1st EMEA Workshop for SMEs

"Navigating the Regulatory Maze"

London, 2 February 2007

Pre-Submission Issues & EMEA meeting opportunities

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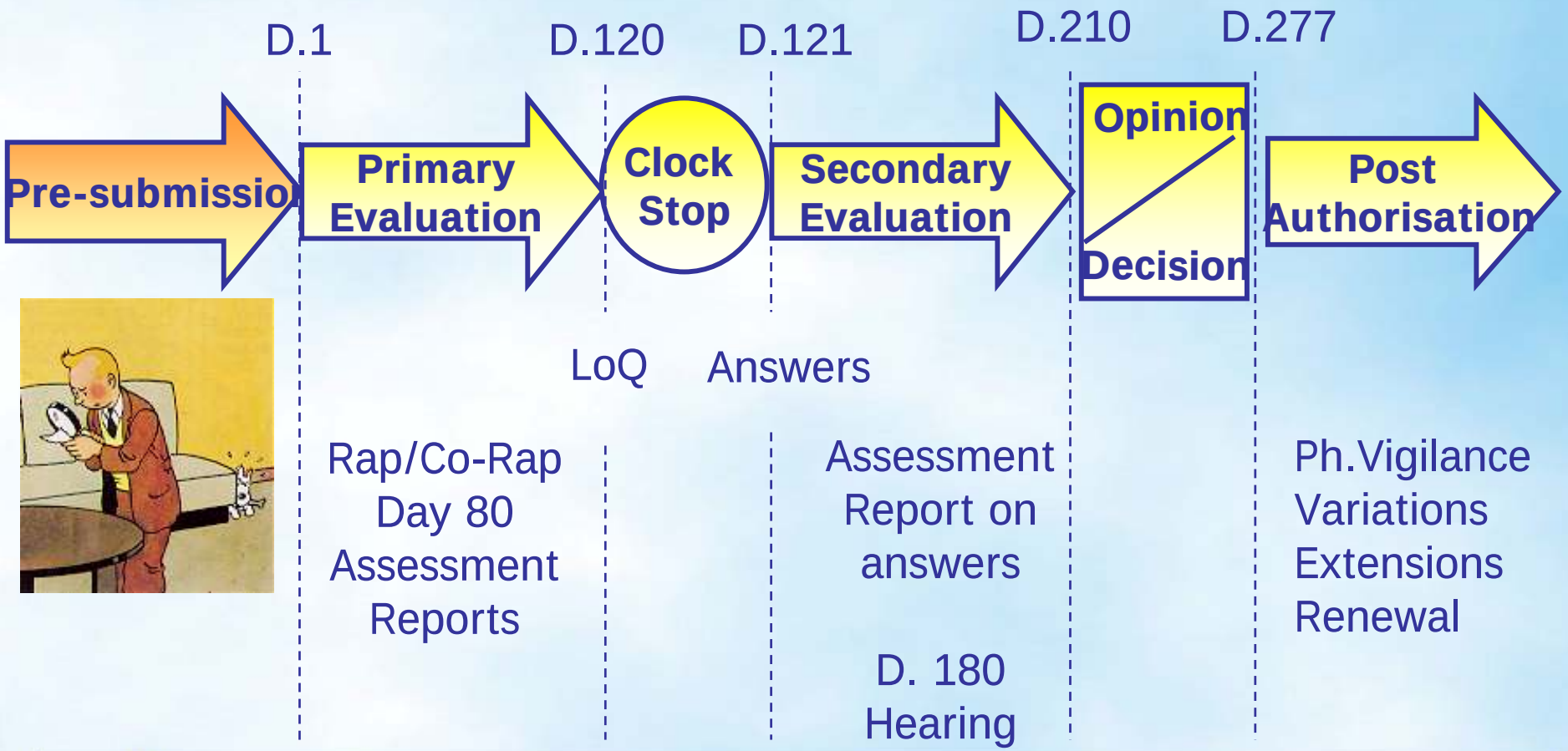
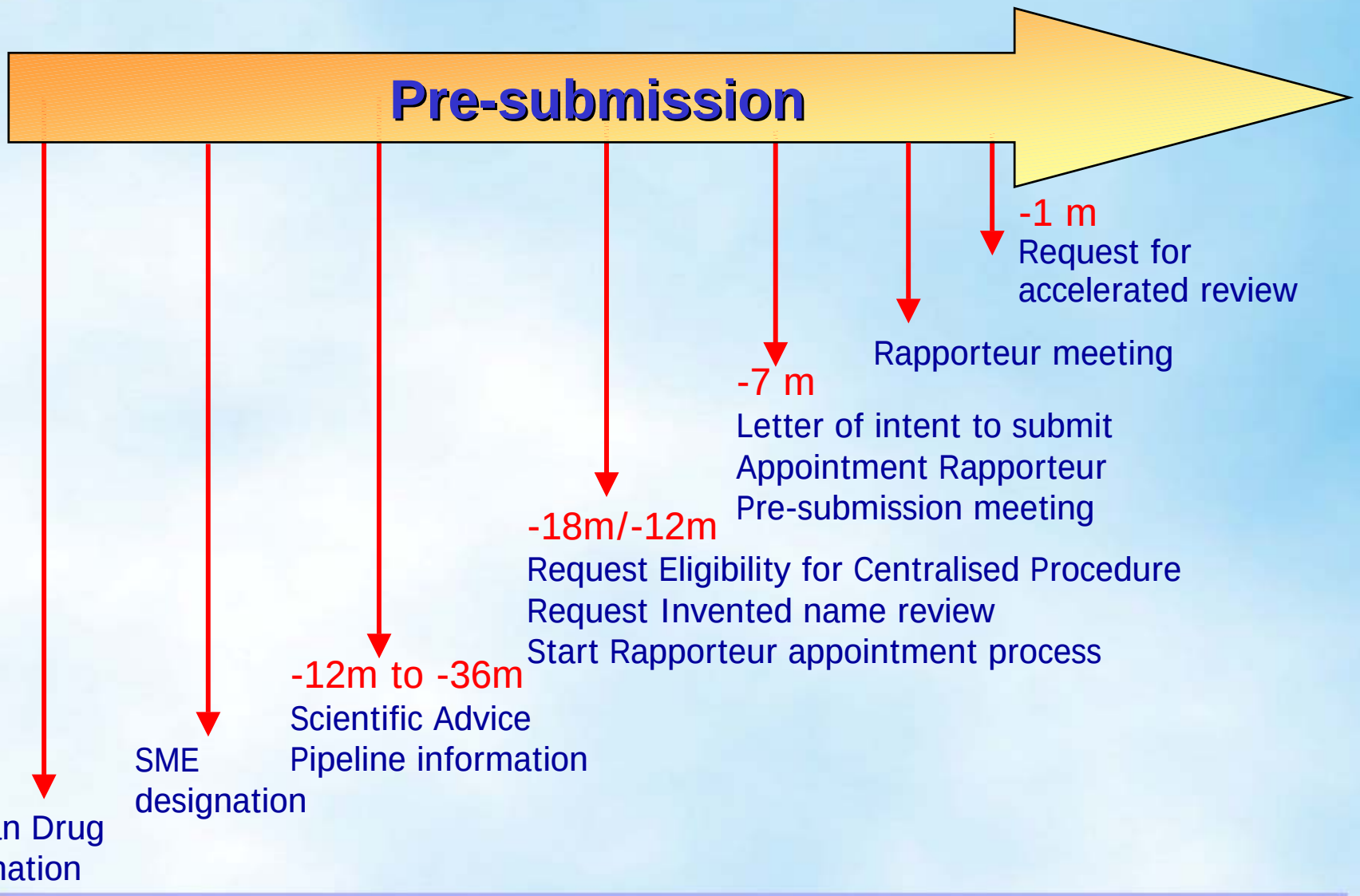
Content

