EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

MAA pre-submission issues and EMA meeting opportunities

Session 4: Regulatory issues in the run-up to dossier submission (part I)

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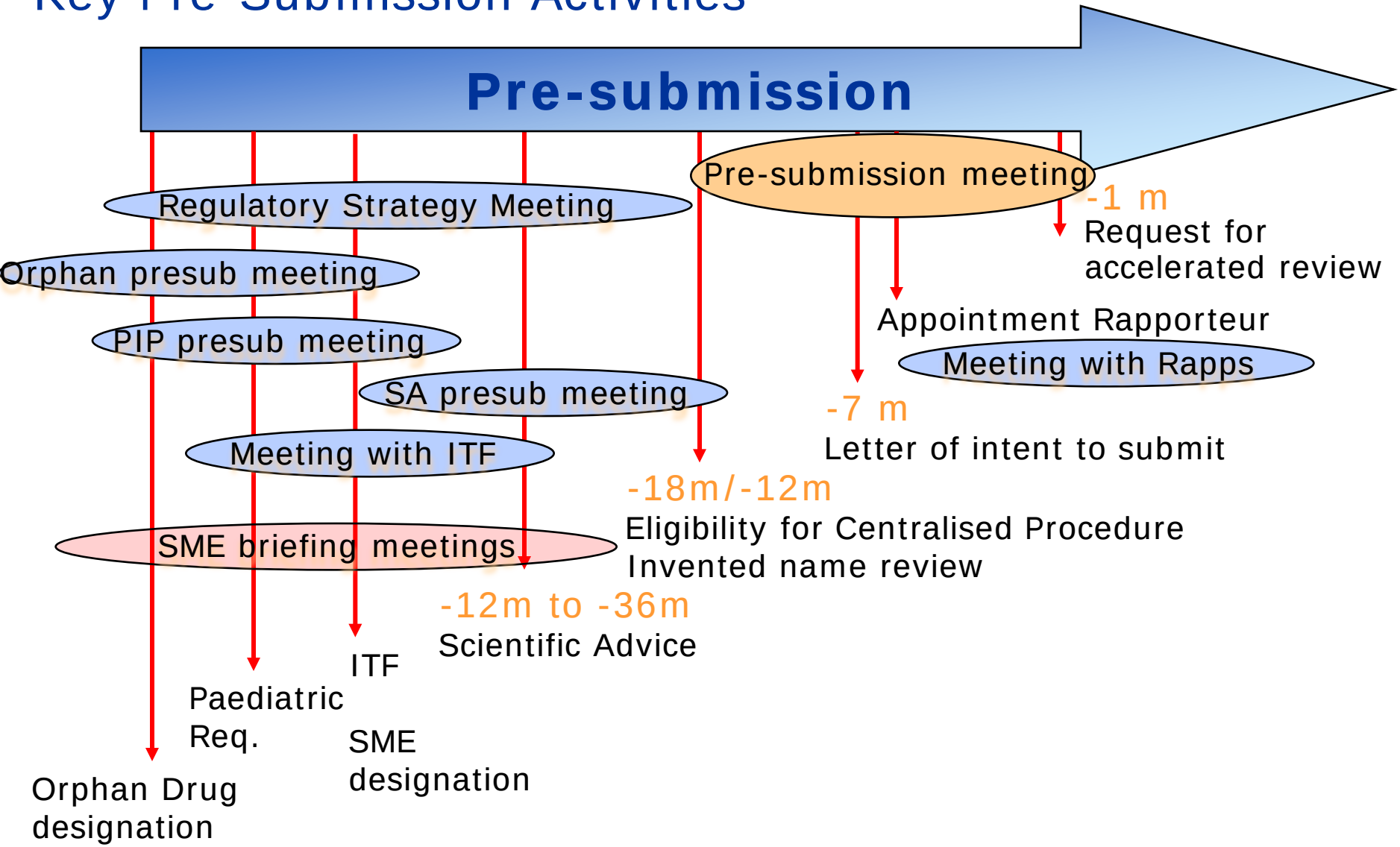
An agency of the European Union

Key Pre-Submission Activities



SME designation

- SME Office
  → facilitate communication with SMEs
- SME Designation
- Practical or procedural enquiries
  → dedicated contact
- Monitor applications

Workshops and Training Sessions for SMEs

Choice of legal basis

- Important driver for the development of the medicinal product
- Dossier requirements linked to legal basis
- Full/Stand-alone submission:
  Articles 8(3), 10(a), 10(b) of Directive 2001/83/EC
- Submission that use a reference medicinal product:
  Articles 10(1), 10(3), 10(4) & 10(c) of Directive 2001/83/EC
- Dossier requirement = Annex I of the Directive

