EUDRAC

QUALITY FOR SUCCESS

OBN Digital Webinar

Maximising your Assets through IP and Regulatory Strategy

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Objective

- To describe opportunities to interact with regulators that should
  - Save you time and money during development
  - Provide you with additional knowledge and expertise
  - Enhance the value of your asset

Agenda

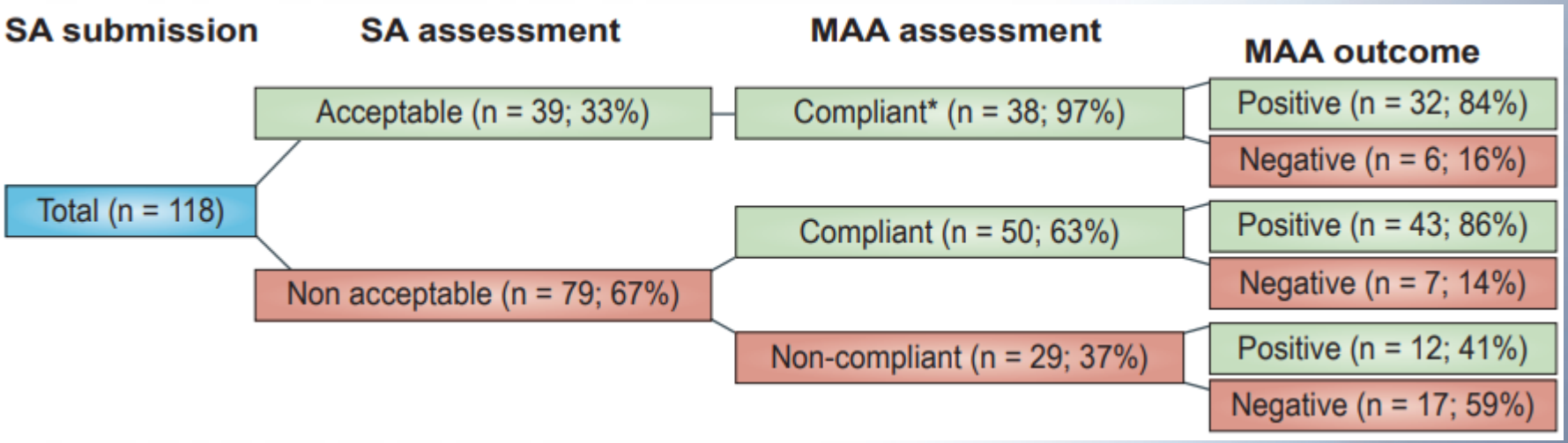
- When to consider regulatory matters?
- Why discuss with the regulators?
- Scientific advice – when?
- Incentives available
- Conclusion

When to consider regulatory matters?

- Integrate a regulatory strategy into your early development plan.
- As soon as a promising candidate emerges from nonclinical pharmacology work / initial toxicology, consider:
  - Focus initially on top level information e.g. is the potential indication for a rare (orphan) disease or not
  - Timing of interactions with regulatory agency
  - Reviewing the applicability of incentives
  - Don’t overlook mandatory requirements
  - Keep the development plan a living document
    - Expand with detail as you move through development

Why discuss with the regulators?

- To strengthen the data package for marketing authorisation application (MAA). An example:
  - Scientific advice: analysis by EMA[1] concluded that requesting and following scientific advice led to a reduction in major objections during MAA assessment and a 2 month shorter approval procedure



[1] Impact of scientific advice from the European Medicines Agency. 2015. Nature Reviews, Drug Discovery.**14**:302

