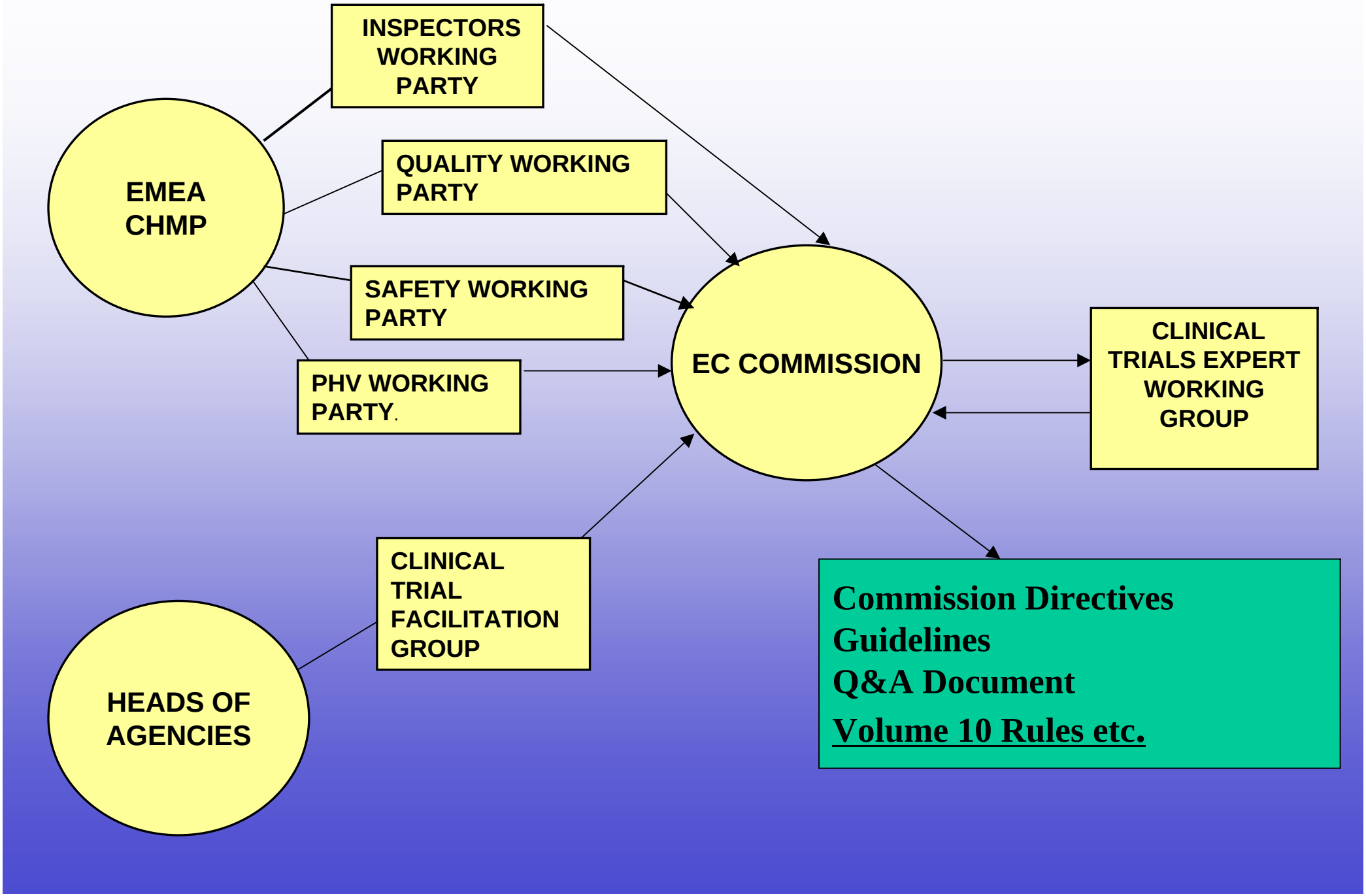
# Guidance on applications for potential high risk medicinal product trials

