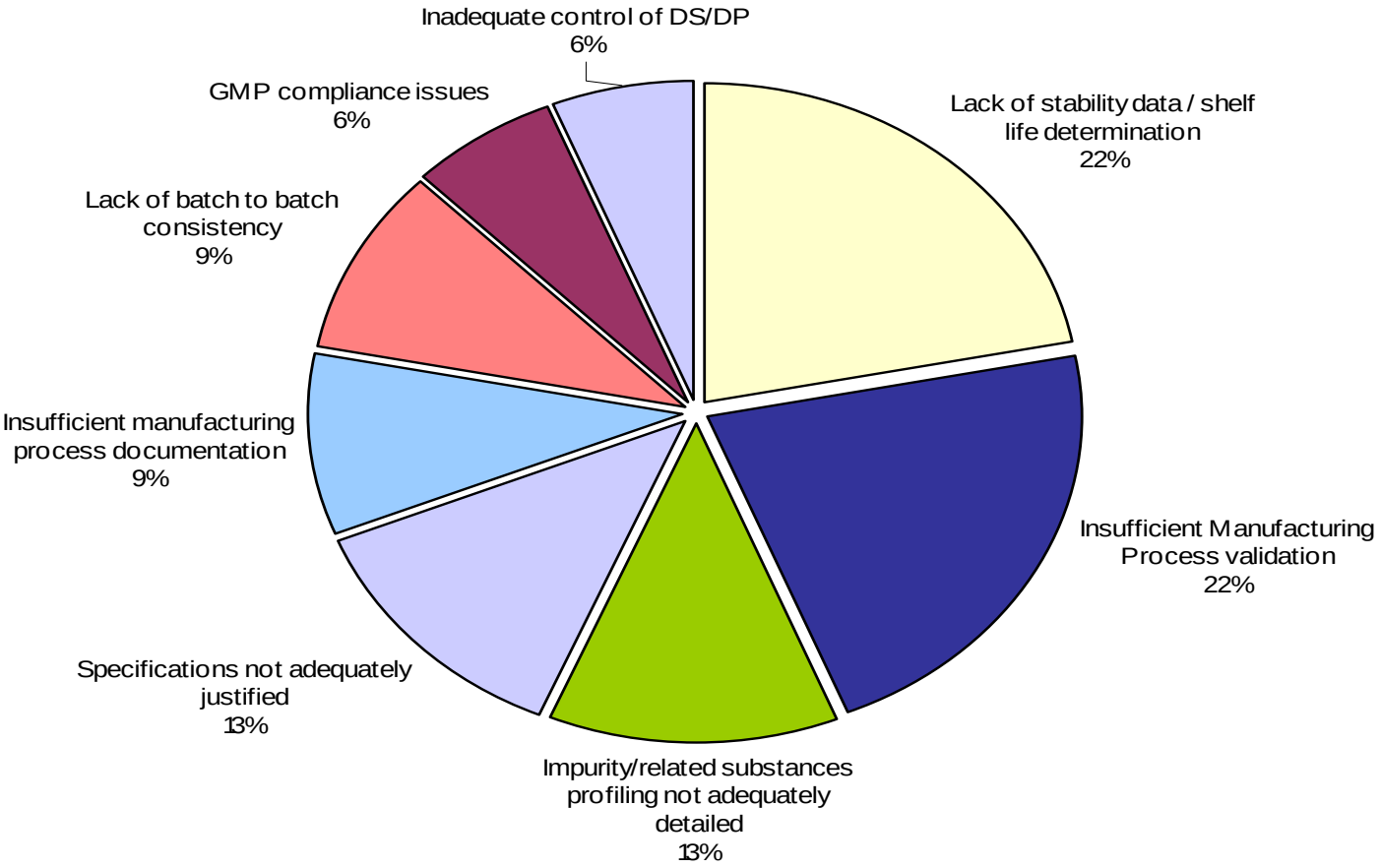
-Clinical Efficacy

-Clinical Safety

Examples of Major Objections "Quality"

- Process documentation incomplete
- Process validation incomplete
- Levels of impurities too high
- Setting of specifications not justified
- Lack of demonstrated consistency of lots
- Comparability between different sites not addressed
- Lack of GMP Certification
- Stability data lacking