- Overview of key pre-submission steps
- Eligibility to centralised procedure
- Rapporteurs appointment
- Invented name review
- EMEA Pre-submission meetings
- Rapporteur meetings

Overview of Centralised Procedure: Timetable



Key Pre-Submission Activities



Pipeline information

- Forecasting SME MA Applications helps EMEA **planning** processes
- The EMEA must be able to accurately forecast the content and status of the EU pharmaceutical pipeline (0-5yrs) in order to:
  - Financially plan and budget
  - Recruit and allocate staff in view of upcoming workload
  - Anticipate advances in new technologies and scientific fields
  - Allocate Rapporteur and Co-Rapporteur to particular MAA
- SME companies should notify the EMEA of a **draft submission date as early as possible** (SME designation, or Scientific Advice)
- EMEA will ask for periodic updates until letter of intent to submit
- Managed by: Tom Cardy: Business Pipeline Manager
  020 7523 7446
  tom.cardy@emea.europa.eu
- Or pass information to SME Office

Eligibility to the CP "Mandatory Scope"

Art. 3(1) of Regulation (EC) No 726/2004 & its Annex		
Indent 1	**Indent 3**	**Indent 4**
"Biotech" products • Recombinant DNA technology • Controlled gene expression • Monoclonal AB	**"Mandatory therapeutic Classes"** New active substance for: • AIDs • Cancer • Neurodeg. disorders • Diabetes	**Orphan Designated Medicinal Products**

