Objectives

• To establish the basic pharmacokinetic properties and safety profile of predefined macrolides.

• To make an inventory of the intrinsic susceptibilities of pathogenic organisms towards macrolides and establish their key pharmacodynamic parameters in relation to potential use.

• The basic indications of macrolides (evidence-based first and second line)

• The problem of resistance and rational approaches to redefining the indications.

• The EU consensus on the indication of macrolides.

• General discussion: towards a consensus.
Recommendations for future research

- Internationally harmonized, evidenced-based guidelines/guidances for preclinical and clinical evaluation need to be developed
- Resistance surveillance data which are prospective, community based, unselected, denominator and geographically defined
- Pharmacodynamic studies in animals and patients should be further developed to form a scientific basis to support dosing recommendations

Recommendations for future research projects in relation to antibiotic use

- More solid information should be generated on correlation between resistance and clinical failures
- Rapid diagnostic tests should be developed to support prudent prescribing
- Strong support should be provided for documentation of basic properties and safety/efficacy of generic antibiotics
- Address the unknown fields such as true intracellular activity of antibiotics
Recommendations for National Health Authorities

• Revisit SPCs for established antibiotics in situations where there is a rapidly changing susceptibility profile which may affect the empirical efficacy.
• Take into account newly emerging safety concerns (e.g. QTc changes)

Recommendations for the EU

• Set up necessary programmes for improving the quality of collection, collation and access to sensitivity data to support prescribers and guide drug regulation
• Promote the standardisation of a European consensus on susceptibility testing
• Promote the development of evidence-based European guidelines for the management of common infectious disease problems
Practical Recommendations for the ESAC project

For the project steering committee

- Develop robust data on antibiotic usage in relation to trends in susceptibility and by indication
Deliverables

- What are the acceptable basic first line and second line indications (given the existence of alternatives) for each macrolide?

**In general**

- mainly community-managed infections
Respiratory tract infections

- streptococcal pharyngitis
  (alternative to penicillin, especially in patients with beta-lactam allergy)
- CAP in outpatients with no signs of severity
- pertussis
- diphtheria

Because of the high prevalence of *H. influenzae*, macrolides should NO LONGER be recommended for the treatment of:

- acute exacerbations of chronic bronchitis
- sinusitis
- otitis media (unless documentation of proven susceptibility of the causative pathogen)
Towards European consensus indications for major antibiotic classes: an exercise with the macrolides

Indications (2/3)

**Genital tract infections**
- chancroid
- gonococcal urethritis/cervicitis
- *Chlamydia* and non specific urethritis/cervicitis (azithromycin only)
- granuloma inguinale

**Gastro-intestinal tract infections**
- *Helicobacter pylori* infections (clarithromycin only)
- *Campylobacter* enteritis

**Dental infections**
- periodontitis
**Indications (3/3)**

**Uncomplicated skin & soft tissue infections**

- impetigo  
  (alternative to penicillin, especially in patients with beta-lactam allergy)
- erysipelas  
  (alternative to penicillin, especially in patients with beta-lactam allergy)
- acne conglobata
- furunculosis

**Ocular infections**

- conjunctivitis (systemically)

**Infections in special populations**

- *Mycobacterium avium* infections (clarithromycin and azithromycin only)  
  (prophylaxis, treatment [as part of a combination therapy])
How should indications be reconsidered in areas where resistance is demonstrated?

- CAP
- Streptococcal pharyngitis
- Otitis media - proven susceptibility (?)
- Impetigo
- Erysipelas
- *Campylobacter* enteritis
- Gonococcal urethritis/cervicitis

Advice should be sought when frequencies of resistance increase significantly in a given geographical area.
Deliverables

• How should resistance practically modify the basic indications of macrolides and can consistent rules be applied?

For each indication local contemporary susceptibility data should be available to guide empirical prescribing for common target pathogens.
Deliverables

• Working text on the way to harmonise indications for macrolides in Europe

• There should be continued data that supports the clinical indications, safety profile and microbiological activity against target pathogens.

• Obstacles which prevent the achievement of these goals should be identified and addressed.