→ Mix & Match approach not possible

'Bible': Pre-submission procedural guidance (Q&A) and NtA

Regulatory advice in the centralised system

- Early possibility to engage with the Agency on regulatory questions
- Frequently encountered topics:
  - Dossier requirements vis-à-vis chosen legal basis
  - Eligiblity to the centralised system
  - Multiple applications
  - OTC switch
  - Reference medicinal product
  - Orphan exclusivity

Regulatory Strategy Meeting

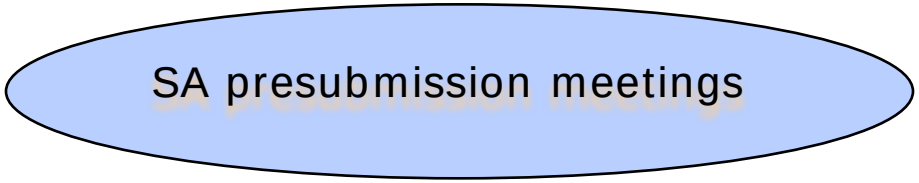
- To request: email SME office

Scientific Advice & Protocol Assistance (1)

- Independent from submission route
- Appropriate tests and studies
  → no major objections regarding the design of the tests/studies
- **Answers questions** posed by companies
- Current scientific knowledge
- Based on the documentation provided by the company
- Does not substitute for the industry's responsibility for the development of their products
- Not legally binding on the Agency

Scientific Advice & Protocol Assistance (2)

- Answers to questions relating to the criteria for authorisation of an orphan medicine, including (demonstration of significant benefit; similarity or clinical superiority over other medicines)
- At any stage of development of a medicine
  - conditional approval
  - exceptional circumstances
  - post-authorisation measures
  - post-approval phase



Paediatric requirements

- Only if either Art. 7 or 8 of the paediatric legislation applies
- Dependant on chosen legal basis
- PIP development starts at the end of PK studies (‘phase I’)
- PIP, class waiver, product specific waiver, deferrals

PIP presubmission meetings
via TC to all applicants

- Modifications after PIP is agreed

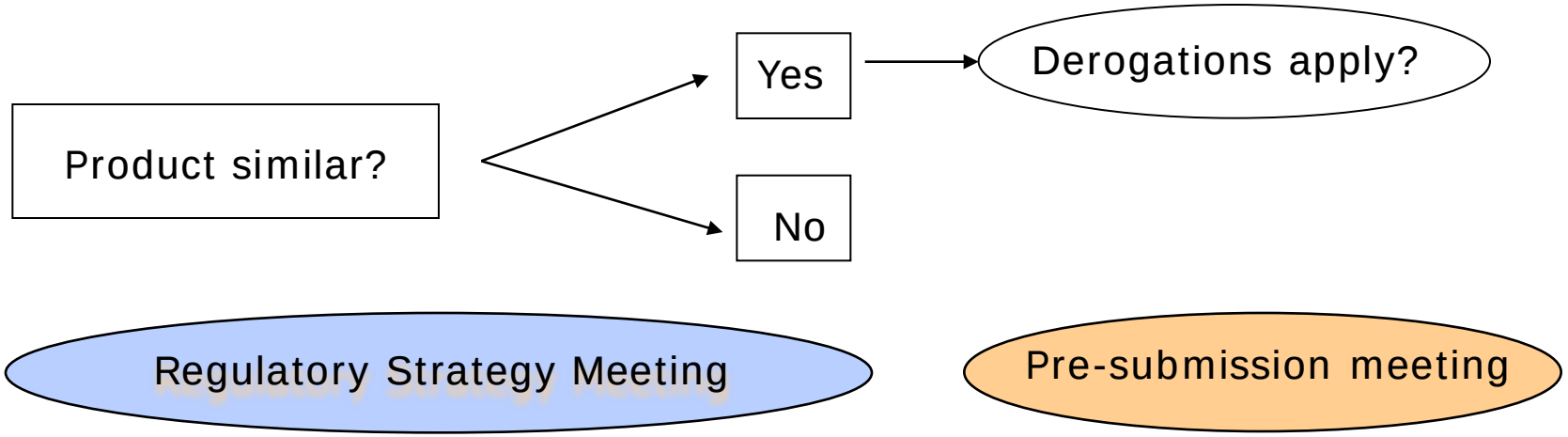
Orphan Designation

- Optional for medicinal products for human use
- Can be requested at any stage of development before MAA
- Sponsor can be either company or individual
- Established in the EEA (EU, Iceland,Lichtenstein, Norway)
- European Commission Decision before MAA submission
- Transfer
- Centralised procedure mandatory for orphans

Orphan designation presubmission meetings via TC

Orphan similarity check & Derogations

- Orphan designation can be granted for the same orphan indication to different sponsors
- First sponsor with MA for an orphan indication obtains exclusivity (for the therapeutic indication)
- Subsequent MAA for the same therapeutic indication:



GMP and PhV Inspections

- Any EU/EEA manufacturing site
  → EU manufacturing authorisation
- EU manufacturing authorisation relevant for the activities
- Sites outside the EU/EEA
  → equivalent to EU manufacturing authorisation
  → GMP standards/ready to pass inspection
- Batch release site in the EU/EAA established at submission
- New requirements for API importation as of 2nd July 2013 (!)
- QPPV established at time of submission

Pre-submission meeting

Eligibility

- Eligibility (mandatory or optional scope) to be requested / confirmed in ALL cases !
- 18 Months before planned submission
  or, at the latest 7 months - as part of 'Letter of Intent'
- Applicants to use only 1 main access criterion
- Concise **justification** to be provided
- 15 Days before CHMP meeting
- Reviewed by the CHMP

Letter of Intent to submit a MAA

- 18 – 4 months before filing (Monthly submission dates)
- Appointment of Rapporteur/Co-Rapporteurs
  - Appointment of Rapporteurs based on objective criteria
  - Use of best available expertise in EU in relevant scientific area
- Check of (Invented) Name
- Correspondence with Commission on proposed multiple applications (Art 82(1) of Regulation (EC) No 726/2004)

Pre-submission meeting

Ancillary requests

- (Extended) Data / Market Exclusivity
- Exceptional Circumstances
- Conditional Marketing Authorisation
- Accelerated Assessment
- New Active Substance status

Pre-submission meeting

Pre-submission meeting

- 6-7 Months before submission
- Discuss final **practical** & **regulatory** aspects of upcoming application
- Clarify application-specific issues not addressed on the EMA website
- Useful step to ensure that application will meet all requirements for **validation**
- **Strongly recommended**, even for experienced users of the centralised procedure

  → Reconfirm various administrative/procedural/legal issues; requirements may have changed

Meeting with Rapporteurs

PIP compliance check

For any measure agreed in a PIP and due at submission

Maximum 60 days procedure

PDCO review

Opinion only for full compliance check, otherwise EMA Letter

Compliance check needed before successful validation

Dedicated application form for compliance check

MAA Submission and Validation

- Applicant established in the EEA
- Dossier in line with chosen legal basis
- GxP requirements met
- Paediatric requirements met
- Orphan similarity clarified

→ successful Validation and Start of procedure

Human medicines
- Pre-authorisation
- Post-opinion
- Post-authorisation
- Product information
- Scientific advice and protocol assistance
- Scientific guidelines
- Innovation Task Force
- Regulatory and procedural guidance
- SME office
- Paediatric medicine
- Orphan designation
- Herbal products
- Referral procedures
- Article 58 applications
- Compassionate use
- Pharmacovigilance
- Advanced therapies
- Inspections
- Product defects and recalls
- Parallel distribution
- Pandemic influenza
- Non-pharmaceutical products
- New countries/EFTA
- Fees
- Veterinary medicines

Home ▸ Regulatory ▸ Human medicines

Human medicines

This section of the website provides information for companies and individuals involved in developing and marketing medicines for use in the European Union.

For further information on EU legislation and procedures for the regulation of medicines, see also Volumes 1-4 and 9-10 of the rules governing medicinal products in the European Union.

Important note on document formats: All Microsoft Office documents submitted to the European Medicines Agency must be in a format compatible with MS Office 2003. Office 2007 and Office 2010 formats cannot currently be accepted.

This section contains the following topics:

- Pre-authorisation
- Post-opinion
- Post-authorisation
- Product information
- Scientific advice and protocol assistance
- Scientific guidelines
- Innovation Task Force
- Regulatory and procedural guidance
- SME office
- Paediatric medicine
- Orphan designation
- Herbal products
- Referral procedures
- Article 58 applications
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- New countries/EFTA
- Fees

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/landing/human_medicines_regulatory.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac058001ff89

Human medicines
Pre-authorisation
Q&A: Presubmission guidance
Questions 1-10
Questions 11-20
Questions 21-30
Questions 31-40
Questions 41-50
Questions 51-60
Q&A: Generic / hybrid applications
Q&A: Similar biological products
Templates for assessors
Templates for industry
Submission dates
Guidance
Post-opinion
Post-authorisation
Product information
Scientific advice and protocol assistance
Scientific guidelines
Innovation Task Force
Regulatory and procedural guidance
SME office
Paediatric medicine

Presubmission guidance: questions and answers

This section of the website contains questions that marketing-authorisation holders (MAHs) may have related to presubmission guidance for innovative medicines. It provides an overview of the European Medicines Agency's position on issues that are typically addressed in discussions or meetings with MAHs.

These pages are updated regularly to reflect new developments, to include guidance on further pre-authorisation procedures and to reflect the implementation of new European legislation. Revised topics are marked 'New' or 'Rev.' on publication.