EMEA "guideline on therapeutic areas within the mandatory scope of the centralised procedure for the evaluation for marketing authorisation applications with reference to Art.3 point 3 of Annex of Regulation (EC) No 726/2004" (EMEA/282954/2005)

“Optional Scope”

Art. 3(2) of Regulation (EC) No 726/2004			
Art. 3(2)(a)	Art. 3(2)(b)		
New Active Substances	Significant Innovation Therapeutic Scientific Technical	OR	Interest of Patients at Community Level

Draft “Guideline concerning the optional scope of the centralised procedure in accordance with Art. 3(2)(b) of Regulation (EC) No No 726/2004” (Pharmacos web)

Art. 3(3) **Generic** of a product authorised via EMEA

Eligibility Request

Eligibility 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 1 main access criterion
  (except possible combination for Art.3(2)(b) significant innovation)
- Concise **justification** to be provided + draft SPC
- 15 Days before CHMP meeting

Reviewed by EMEA → Discussion & agreement by CHMP

Rapporteur & Co-Rapporteur Appointment

- New Legislation no longer refers to Applicant's preferences or equal distribution of workload
- Appointment of Rapporteurs based on **objective criteria**
  → Use of best available expertise in relevant scientific area
- Criteria + appointment process detailed in EMEA guidance:
  "CHMP rapporteur/co-rapporteur appointment: principles, objective criteria and methodology" (EMEA/124066/2005)
- Appointment process = **two-phase** approach
  1st phase: Pre-awareness step
  2nd phase: Appointment of Rap. & Assessment teams

Appointment Process

1st Phase

18 months before submission

Based on pipeline & filing info
→ EMEA informs CHMP & Heads of Agencies; twice yearly

CHMP: expression of interest & availability of scientific competences

Allow resource planning

2nd Phase

7 months before submission

Following applicant's letter of intent
→ 1 month appointment process

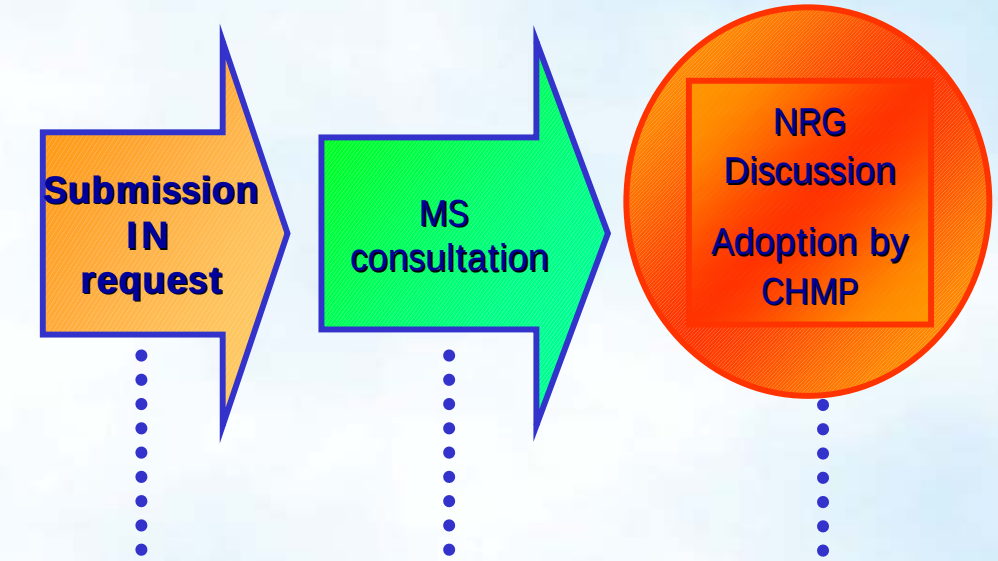
CHMP members submit nominations for Rap/Co-Rap + assessment teams

CHMP chair proposes Rap/Co-Rap nominations based on objective criteria → adopted by CHMP → applicant informed

Invented Name Review

- **Single name** for Centrally Authorised Products in whole EU
- Proposed invented name to be checked if it could create a public-health concern or potential safety risk in EU member states
- invented Name Review Group (**NRG**) set-up at EMEA
  Monthly meetings at EMEA
  Representatives from EMEA, member states, EC + experts (e.g. WHO)
- Review criteria are detailed in:
  "Guideline on the acceptability of invented names for human medicinal products processed through the centralised procedure (CPMP/328/98)"
- **Check** to be requested **12-4 months before** submission of applicat.
  Monthly submission dates published on EMEA website
- Review process & Invented Name submission form are described in
  "EMEA Pre-Submission Guidance" (Q&A 4)

