

TOWARDS A GLOBAL DEVELOPMENT

Eric Abadie, MD,MBA
AFSSAPS, CPMP,COMP

FACTS

- Money spent in R/D increasing
- Number of IND's remain steady (400-500/year)
- Products longer in phase II
- Increased attrition rate at end Phase II
- Success rate at the submission stage remains the same

POSSIBLE REASONS

- Regulatory environment
- Business environment
- Concentration on economically viable products
- Demonstrate the value of medicines

HOW REGULATORS CAN HELP

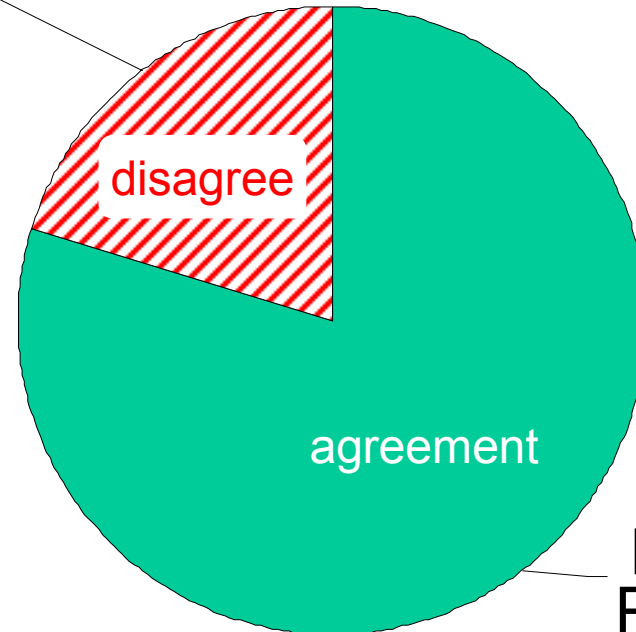
- Facilitation of dialogue
- Facilitation of global development

GLOBAL DEVELOPMENT

- Myth or reality ?
- EMEA outcome for FDA positive applications (n=139)
- FDA outcome for EMEA negative applications (n=74)

EMEA outcome for **FDA positive** applications (n=139)

EMEA Negative 20%

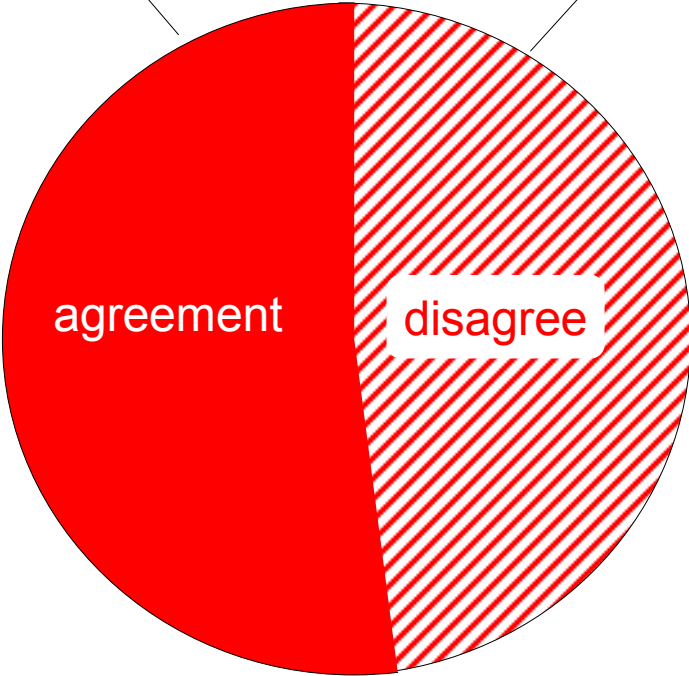


EMEA
Positive
80%

FDA outcome for **EMEA negative** applications (n=74)

FDA Negative 51%

FDA Positive 49%



DIVERGENCES EU/FDA (frequently associated factors)

- 35 products EMEA negative and FDA positive
- 20 products EMEA negative and FDA positive without hearing
- 15 products EMEA negative and FDA positive with hearing
- Submission not more than two years apart in both regions

RESULTS (1)

- ATC code: V most frequent
- Major objections not solved
 - Quality: 1 (comparability)
 - Preclinical: 3 (toxic effects, pharmacodynamics, reprotoxicity)
 - Clinical efficacy: 44
 - Clinical safety: 11

RESULTS (2)

- Clinical efficacy (44 major objections)
 - Marginal efficacy, size of effect (31%)
 - Selected population (22%)
 - Lack of RCT (9%)
 - Choice of endpoint (9%)

RESULTS (3)

- Clinical safety (11 Major objections)
 - Serious AEs (63%)
 - Size/quality/long term data (18%)
 - Dose justification in at risk population (18%)

Summary

- High degree of concordance, but differences exist between EU and US approvals
- Demonstration of efficacy seems to be the main pitfall
- Target population, size of the difference and comparative B/R assessment are key points (EU)
- Inter regulatory dialogue needed for disease specific guidelines and scientific advices