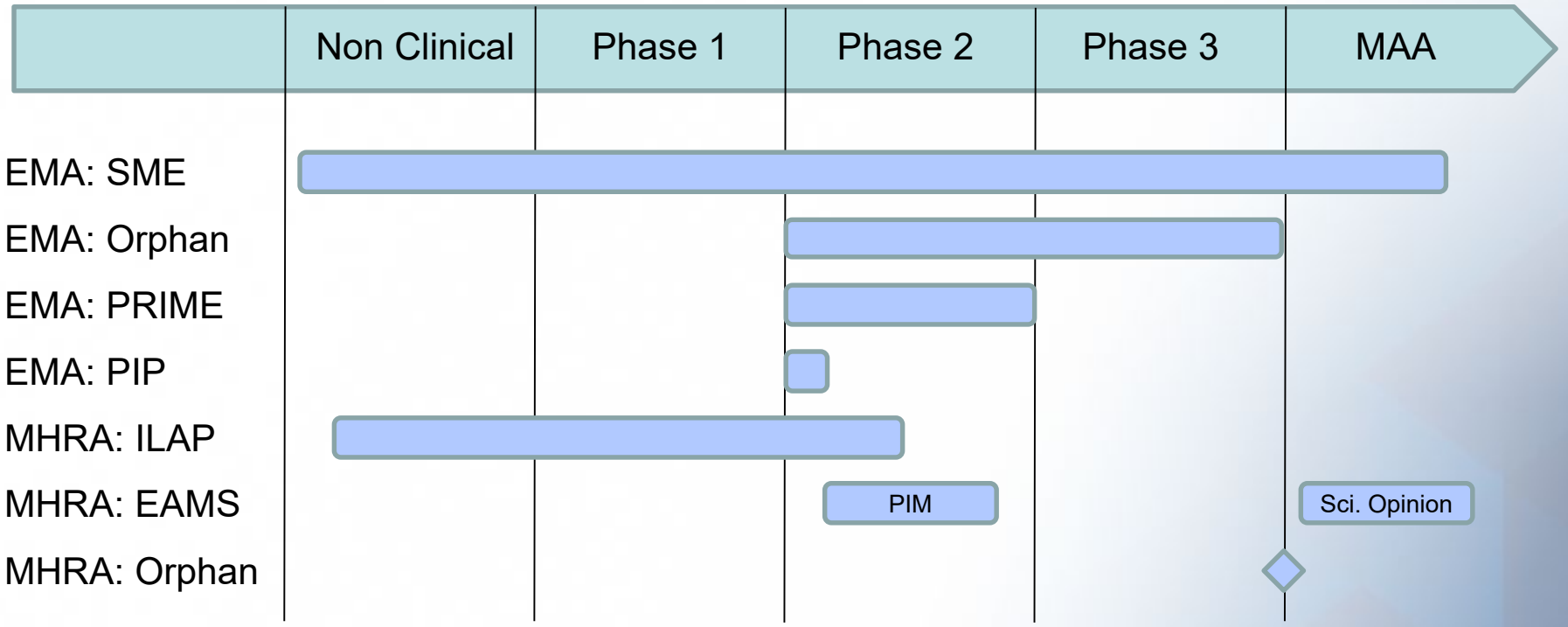
Scientific advice – When?

- Early development
  - Particularly if novel compound / platform technology, gene therapy
  - Prior to deciding which indication to target
- Always before finalisation of phase 3 protocol(s)
  - If global development, plan early enough to allow input from key regions and time to resolve if receive conflicting advice
  - Need a clear definition of indication, justification of posology
  - Focus may be on clinical phase 3 however is also opportunity to ensure nonclinical programme is adequate for registration
- All scientific advice will need to be submitted in future clinical trial applications, MAA and other procedures
- Only ask the questions you are prepared to react to!

Incentives Available from Regulators

- EMA: SME Status
- EMA: EU Orphan Drug Designation
- EMA: Priority Medicines (PRIME) scheme
- EMA: Paediatric Investigation Plan (PIP)
- MHRA: Innovative Licensing & Access Pathway (ILAP)
- MHRA: Early Access to Medicines Scheme (EAMS)
- MHRA: Orphan Medicinal Products

Incentive Applications Timings



EMA SME Status
(micro, small and medium-sized enterprises)

- Criteria:
  - < 250 employees
  - annual turnover of ≤ €50 million, or an annual balance-sheet total of ≤ €43 million
- Simple application (few hours to complete) showing ownership structure, financial figures and supporting documents
- EU based or can link to an EU consultancy company
- Simple annual renewal required