Invented Name (IN) Review Process



- Submission of new name, or
- Justification for retaining proposed name
- New name or justification reviewed by NRG
- MAA can present matter to CHMP (exceptional)
- CHMP Opinion using: 'Common/scientific name + MAH'

- Name can be used for MA

up to 4 INs/appl. 4 - 6 months prior MAA (max 12 months before)

Objections / comments on grounds of safety concerns or other

Review of objections received based on IN guideline

Letter of Intent

- Formal letter from Applicant notifying CHMP of their intention to submit an application via the Centr. Procedure
- Information on upcoming application to be provided e.g. **date**, legal basis, SPC, intention to request conditional MA, batch release info, use of ASMF ....
  → Full list: see NTA Vol 2A Chapter 4 (Pharmacos website)
- Include request + justification for Eligibility, if not yet done before
- Will trigger 2nd phase of **Rapporteur** appointment
- Letter to be sent to CIG (Central Information Group)

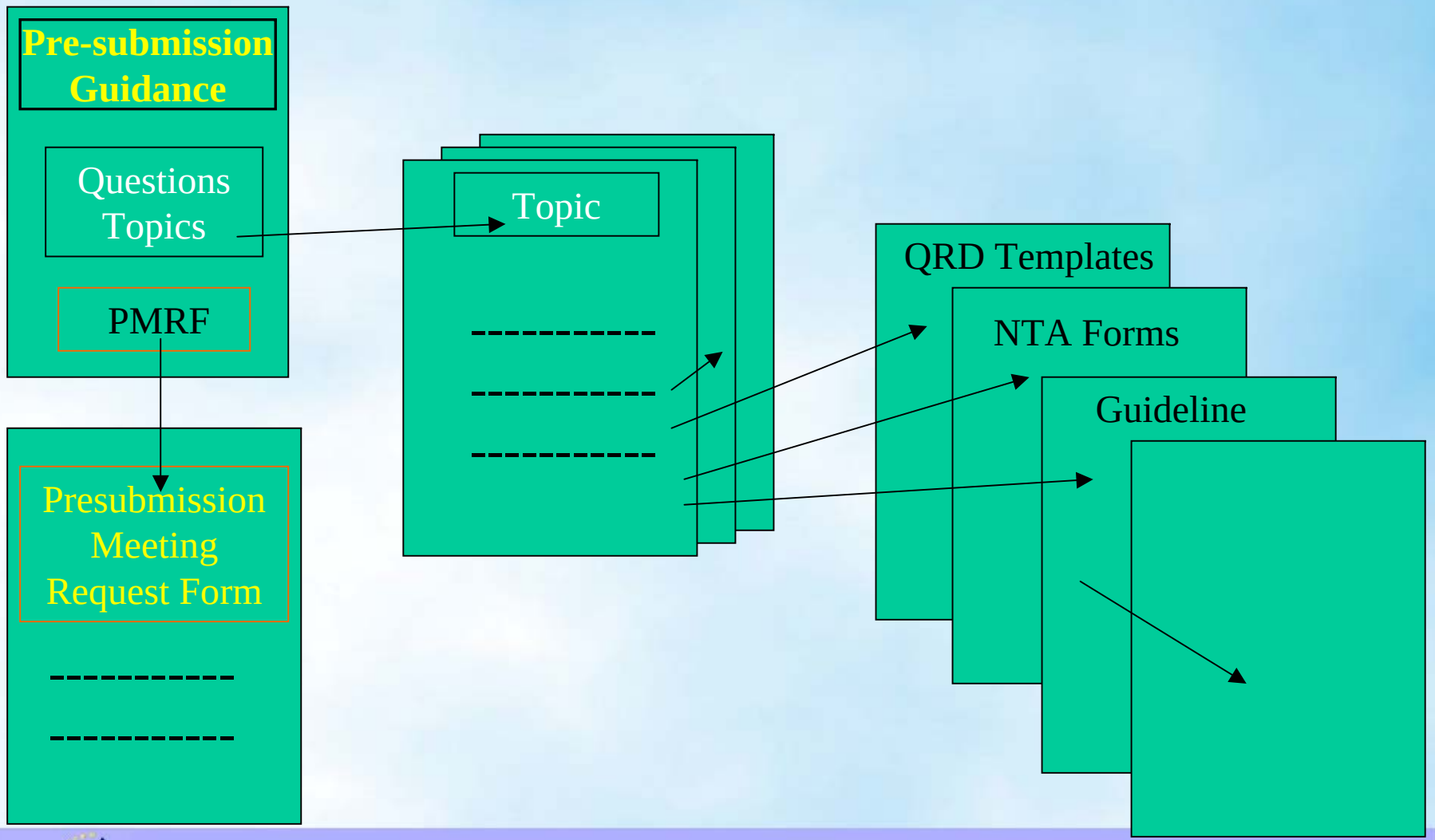
  h-cig2@emea.europa.eu

EMEA Pre-submission Guidance

- Answer to **frequently asked questions** from users of the Centralised Procedure.
- Overview of important regulatory, procedural issues to be considered when preparing MA application
- Includes links to useful reference documents, templates, forms etc ...
- Frequently updated by the EMEA
- **Separate** document for **generic/hybrid** applications, providing specific guidance on issues, timeframes ... in relation to such applications

