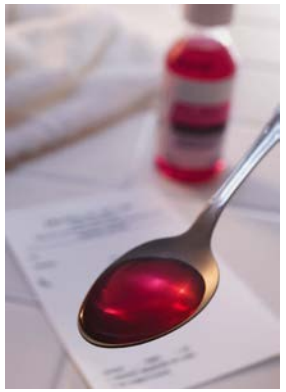
Workshop on Paediatric Investigation Plans in Type 2 Diabetes Mellitus

Conclusions

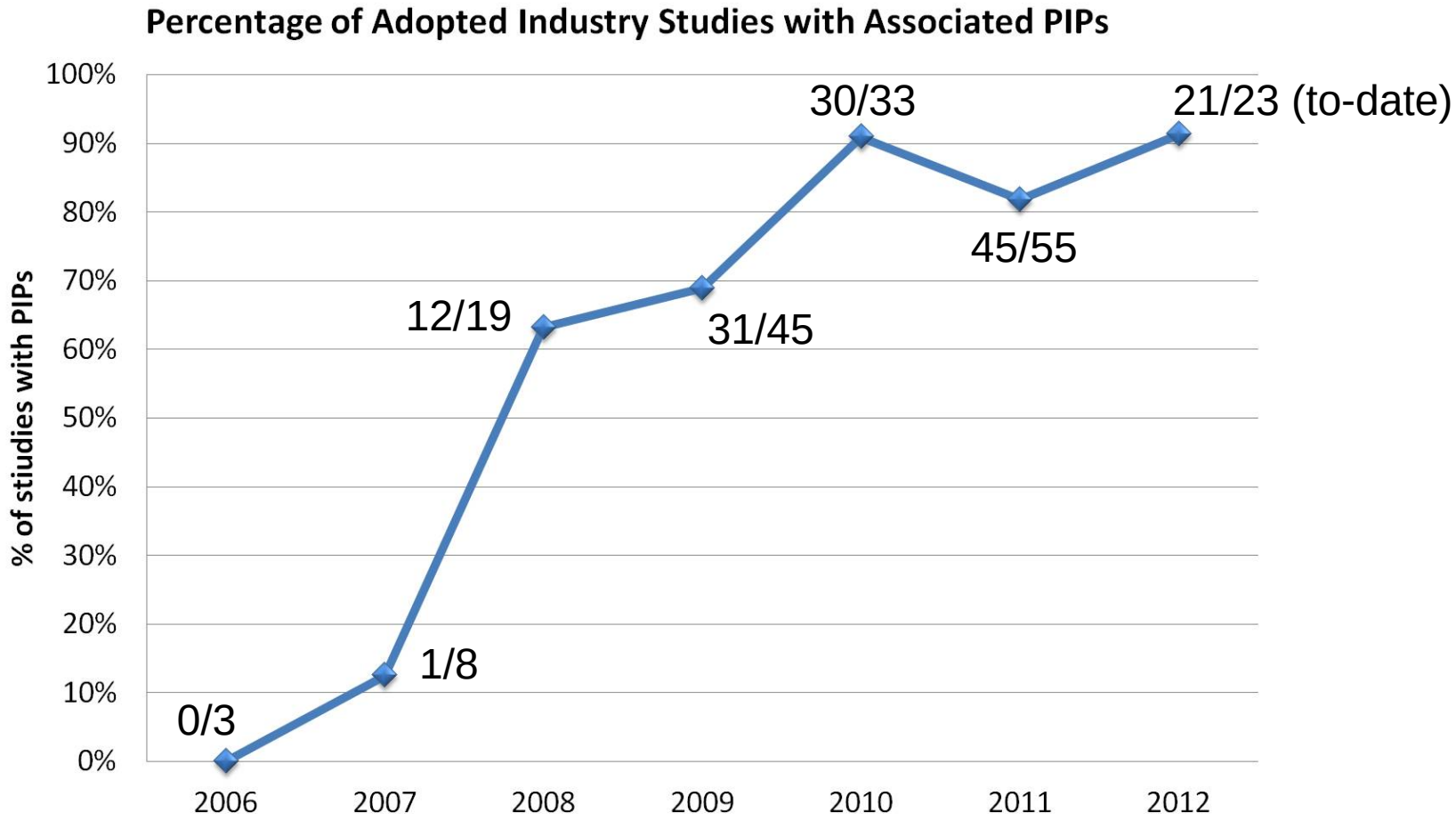
Paolo Tomasi MD PhD

Head of Paediatric Medicines, EMA



NIHR Medicines for Children Research Network (MCRN)

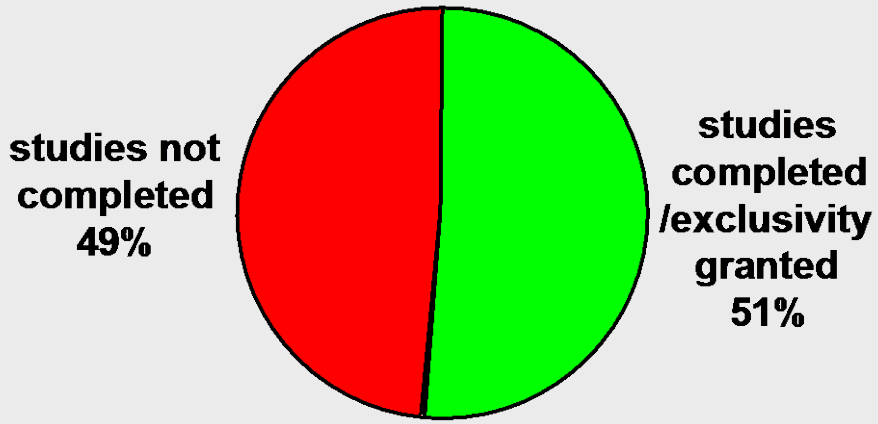
National Institute for Health Research
Clinical Research Network



industry@mcrn.org.uk - www.mcrn.org.uk

Will all Paediatric Investigation Plans be completed?

Completion of studies under BPCA written request
(optional, but 80% suggested by applicant)



Source: IOM report on “Safe and Effective Medicines for Children: Pediatric Studies Conducted Under BPCA and PREA”

Main concerns for pharma companies (feasibility):

- Few available patients in total for all the studies.
- Widespread insulin (and metformin) use needs to be addressed – weaning not always feasible.
- 30% patients to be recruited in EU-like countries: difficult to achieve due to rarity in EU
- Many patients do not meet HbA1c inclusion criteria

Potential solutions

- Broadened role for extrapolation (for efficacy) / sample size reduction
  - ✓ Use of Bayesian methods with adult priors
  - ✓ Acceptance of lower significance levels (p=0.07, p=0.10)
  - ✓ Safety study only (pre or post authorization in children?)
- Studies in related diseases (prediabetes? T1DM?)
- Staggered development of products (in same class) / deferrals
- Broadened inclusion criteria:
  - ✓ For insulin treatment
  - ✓ For age (up to 22? 25?)
  - ✓ For HbA1c range
  - ✓ For geographical origin (non-EU)
  - ✓ What else?
- **Multi-company study** (paediatric incentive and obligations are irrespective of outcome of studies)
- Single company with multiple agents
- Simplification of PK studies (peak and trough levels, dried blood spots)

Conclusions

- Number of patients required is high (and it's a minimum number).
- A change in paradigm for diabetes PIPs seems necessary, to maximize feasibility and obtain significant data.
- Staggered development, followed potentially by greater extrapolation and/or reduced requirements could be a solution.
- Several of the proposed solutions may be applicable in practice.
- SAWP/CHMP needs to be included in the equation; Extrapolation working group will act as the glue (chairs of SAWP and CHMP are members).
- Companies may re-consider their options (multi-company studies, modification of previously agreed PIPs…)