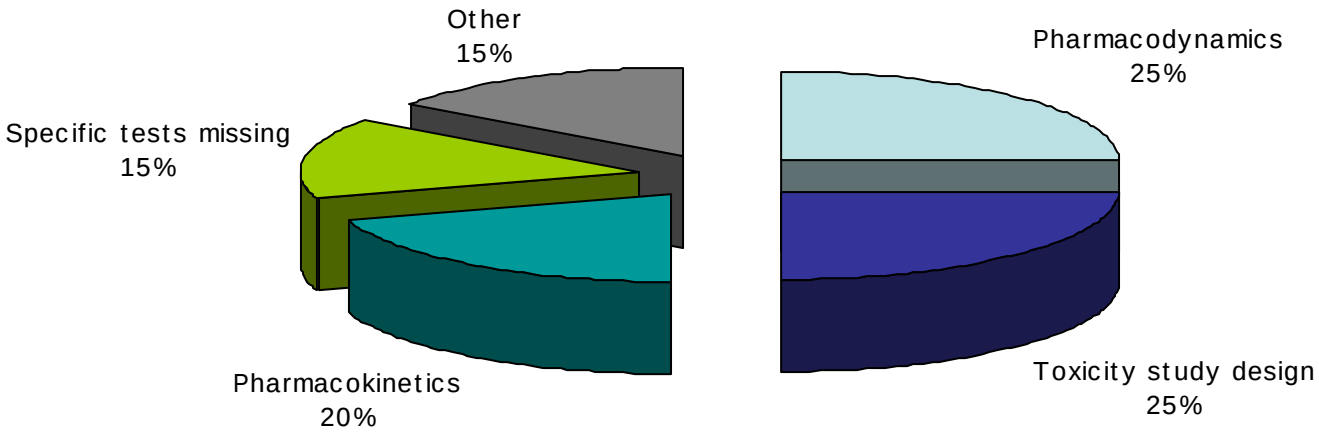
Distribution of 8 most frequent major objections in **quality** for SME applications



Examples of Major Objections "Non- clinical"

- Need to provide evidence of pharmacological activity
- No biodistribution study provided reflecting the intended clinical application
- Design of repeated dose toxicity studies not to current standards
- Need to justify relevance of the species and doses chosen
- Toxicity studies do not reflect intended clinical scheme of dosing
- Lack of data concerning impurities
- Local tolerance should be investigated with product intended for marketing

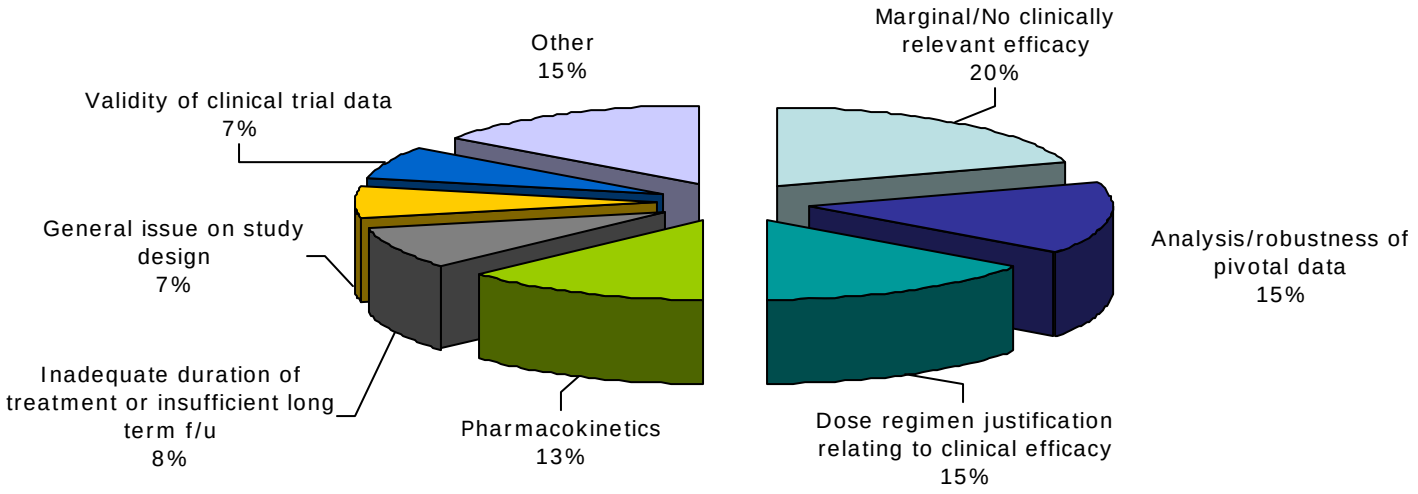
Distribution of **non-clinical** major objections for SME applications



