Draft Guideline Rheumatoid Arthritis 2015 (revision 2004)

Introduction

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EMA Guidelines

- **Aims:**
- To help applicants to prepare marketing-authorisation applications for human medicines, in a legislative framework.

- To clarify requirements regarding Efficacy & Safety evaluation (endpoints, design, populations)

- Harmonised view of the EU Member States/EMA

- Based on the up-to-date scientific knowledge (Scientific Advices/regulatory experience)

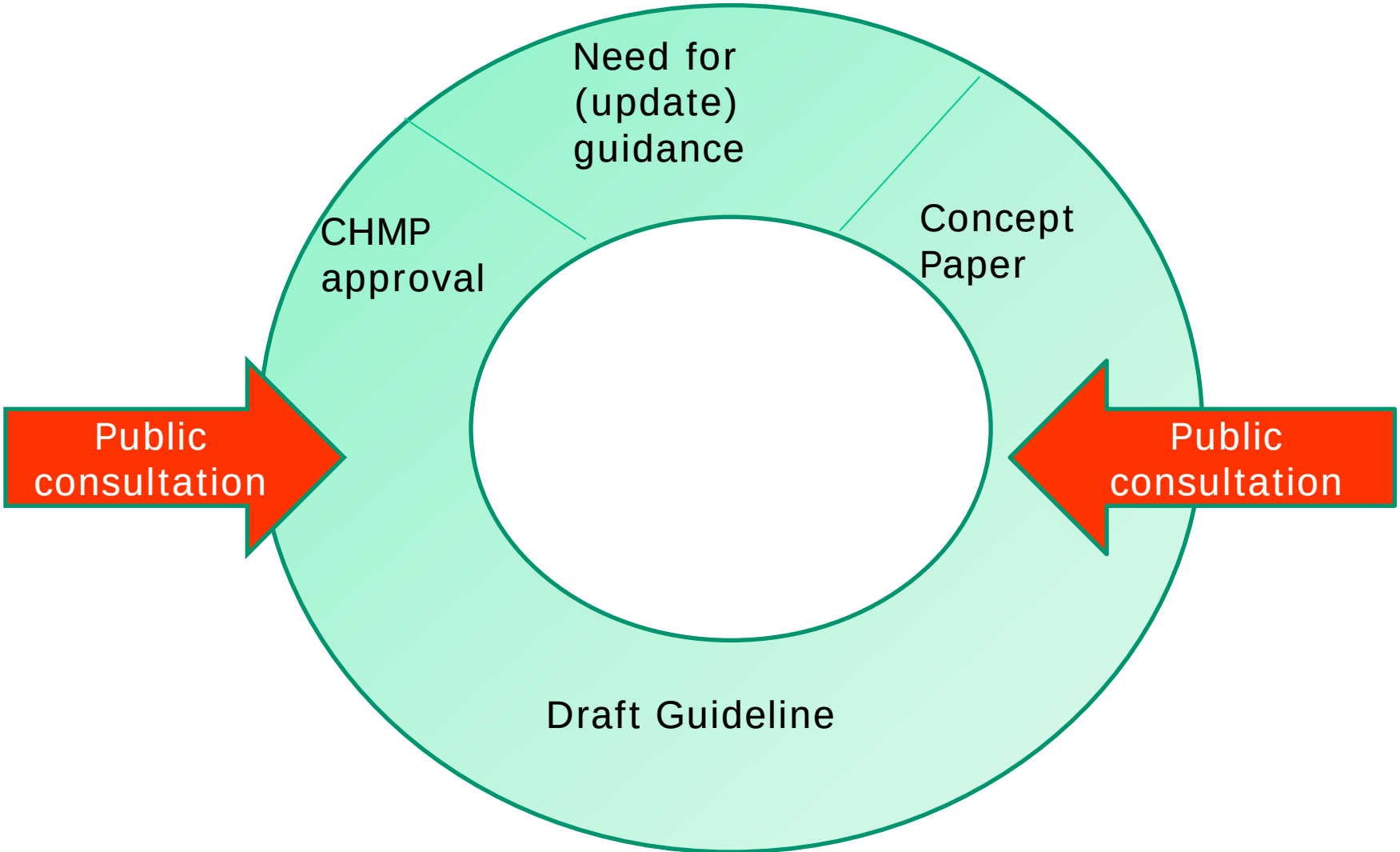
EMA Guidelines

- **How prepared:**
- Rheumatoid Arthritis Guideline: prepared by the RIWP (Rheumatology-Immunology Working Party)
- Experts European Agencies
- Under auspices of the Committee for Medicinal Products for Human Use (CHMP)