  "EMEA guidance for users of the centralised procedure for generics/hybrid applications" (EMEA/CHMP/225411/2006)

EMEA Pre-submission Guidance

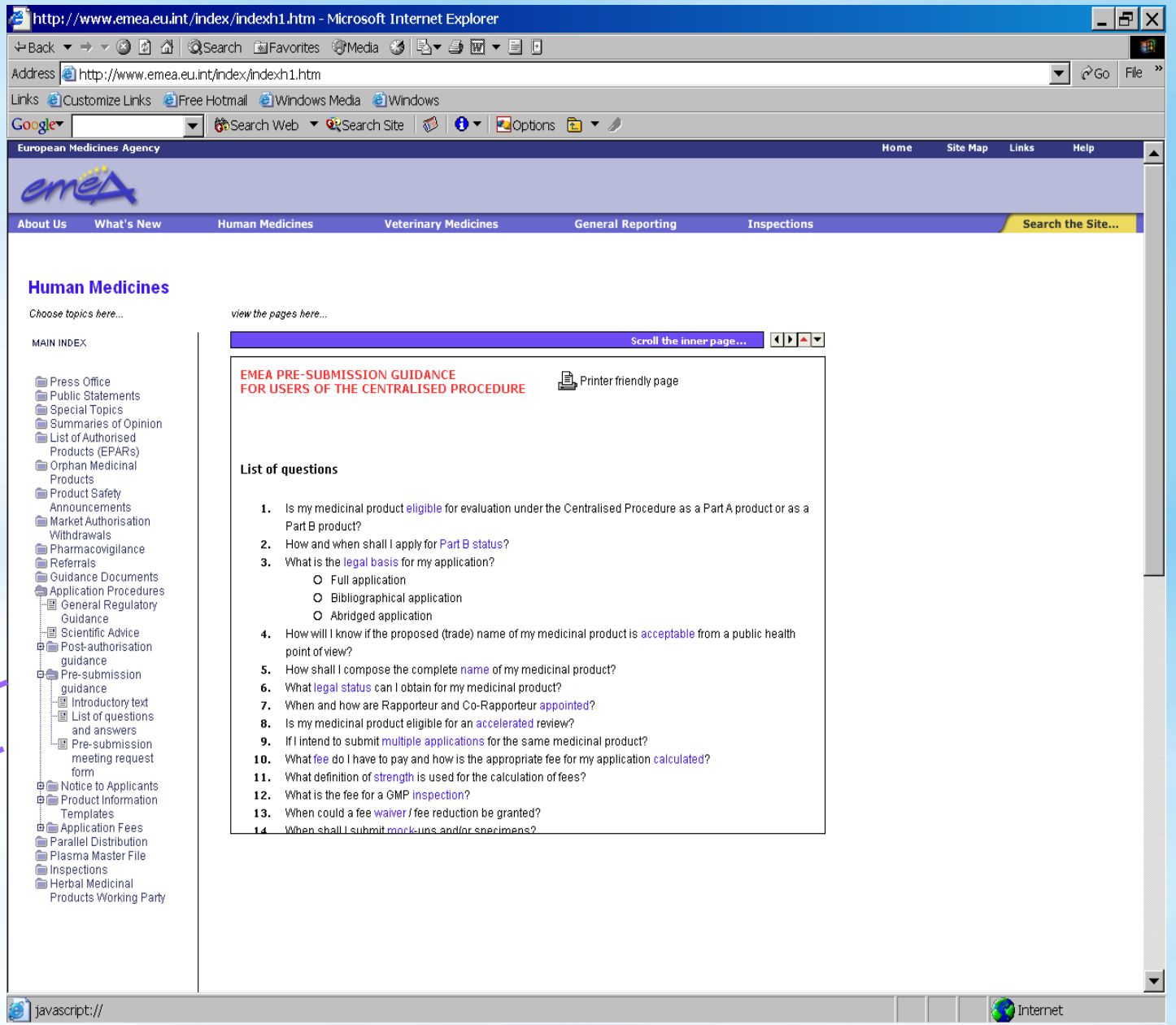


Human Medicines

Application Procedures

PSM Guidance

PSM Request Form



EMEA Pre-submission Guidance
(example topics)

- When and how are Rap/Co-Rap appointed?
- How, when and to whom shall I submit my application?
- When can I expect a GMP inspection?
- How is the fee for my application calculated?
- Do I need to perform User Consultation on the PL?