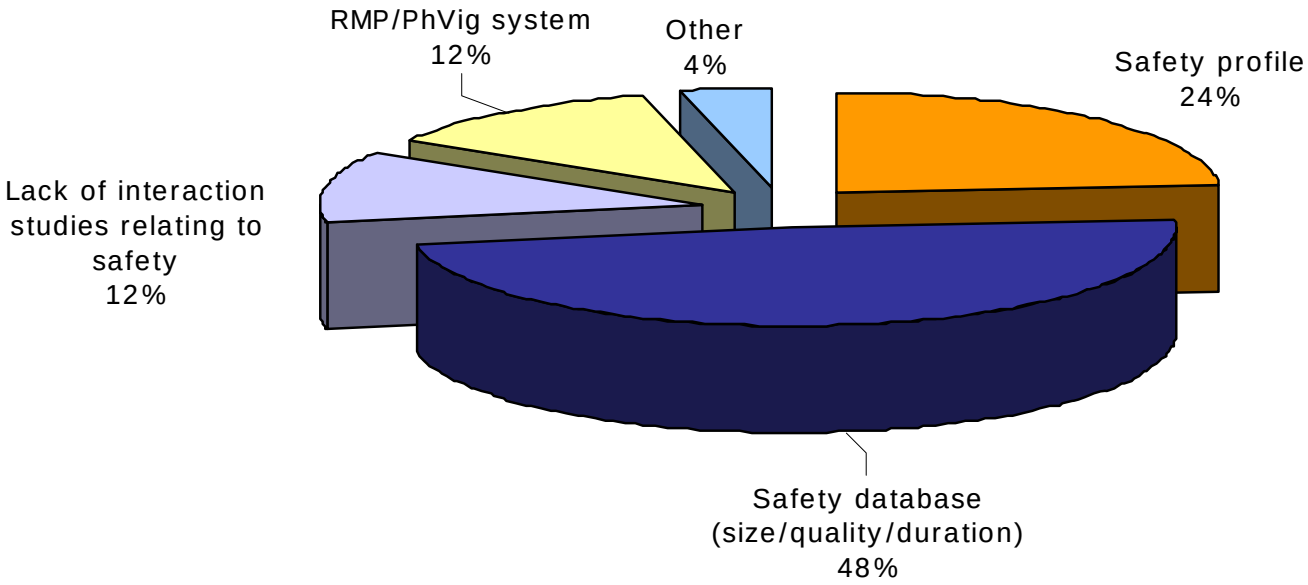
Examples of Major Objections “Clinical”

- Discrepancy between studied patients & proposed indications
- Insufficient clinical package – one pivotal study
- Inadequate trial design
- Efficacy not demonstrated to significantly robust level
- Primary endpoint is not statistically significant
- Choice of dose not sufficiently justified
- Predefined criteria for clinical relevance not met
- Inconsistency in statistical methods between protocol & report
- Multiplicity issues
- Data do not allow comprehensive evaluation of safety profile

Distribution of major objections relating to clinical **efficacy** for SME applications



Distribution of major objections relating to clinical **safety** for SME applications



Closing Remarks

Observations:

With increasing experience can identify areas where SMEs encounter problems

Major objections run high particularly in area of quality and clinical efficacy

Objections raised highlight need for scientific advice in specific areas

Recommendations:

Early Scientific advice is strongly encouraged

Maximise dialogue with regulatory authorities through various entry doors as development proceeds

The various entry doors:
for scientific advice & regulatory assistance

Thanks to following colleagues for contribution to this presentation:

- Laetitia Radal
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Thank you for your attention