Regulatory Aspects in Europe (EMA) – Considerations in Medicinal Discovery & Development

- Regulatory approval & evaluation processes
- Dialogue opportunities with EMA
- Information to be submitted to EMA
- Discovery & Development processes and data generation
- Successful fundraising – some considerations
- Start-up challenges – a personal perspective
Regulatory Approval Processes (EU)

- Local authority
- Mutual recognition (decentralized procedure)
- **Centralized marketing authorisation by EMA**
How EMA evaluates Medicines for Human Use

1. **Pre-submission meeting**
   - 6-7 months before submission
   - Avoid unnecessary delays

2. **Guidance**
   - Prior assessment

3. **Assessment**
   - Thorough evaluation of the data provided
   - Decision on whether the medicine is safe, effective and of good quality and is therefore suitable for use in patients
Who is involved in the Assessment?

**CHMP (Committee for Medicinal Products for Human Use):**

- Assesses applications submitted by medicine developers
- Composed of one member and an alternate from each EU Member State (+ Iceland and Norway) & up to five EU experts in relevant fields, who are nominated by the European Commission.
- Rapporteur & co-rapporteur assessment teams conduct the scientific evaluation independently of each other

**Other**

- CAT (Committee for Advanced Therapies)
- PRAC (Pharmacovigilance Risk Assessment Committee)
- PDCO (Paediatric Committee)
- COMP (Committee for Orphan-designated Medicines)
How does the Evaluation Process look like?

- Initial assessment
- Further assessment
- Further Consultations
- Final discussions/adoption of opinion
- Possible re-examination

Day 120 (3-6mo)

Day 180 (1-3mo)

Reduced to 150 days, if accelerated approval is granted
What Dialogue Opportunities are offered by EMA?

- **Discovery / synthesis**
  - Screening on pharmacological activity
  - Purification
  - Formulation

- **Toxicology**
  - Pharmacology
  - Pharmacodynamics (Phase I)
  - Pharmacokinetics (Phase I)
  - Dose finding / exploratory (Phase II)
  - Confirmatory Efficacy / Safety (Phase III)

- **REVIEW**
  - Therapeutic use (Phase IV)
  - Post-authorisation efficacy/Safety studies
  - Specific obligations
  - Pharmacovigilance

- **Paediatric requirements and incentives**
  - Paediatric investigation plan (PIP), deferral or waiver, PIP modification, MA compliance, scientific advice, and post-authorisation requirements.

- **PRIME Scheme**
  - Reinforced scientific and regulatory support. Early rapporteur appointment and early identification of candidates for accelerated assessment.

- **Orphan Drug Designation and incentives**
  - Orphan designation/incentives for products being developed and authorised for rare conditions.

- **Certification procedure for ATMPs**
  - Scientific evaluation of quality/ non clinical data.

- **Scientific Advice/Protocol Assistance**

- **Classification as ATMPs**
  - Confirmation that the product falls within the definition of an advanced therapy medicinal product.

- **Innovation Task Force**
  - Briefing meetings. Provision of guidance early in the development process.
Innovation Task Force

**Multidisciplinary group** (scientific, regulatory and legal competences) to ensure

• Coordination across the Agency
• Provide a forum for early dialogue with applicants on innovative aspects in medicines development especially micro, small and medium-sized enterprises, academics and researchers
  o Impact on current scientific, legal, regulatory requirements?
  o Need for specialized expertise?
  o Eligibility to agency procedures relating to research and development?

**Recently discussed topics:**

• Nanomedicines, biomaterials, modelling and simulation, mobile health ...
## Scientific Advice

### When it is useful
- Development of innovative medicine
- Deviation from scientific guidelines
- Limited knowledge about medicine regulation

### How it works
- Scientific advice by responding to **specific** questions on the development of a particular medicine
- Prospective in nature
- No-pre-evaluation
- Not legally binding

### Types of questions addressed
- Quality aspects
- Non-clinical aspects
- Clinical aspects
- Methodological issues

### Other forms of scientific advice
- Designated orphan diseases protocol/authorisation criteria assistance
- Parallel scientific advice with the FDA
- Parallel consultations with HTA
- Tailored scientific advice biosimilars
Rare Diseases - Overview

• Between 5,000 and 8,000 rare diseases exist affecting 6-8% of the population in total (27-46 million people in the EU)

• 80% of rare diseases have identified genetic origins
  o Affect 3-4% of births
  o Other diseases are due to degenerative and proliferative causes.

• Symptoms of some rare diseases may appear
  o At birth or in childhood (e.g. spinal muscular atrophy, lysosomal storage orders, cystic fibrosis)
  o During adulthood (e.g. renal-cell carcinoma, glioma, acute myeloid leukaemia).
Orphan Designation – Qualification Criteria

• Treatment, prevention or diagnosis of a **life-threatening or chronically debilitating disease**

• **Prevalence** in the EU not more than 5 in 10,000* or it must be unlikely that marketing of the medicine would generate sufficient returns to justify the investment needed for its development

• No satisfactory method of diagnosis, prevention or treatment of the condition concerned can be authorised, or, if such a method exists, the medicine must be **significant benefit** to those affected by the condition**

*FDA Prevalence: <200,000
**not required by FDA
Orphan Designation – Assessment

- **COMP**: granting by European Commission
- Evaluation process takes max. **90 days**
- Close collaboration with
  - FDA
    - Information sharing
    - Common procedures (application format, annual reports on the status of development of designated orphan medicines)
    - EMA encourages applicant to at the same time seek for scientific advice by FDA
Orphan Designation - Incentives