Dr Brian Davis MHRA

# Overview

- Current guidance on commencing and conducting clinical trials;
- Issues for high risk medicinal product (HRMP) trials:
  - Clinical trial site and facilities.
  - Choice of subjects;
  - Management of adverse events;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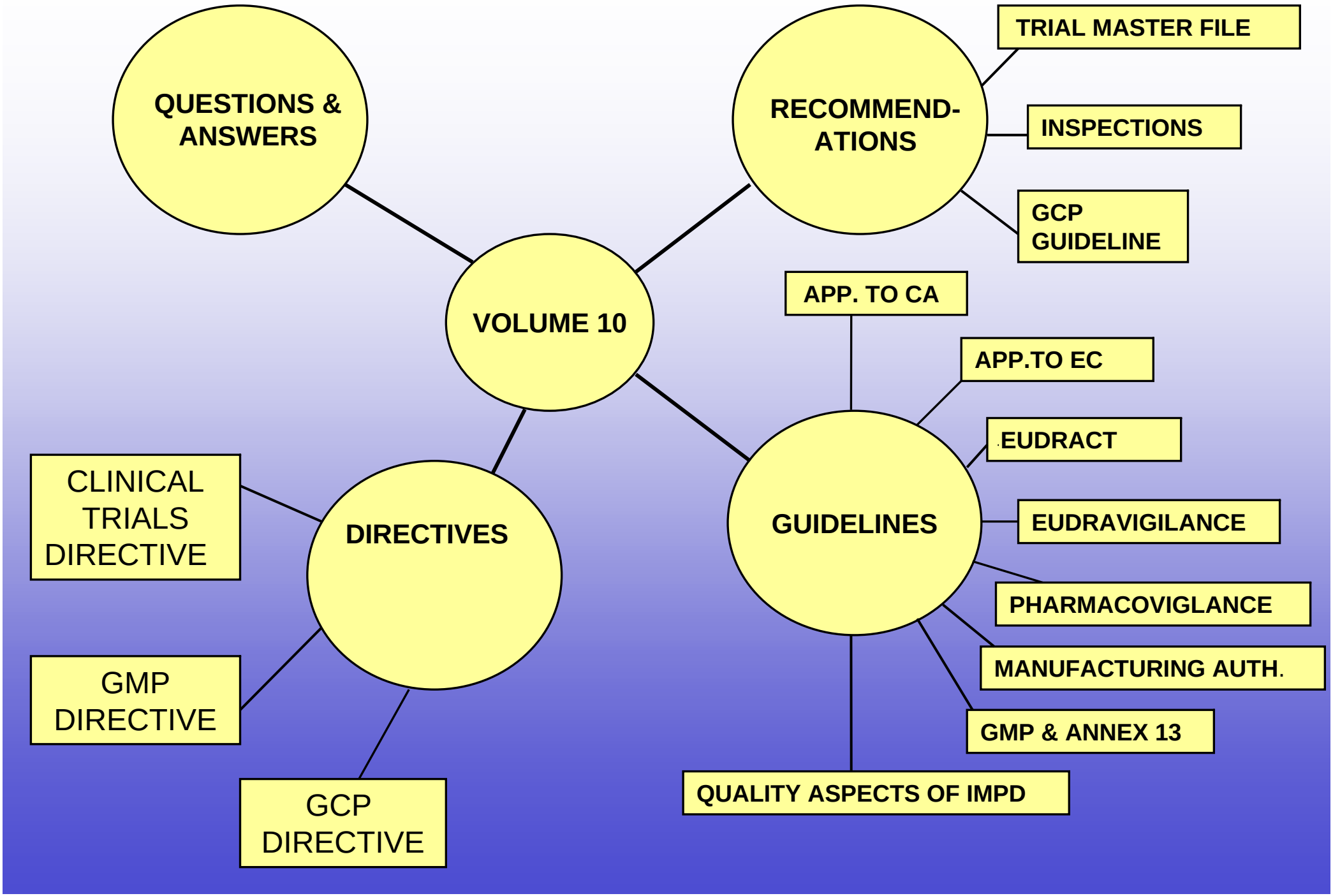
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# High Risk Medicinal Product (HRMP) Trials

# Protocol and Application

- **Protocol should take into account**:
  - All available preclinical data;
  - All identified risk factors; and
  - Provide specific risk management strategy.

# Protocol and application should discuss:

*Site of the clinical trial including its clinical environment*:

- One research centre v several locations;
- Availability of data from all treated volunteer(s);
- Information system that will provide immediate access to information;
- Staff – their level of training and expertise;
- Qualifications and skills of the person(s) or the body (e.g. IDSMB) responsible for stopping trial;
- Immediate access to facilities for emergency treatment;
- Ready access to ITU.

# Comments on trial site

- Single site – exception for patient studies;
- Information communication system; described;
- Standards for level of staff training and updating; e.g. *experience in early clinical drug development; training in Good Clinical Practice, safety training and basic life support;*
- MoU with ITU on responsibilities;
- Assessment by criteria or accreditation.

# Protocol and application should discuss:

- Choice of subjects :
  - Patients or healthy subjects;
  - High risk potential from the IMP; and
  - Possible long-term risks.

# Protocol and application should discuss:

*Management of adverse events:*

- Parameters used to evaluate tolerance and/or pharmacological activity, based on non-clinical data;
- Procedures for monitoring and caring for volunteers:
  - during their stay in the research centre (including stopping rules and any emergency); and
  - during the ambulatory period if applicable;
- Emergency treatment strategy when required;
- Provision of supportive treatment;
- Rapid access to urgent treatment;
- Availability of specific antidotes where they exist.

# Comments on managing ADEs

- Demonstrable PD effect persisting beyond the duration of the trial;
- Communicate to trial participants; Use patients;
- Duration of monitoring based on PK/PD data;
- Rapid access to treatment allocation codes;
- Clarify ‘immediate access’ to ITU facilities;
- Issue a pass to participants; Contact plan for participants;
- Follow up for potential long-term effects, especially immune-modulators; too vague.

# Conclusion

- Guidance is available on commencing and conducting clinical trials in the EU;
- No current guidance on HRMP trials;
- Need to provide guidance on:
  - Clinical trial site and facilities;
  - Choice of participants;
  - Management of ADEs.