- **Public consultation** is sought during development
- Transparent procedure

EMA Guidelines

- **Life cycle:**



EMA Guidelines

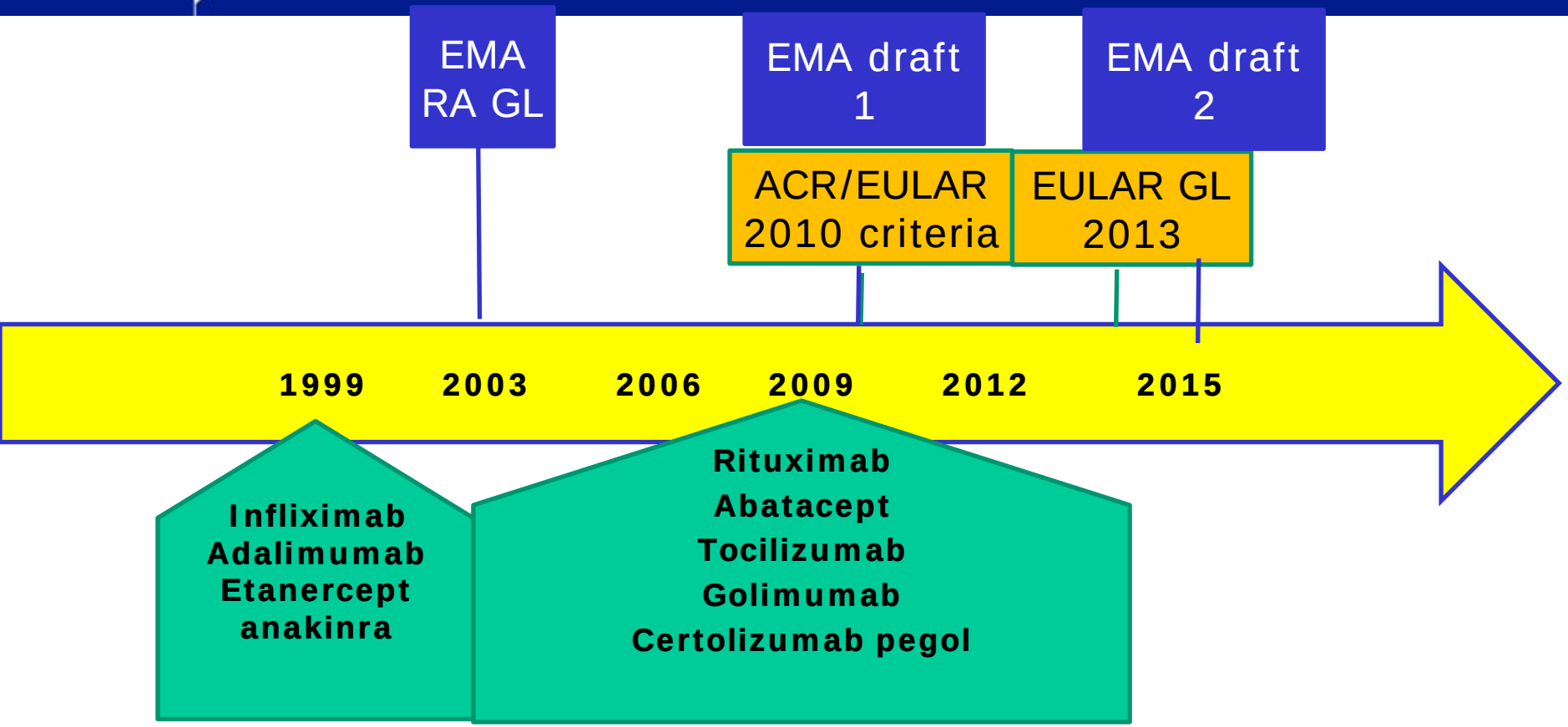
- **Status**
- Guideline, not a law
- Not intended to raise unreasonable hurdles, but good quality data and consistency
- Deviations: adequately justified, SAWP advice recommended

RA guideline development

- **Present RA guideline (2003)**

- **Endpoints:** core set of signs/symptoms (TJC, SJC, PGA, pain, acute phase reactants),
- Composite endpoint (e.g. DAS (EULAR categories), Paulus, ACR)
- Physical function + X-rays
- QOL (AIMS), biomarkers, extra-articular
- **Design:** parallel, Placebo (3-6 m), Active Control (MTX or Sulfasalazin)
- **Study population:** no specific recommendations

Recent developments



Milestones RA treatment

- Rapidly developing field, need from revision

- **Milestones in RA:**
- More therapeutic options of efficacious DMARDs
- Optimised Standard of Care (BeSt, COBRA)

- Change treatment paradigm: earlier intervention with DMARDs, more intensive
- ACR/EULAR classification criteria 2010: DMARDs available in Early RA
- EULAR RA treatment guidance 2013: Treatment-to-target: remission/low disease activity

Milestones in RA, continued…

- Development of outcome measures (SDAI, CDAI)
- ACR/EULAR remission criteria 2011

- Development of imaging techniques and scales (MRI (RAMRIS), ultrasound)

- RA Registries (biologics) in different EU countries

- Search for tapering/stopping criteria

- Biosimilars (beyond the scope RA Guideline/RIWP)

Challenges of new developments

- **Endpoints**

- ACR20: still clinically relevant?
- T2T: targeted endpoints versus relative change (ACR)
- Definition LDA/remission: DAS28 cut-offs, or SDAI/CDAI/Boolean?

Challenges new developments

- Feasibility structural damage studies (patients better controlled, treated earlier, short placebo), validity MRI/US?
- Choice of the Active Control (multiple options)
- More options/more experience, different weight on safety
- FDA guideline differentiation

Outline 2015 version

	GL 2003	GL 2015
End-points	ACR20, Month 6 Sharp (X-ray)	Remission/LDA as defined by DAS28 cut-off 2.6/3.2, X-Ray control (Sharp-vdHeijde)
Target	All RA patients	-Naive: 'remission' 3-6 Months -MTX-IR: 'remission'/LDA 3-6 Months -TNF-IR: LDA 6 Month -Treatment resistant (IR multiple biologicals): ACR20
Design	Placebo 3-6 m Active Control: MTX/SLZ	Placebo 6-12 weeks (rescue) -naive: MTX -MTX-IR/TNF-IR: a biological DMARD Tapering study encouraged

Points for discussion

- Rigid framework vs. flexibility
- Time for us to provide clarity and harmonised vision!

- Endpoints (Arantxa Sancho)
- Trial design (Andreas Kouroumalis)
- Populations (Jan Müller-Berghaus)