Further clarification ? Other questions ?

⇓ **Request Meeting** at EMEA via

"Pre-Submission Meeting Request Form"

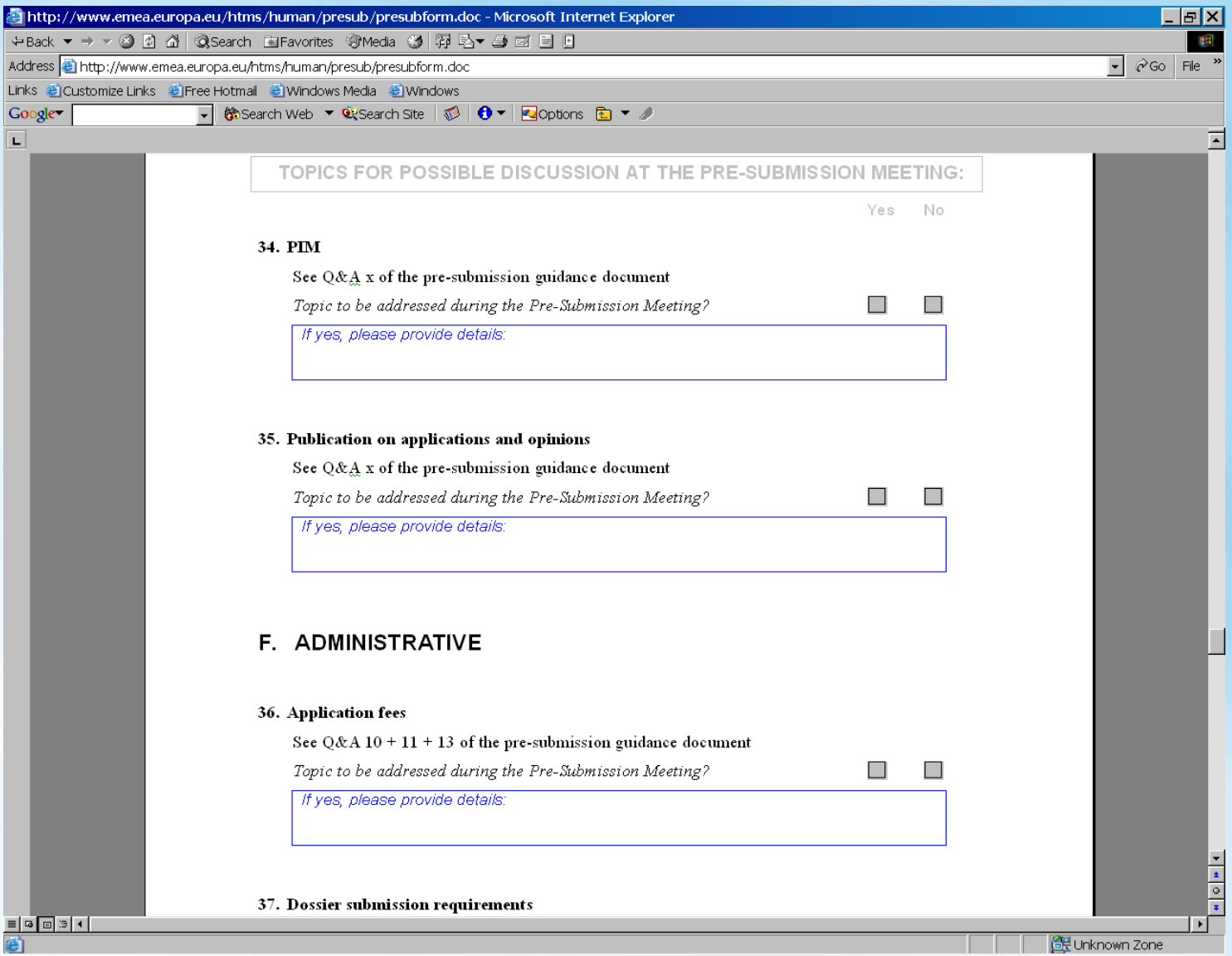
EMEA Pre-submission Meetings

- 6-7 Months before submission **Free service**
- Discuss final **practical** & **regulatory** aspects of upcoming application
- Clarify application-specific issues not addressed in the Pre-Submission Guidance
- 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