• **Protocol assistance** (scientific advice specifically for orphan medicines) at reduced charge and with no restriction on the number of times a sponsor can request protocol assistance

• Access to **centralized procedure**

• **10 years market exclusivity** (extended by 2 years for medicines that also have complied with an agreed paediatric investigation plan granted at the same time of the orphan medicine designation)

**SMEs:**

  o Administrative and procedural assistance

  o Fee reductions (protocol assistance, marketing-authorisation applications, inspections prior authorisation etc.)
PRIME (Priority Medicines)

**Purpose:**
- Enhance support for the development of medicines that target an unmet medical need.

**Requirement:**
- Medicine has to show its potential to benefit patients with unmet medical needs based on early clinical data; **SMEs/ academic sector can apply earlier** on the basis of compelling non-clinical data and tolerability data from initial clinical trials.

**Benefits for applicants**
- Dedicated contact point (rapporteur from CHMP or CAT appointed by agency)
- Kick-off meeting for guidance on the overall development plan and regulatory strategy
- Scientific advice at key development milestones
- Accelerated assessment at the time of application for marketing authorisation.
PRIME Eligibility Requests

Therapeutic Areas (cumulative recommendations up to the latests CHMP meeting)

- Oncology: 19
- Neurology: 5
- Infectious diseases: 6
- Endocrinology-Gynaecology-Fertility-Metabolism: 6
- Haematology-haemostaseology: 13
- Immunology-rheumatology-transplantation: 3
- Cardiovascular diseases: 2
- Pneumology-allergology: 12
- Gastroenterology-Hepatology: 2
- Dermatology: 2
- Ophthalmology: 3
- Vaccines: 4
- Uro-nephrology: 1
- Psychiatric: 2
- Neonatology-paediatric intensive care: 2
- Diagnostic: 1
- Musculo-skeletal system: 1
- Oto-rhino-laryngology: 1

Type of applicant

- SME: 33
- Other: 93

Recommendations adopted by 23 July 2020

* Out of scope applications are not included in the breakdown by type of applicant or by therapeutic area
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<th>Headcount: annual work unit (AWU)</th>
<th>Annual turnover</th>
<th>Annual balance sheet total</th>
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<td>&lt; 250</td>
<td>≤ EUR 50 million</td>
<td>≤ EUR 43 million</td>
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<td>&lt; 50</td>
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<td>Micro</td>
<td>&lt; 10</td>
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<td>≤ EUR 2 million</td>
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Micro, small or medium-sized Enterprise – User Guide

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ANNEXE 1

National provisions for SMEs applicable to the pharmaceutical sector

Appendix
What Information needs to be submitted?

• The medicine’s mechanism of action, as investigated in laboratory studies;
• How the medicine is distributed in, and eliminated by the body;
• The medicine’s side effects observed in patients, including in special populations such as children or the elderly;
• The quality of the medicine including its chemical and physical properties, such as its stability, its purity and biological activity;
• Compliance with international requirements for laboratory testing, medicine manufacture and conduct of clinical trials (GXP);
• The group of patients the medicine is proposed to treat, and whether there is an unmet medical need addressed by the medicine;
• The benefits observed in the patient group at whom the medicine is aimed;
• The way risks will be managed and monitored once the medicine is authorised;
• What information is intended to be gathered from follow-up studies after authorisation.
Data Generation and Documentation starts early

- **Discovery**
  - Target Hits
  - Lead(s)
  - Candidate(s)

- **Preclinical Development**
  - PoC
  - Target Product Profile
    - Quality
    - Pharmacokinetics & Metabolism
    - Pharmacology
    - Toxicology

- **Clinical Development**
  - CTA
  - IND
  - Clinical Development
    - Phase I/II/III Quality
    - Non-clin.

- **Increase of Complexity**
- **Cross-disciplinary**
What to consider in Medicinal Product Discovery & Development

- Have a drug candidate selection strategy to minimize attrition
R&D – Analysis of Attrition

What to consider in Medicinal Product Discovery & Development

- Define a development goal
- Define a development strategy & plan
  - Be aware of regulatory requirements and create relevant data and proper documentation
  - Think cross-disciplinary & specific expertise
  - Be aware of the risks you take and consider risk mitigation strategies
- Consider potential designation options & incorporate authority contacts into your strategy
What to consider for successful Fundraising?

**Demonstrate the quality of research/ discovery & development**

- Valuable target addressing a medical need
- Solid drug development candidate identification & selection process
- Preclinical PoC

**Show that you know which direction to go**

- Show the overall pathway to approval/ exit
- Demonstrate in detail what you would like to achieve with the investment and how this adds to your overall goal
- Show that you understand regulatory requirements
- Show that you are aware of your projects strengths & weaknesses
What to consider for successful Fundraising? (cont.)

**Demonstrate how you are to realize your goal**

- Describe how you are to operate: Who is to take responsibility for what
- Identify collaboration partners/ external development expertise
- Show that you are aware of the complexity/ cross-disciplinary needs and proper project management

**Demonstrate the commercial potential of your product**

- Market size and positioning towards competition
What are the biggest Challenges for Start-ups? – A personal perspective

• Consider regulatory requirements early

• Accept the importance of proper documentation

• Understand the difference between academic research and drug development and act respectively

• Be ambitious & realistic about anticipated achievements
Any Questions or Comments?

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