	Fee Reductions
Scientific advice	90%
MAA	Deferral until Opinion
Inspections	90%
Post-authorisation, including annual fees	40%

EMA/EU Orphan Drug Designation

- Criteria
  - A product to treat, prevent or diagnose a disease that is life-threatening or chronically debilitating
  - Prevalence in EU ≤ 5 in 10,000
  - No other product exists or, if so, must be of significant benefit
- Designations published by the European Commission

  https://ec.europa.eu/health/medicinal-products/orphan-medicinal-products_en
- Similar system in US but with different prevalence criterion
- 10 years market exclusivity plus 2 years if comply with agreed paediatric investigation plan (PIP)
- Access to the centralised procedure for the MAA
  - One MA covers all EU/EEA; ongoing maintenance more efficient

EMA Orphan Drug Designation

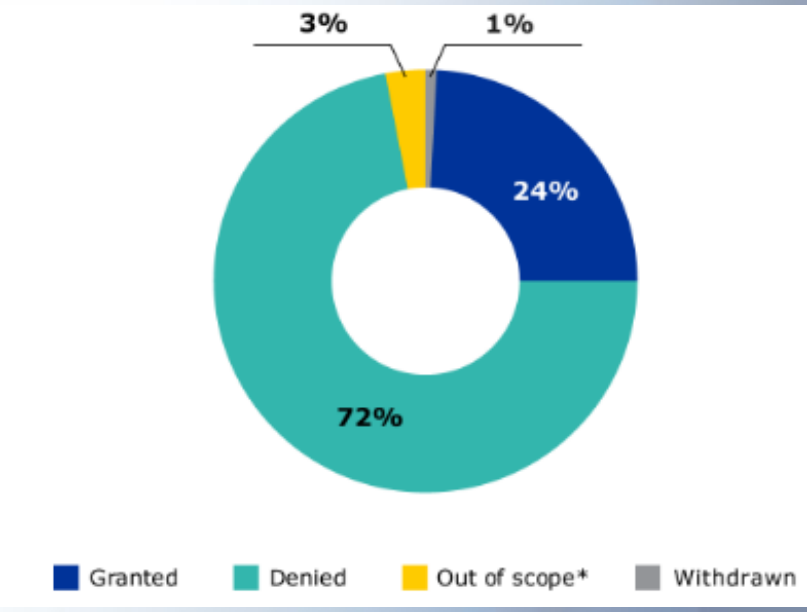
- Fee reductions

	Reductions: SME	Reductions: Non-SME
Protocol assistance (paediatric)	100%	75%
Protocol assistance (non-paediatric)	100%	100%
MAA	100%	10%
Inspections	100% (pre-MA) 90% (post-MA)	100% (pre-MA)
Post-authorisation, including annual fees	100% for 1st year	-

- EU Member States often have different (easier?) pricing and reimbursement pathway for orphan products
  - Long term incentive

EMA Priority Medicines (PRIME) scheme

- Criteria
  - May offer a major therapeutic advantage over existing treatments or benefit patients without treatment options
  - Need early clinical data
  - Very high hurdle
  - Cumulative recommendations to 27 Jan 2022
    (source EMA website, Feb 2022)



EMA PRIME scheme

- Incentives
  - Regular engagement with consistent Rapporteur and EMA throughout development programme ➡ builds knowledge ahead of MAA
  - Provide scientific advice involving additional stakeholders e.g. health technology assessment bodies
  - Potential for accelerated assessment of MAA
    - 150 days compared to 210 days

EMA Paediatric Investigation Plan (PIP)

- Carrot and a stick!
  - Stick = mandatory submission unless class waiver; PIP must be complied with for future submissions (MAA, variations) to be validated
  - Carrot = extension of supplementary protection certificate by 6 months (even if study results are negative)
  - Carrot = free scientific advice for paediatric questions
  - Should be submitted at end of adult PK studies