EMEA Pre-submission Meeting Request Form

- Checklist of topics to be considered
- Grouped per area (Quality, Regulatory, Inspections, ...)
  → serve as **agenda** for meeting
- Tick topics proposed for discussion, and include relevant background information on issues
- Other topics can be proposed; go beyond list as required for your application.
- Send form + SPC to EMEA **6 weeks in advance** of proposed meeting dates to CIG (Central Information Group)

  h-cig2@emea.europa.eu



Human Medicines – Application Procedures – PreSubmission Guidance

EMEA Pre-submission Meeting Documents

- Pre-Submission Meeting Request Form
- Overview of product development programme
- Draft NTA application form (Module 1.2)
- Draft SPC, labelling, PL (1 example)
- Draft Table of Contents of application
- Copy of scientific advice
- Any topic-specific documents
- Applicant's presentation

Pre-submission Meetings

EMEA Participants:

- Product Team Leader
- Product Team Members
  - S/E-PRE or Quality
  - Regulatory Affairs
- Optional
  Specialised Group Leader, representatives from CIG, Inspectorate, Orphan Drugs, S/E-Post, Risk Management, Medical Information, ...

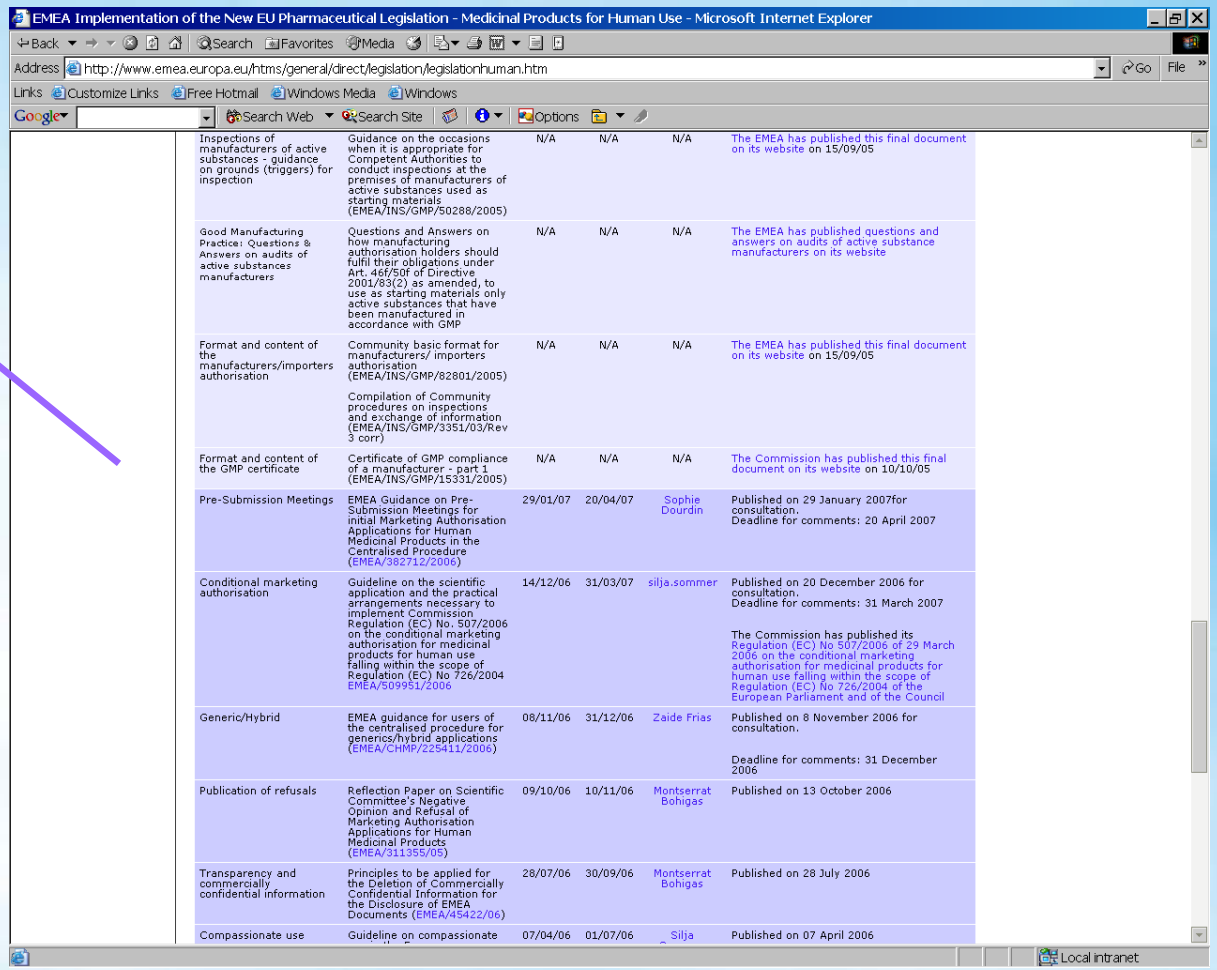
Minutes of meeting reviewed & agreed by EMEA