These questions and answers have been produced for guidance only and should be read in conjunction with the rules governing medicinal products in the European Union, volume 2, notice to applicants.

All of the information previously available on the European Commission's website in chapter 7 of the notice to applicants (volume 2A) related to marketing-authorisation applications for centrally authorised medicines is now primarily available in these questions and answers. For details, see the table below:

▸ European Medicines Agency / European Commission website references substituting information previously available in notice to applicants – chapter 7 of volume 2A

MAHs must in all cases comply with the requirements of Community legislation. Provisions that extend to Iceland, Liechtenstein and Norway by virtue of the European Economic Area agreement are outlined in the relevant sections of the text.

PDF version of questions and answers

European Medicines Agency pre-authorisation procedural advice for users of the centralised procedure (26/03/2013)

Related information

Presubmission request form (15/03/2010)

Explanatory note on the presubmission request form (05/02/2010)

Contact point:

Product and Application Business Support
Tel. +44 (0)20 7418 8433
Fax +44 (0)20 7523 7051
E-mail: pa-bus@ema.europa.eu

Presubmission guidance: Topics

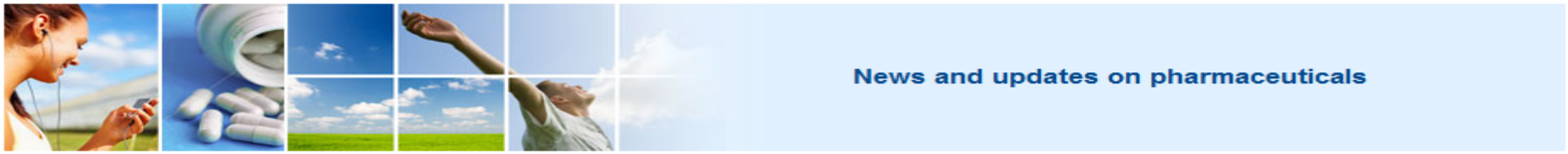
These questions and answers on **presubmission guidance** address these topics:

Questions 1-10
- Eligibility
- Legal basis and status
- Invented names
- Submission dates
- Rapporteurs
- Accelerated assessment
- Multiple applications
- Orphan aspects

Questions 11-20

Questions 31-40
- Application numbers
- European Union (EU) numl
- Good-manufacturing-pract good-clinical-practice inspe
- Quality Review of Docume information
- Presubmission meetings
- Exceptional circumstances
- User consultations
- Braille

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/landing/human_medicines_regulatory.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac058001ff89



Useful links

EudraLex

Community Register

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Pharmaceutical Committee

http://ec.europa.eu/health/documents/eudralex/index_en.htm

Go back to » News and updates on pharmaceuticals » Eudralex » Vol 2: Notice to Applicants Human

EudraLex - Volume 2 - Pharmaceutical Legislation Notice to applicants and regulatory guidelines medicinal products for human use.

Volume 2 of the publications "The rules governing medicinal products in the European Union" contains a list of regulatory guidelines related to procedural and regulatory requirements such as renewal procedures, dossier requirements for Type IA/IB variation notifications, summary of product characteristics (SPC), package information and classification for the supply, readability of the label and package leaflet requirements.

The Notice to Applicants below has been prepared by the European Commission, in consultation with the competent authorities of the Member States and the European Medicines Agency (EMA) . This Notice has no legal force anddoes not necessarily represent the final views of the Commission. In case of doubt, therefore, reference should be made to the appropriate Community Directives and Regulations.

The Notice to Applicants was first published in 1986 and is regularly updated.

Volume 2A - Procedures for marketing authorisation

- Chapter 1 - Marketing Authorisation (updated version - November 2005) **(169 KB)**
- Chapter 2 - Mutual Recognition (updated version - February 2007) **(526 KB)**
- Chapter 3 - Community Referral (updated version - September 2007) - PDF Version of Chapter 3 **(117 KB)** - Word Version of Chapter 3 **(211 KB)**
- Chapter 4 - Centralised Procedure (updated version - Avril 2006) **(162 KB)**
- Chapter 5 - Guideline on the operation of the procedures laid down in Chapters II, III and IV of Commission Regulation (EC) No 1234/2008 of 24 November 2008 as well as on the documentation to be submitted pursuant to these procedures. - (February 2010) **(805 KB)**
  - Procedural note **(9 KB)** concerning the application of articles 28(3), 36 and 37 of regulation 1901/2006 (August 2012)
  - Procedural note **(9 KB)** concerning the Guideline on the operation of the procedures laid down in chapters II, III, and IV of commission regulation (ec) 1234/2008 of concerning the examination of variations to the Terms of Marketing Authorisations for Medicinal Products for human use and veterinary medicinal products (March 2011)