MHRA Innovative Licensing and Access Pathway

- ILAP - including the Innovation Passport
  - Aim is to accelerate time to market for NCE, biological medicines, new indications and repurposed medicines
    - Broader scope than EAMS (see later)
  - Opportunities for enhanced regulatory and other stakeholder input (e.g. NICE, SMC)
  - Apply early to mid-development so you can implement the recommendations

MHRA Innovative Licensing and Access Pathway

- Step 1 = apply for Innovation Passport
  - 3 criteria considered
    1. Condition is life-threatening or seriously debilitating or there is a significant patient or public health need
    2. Product is innovative or for significantly new indication or rare disease and/or other special populations or aligns with UK public health priorities
    3. Product has potential to offer benefits to patients (nonclinical data can be sufficient)
- Step 2 = Target Development Profile (TDP)
  - Roadmap is developed in conjunction with regulatory and access experts using a “toolkit”, examples
    - Adaptive inspections
    - Certifications (pre-review of certain parts of MAA)
    - Continuous Benefit Risk Assessment integrating Real World Evidence
    - Assisted patient recruitment (via CPRD)
    - Innovative and flexible licensing routes
    - Rapid clinical trial dossier pre-assessment

MHRA Innovative Licensing and Access Pathway

- ILAP - including the Innovation Passport
  - Statistics up to 28 Dec 2021 (Source: MHRA website, Feb 2022)

    - Total applications received (cumulative): 71
    - Numbers of Innovation Passports awarded: 41
    - Numbers of Innovation Passports not awarded: 7
    - Applications in process: 22

MHRA Early Access to Medicines Scheme (EAMS)

- Provides access prior to receiving MA when there is a clear unmet medical need for a life-threatening or seriously debilitating condition
- MHRA will provide a scientific opinion on B:R valid for one year and then renewed
- Two steps
  - Promising Innovative Medicine (PIM) designation
    - Based on early clinical data
  - EAMS scientific opinion
    - Based on completed Phase 3 or exceptionally, Phase 2 studies
    - Opinion supports the prescriber and patient to decide whether to use the product before it is approved
    - Public Assessment Report published

MHRA EAMS

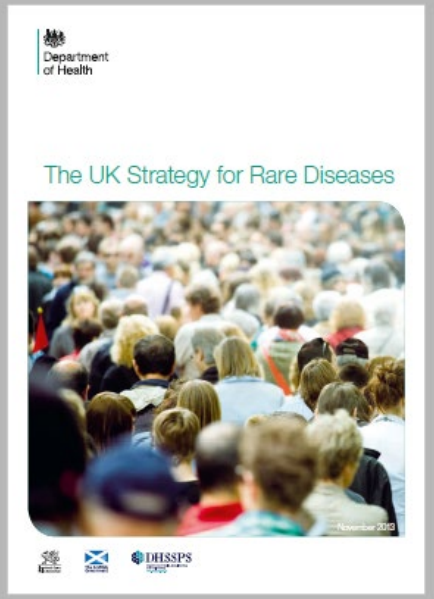
- Statistics (Source: MHRA website, Feb 2022)

EAMS step I PIM designations - April 2014 to October 2021	
Applications received	143
PIM designations granted	110
PIM designations refused	21
PIM designations withdrawn	4
PIM designations pending	8

EAMS step II applications - April 2014 to October 2021	
Applications received	56
Opinions awarded	42
Opinions refused	3
Opinions Withdrawn	8
Opinions pending	3

MHRA Orphan Medicinal Products

- Incentives offered, similar to EU - market exclusivity, reduced/zero MAA fee
  - But no requirement to apply for orphan designation during development (and maintain)
- Decision made at time of MA
- Designation can facilitate pricing and reimbursement



Conclusion

- Consider regulatory activities early in development
- Consider the applicability of your programme to incentive opportunities
- Maximise incentives by exploiting them as early as possible
  - Saving money across the development lifecycle
  - Enhancing the value of your asset
    - Strengthen the data package for MAA
    - Optimising pricing and reimbursement
    - Attractiveness to investors / out-licensing partners

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Thank you for your attention

Questions will be taken at the end of both presentations

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