Pre-submission Meetings

Draft

"EMEA Guidance on **Pre-Submission Meetings** for initial MA Applications for Human Medicinal Products in the CP" (EMEA/382712/2006)

For comments by 20/04



Inspections of manufacturers of active substances - guidance on grounds (triggers) for inspection	Guidance on the occasions when it is appropriate for Competent Authorities to conduct inspections at the premises of manufacturers of active substances used as starting materials (EMEA/INS/GMP/50288/2005)	N/A	N/A	N/A	The EMEA has published this final document on its website on 15/09/05
Good Manufacturing Practice: Questions & Answers on audits of active substances manufacturers	Questions and Answers on how manufacturing authorisation holders should fulfil their obligations under Art. 46f/50f of Directive 2001/83(2) as amended, to use as starting materials only active substances that have been manufactured in accordance with GMP	N/A	N/A	N/A	The EMEA has published questions and answers on audits of active substance manufacturers on its website
Format and content of the manufacturers/importers authorisation	Community basic format for manufacturers/ importers authorisation (EMEA/INS/GMP/82801/2005) Compilation of Community procedures on inspections and exchange of information (EMEA/INS/GMP/3351/03/Rev 3 corr)	N/A	N/A	N/A	The EMEA has published this final document on its website on 15/09/05
Format and content of the GMP certificate	Certificate of GMP compliance of a manufacturer - part 1 (EMEA/INS/GMP/15331/2005)	N/A	N/A	N/A	The Commission has published this final document on its website on 10/10/05
Pre-Submission Meetings	EMEA Guidance on Pre-Submission Meetings for initial Marketing Authorisation Applications for Human Medicinal Products in the Centralised Procedure (EMEA/382712/2006)	29/01/07	20/04/07	Sophie Dourdin	Published on 29 January 2007for consultation. Deadline for comments: 20 April 2007
Conditional marketing authorisation	Guideline on the scientific application and the practical arrangements necessary to implement Commission Regulation (EC) No. 507/2006 on the conditional marketing authorisation for medicinal products for human use falling within the scope of Regulation (EC) No 726/2004 EMEA/509951/2006	14/12/06	31/03/07	silja.sommer	Published on 20 December 2006 for consultation. Deadline for comments: 31 March 2007 The Commission has published its Regulation (EC) No 507/2006 of 29 March 2006 on the conditional marketing authorisation for medicinal products for human use falling within the scope of Regulation (EC) No 726/2004 of the European Parliament and of the Council
Generic/Hybrid	EMEA guidance for users of the centralised procedure for generics/hybrid applications (EMEA/CHMP/225411/2006)	08/11/06	31/12/06	Zaide Frias	Published on 8 November 2006 for consultation. Deadline for comments: 31 December 2006
Publication of refusals	Reflection Paper on Scientific Committee's Negative Opinion and Refusal of Marketing Authorisation Applications for Human Medicinal Products (EMEA/311355/05)	09/10/06	10/11/06	Montserrat Bohigas	Published on 13 October 2006
Transparency and commercially confidential information	Principles to be applied for the Deletion of Commercially Confidential Information for the Disclosure of EMEA Documents (EMEA/45422/06)	28/07/06	30/09/06	Montserrat Bohigas	Published on 28 July 2006
Compassionate use	Guideline on compassionate	07/04/06	01/07/06	Silja	Published on 07 April 2006

EMEA Homepage – New EU legislation – Human Medicines

Rapporteur
Pre-Submission Meetings

- Meetings useful to inform (Co-)Rap & Assessors and to discuss practicalities on future filing
  - Present product & dossier
  - Discuss (e)CTD + dossier requirements
  - Discuss possibility for accelerated review
  - →Should not lead to pre-assessment of dossier
- EMEA PTL to participate via teleconference
- Minutes of the meetings to be circulated to EMEA and to (Co-)Rapporteur
- Companies to discuss regulatory/procedural issues with EMEA rather than with (Co-)Rapporteur

Thank you

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List of Abbreviations

- ASMF Active Substance Master File
- CHMP Committee for Medicinal Products for Human Use
- CIG Central Information Group
- EC European Commission
- (e)CTD (electronic) Common Technical Document
- GMP Good Manufacturing Practices
- IN Invented Name
- ITF Innovation Task Force
- LoQ List of Questions
- MA(H) Marketing Authorisation (Holder)
- MS Member State
- NRG invented Name Review Group
- NTA Notice to Applicants
- PL Package Leaflet
- PSM Pre-Submission Meeting
- PMRF Pre-Submission Meeting Request Form
- S/E Safety and Efficacy
- SPC Summary of Product Characteristics