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Incentives and Disincentives for Pediatric Drug Development

- Industry Perspective

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Environment

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- Incentives and requirements exist for industry to generate data on the use of drugs/ biologics in paediatric patients
- Shift from protecting paediatric patients ***against*** drug trials to protecting them ***through*** drug trials and data generation
- Paediatric trials are becoming a routine part of drug development
- Experience with paediatric trial design and operational execution is still growing within industry
- Many special considerations exist for planning and conducting paediatric trials compared to adult trials

Incentives
Regulatory Incentives

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Mandatory – (PREA, US)

- Requires that sponsors submit pediatric data in every application for a new ingredient, new indication, new dosage form, dosage regimen or route of administration
- Mandatory for all drugs and biologics

Voluntary – (BPCA, US)

- Voluntary incentive program that allows sponsors to gain 6 months exclusivity for conducting pediatric trials
- Not available to biologic, generics, off-patent or “old” antibiotic drugs
- Linked to active moiety rather than drug product/ indications

EU Regulations

- Combine incentives and requirements for paediatric studies

Incentives
Ethical Incentives

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- Responsibility to share pharmaceutical knowledge with treating community
- Responsibility to protect paediatric patients through provision of data
- Responsibility to further treatment of paediatric patients through provision of data
- Responsibility to work with Health Authorities and Clinicians to further area of paediatric drug development in general

Disincentives
Trial Design Challenges

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Trial design for paediatric patients differs widely from adult patients in the same disease area, e.g.:

- Nature of disease can be different -> different endpoints
- More restrictive assessments e.g. volume of samples that can be taken -> more innovative statistical design
- Additional safety considerations e.g. growth and development
- “Paediatric” patients cover neonates -> adolescents, but very different considerations for each age group
- Formulation of drug

-> Expertise is often not “in house”, external experts need to be consulted

Disincentives
Operational Difficulties

Running paediatric trials also poses challenges:

- Speciality sites often needed
- Networks and infrastructure not in place for paediatric trials in some disease areas
- Recruitment difficulties:
  - Paediatric population for same disease smaller
  - Sufficient patients for trials do not always exist in US/ EU (particularly in younger age groups)
  - Drugs competing for paediatric patient to complete mandatory trials

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Disincentives
Ethical/ Regulatory Difficulties

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Gaining Ethics Committee and Health Authority approvals/ agreements can be challenging, e.g.:

- Local ethics committees raise concerns regarding trials, particularly if conducted in ex-US paediatric patients to meet US regulatory requirements (e.g. when sufficient patients do not exist in US/ EU)
- Regulatory agreements on protocol or Written Requests can take many rounds of feedback and sometimes years to reach agreement (particularly if more than one Health Authority is involved)

Disincentives
Technical/ Preclinical Difficulties

Adult formulations are not always suitable for paediatric patients:

- Re-formulation work can take years
- Paediatric formulation sometimes is not possible or feasible
- Can take years to get agreement that “due diligence” has been exercised.

Studies in juvenile adults can be a useful predictor of toxicity in children:

- Need to consider whether additional preclinical (e.g. juvenile toxicology) data is required before entry into human paeds.
- Add relevant duration of preclinical trials onto timeline for paediatric programme

Considerations for Development
Designing a Paediatric Programme

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- What Type of Study is optimal?
  - Nature of disease (i.e. similar to adults?),
  - Amount already known about product in paeds,
  - Use and benefit in each age group, etc
- Timing of the Study/ies?
  - How life threatening is the disease?,
  - Extent of other therapies for paeds,
  - Therapeutic index,
  - Expected benefit.
  - Likelihood that drug will continue to NDA/ MAA

Considerations for Development
Designing a Paediatric Programme (cont.)

- Have suitable study centres been identified?
- Is exclusivity required?
- Is there a suitable formulation?
- Are racial and ethnic groups adequately represented?
- Will pre-clinical data be required?
- Are pediatric age groups appropriate or is another characteristic more suitable (e.g weight)?
- What label is targeted as a result of the studies?
- Is there sufficient time before patent expiry for submission of PPSR, FDA review, discussion with FDA, issue of a WR, study initiation and conduct, report writing and filing

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Support and Successes

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- Paediatric legislation has given a framework and structure for paediatric research and helped to remove barriers
- Dialogue with FDA is encouraged as a partner in paediatric trials
- Industry experience in conducting paediatric trials in increasing
- Increased co-operation between all stakeholders as process becomes more routine

Working Towards the Future

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- Generation of paediatric data is becoming routine
- Inclusion of paediatric trials in drug development programme is becoming routine
- Paediatric drug development acknowledged to be a shared responsibility between Industry, Regulators and Clinicians
- Best results will be achieved as these groups continue to work together towards effective generation and dissemination of meaningful paediatric data
- Working towards the ideal of a single, globally accepted (EU/US) paediatric programme to cover both mandatory requirements and regulatory incentives.

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THANK YOU FOR YOUR TIME AND ATTENTION