

Clinical Studies in the United Kingdom



SMERUD
Medical Research

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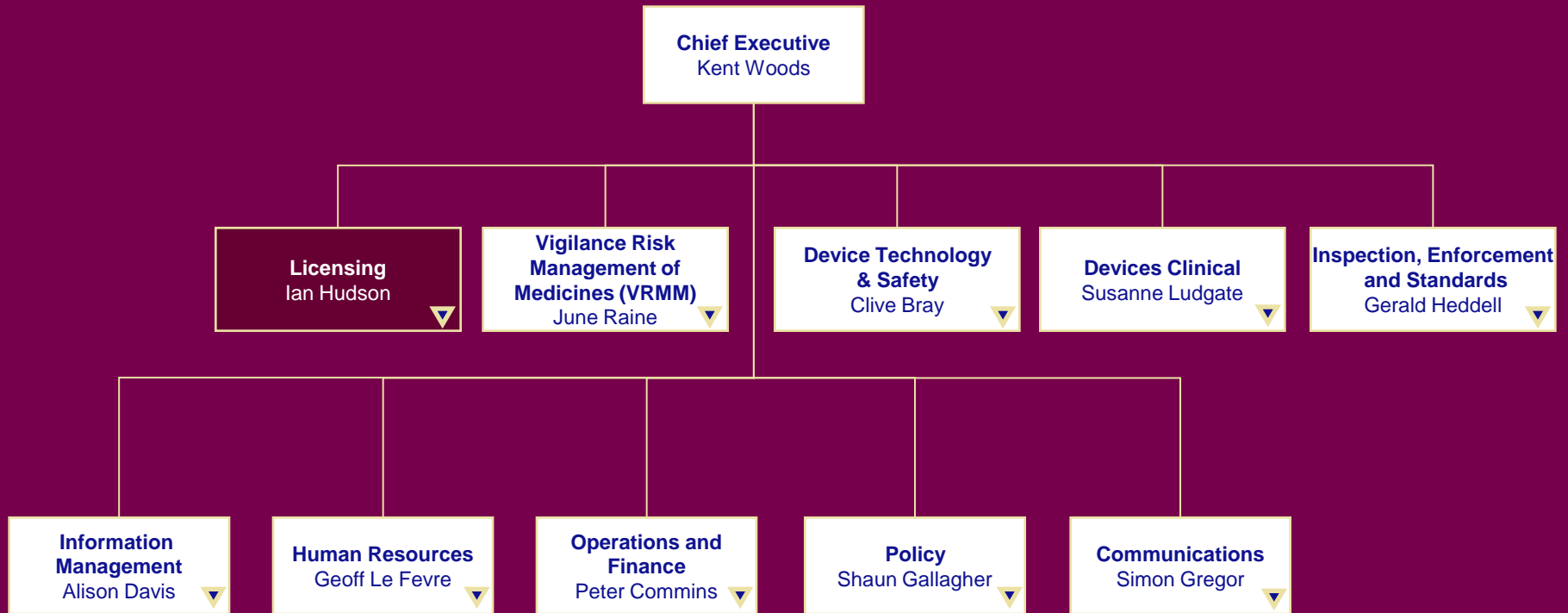
Summary

- MHRA
 - Organisation
- UK Regulatory Framework
 - Legislation, regulation and guidance
- The CTA
- The EC
- Contracting
- Clinical Trial Insurance
- Investigator Selection
- Geographic Factors

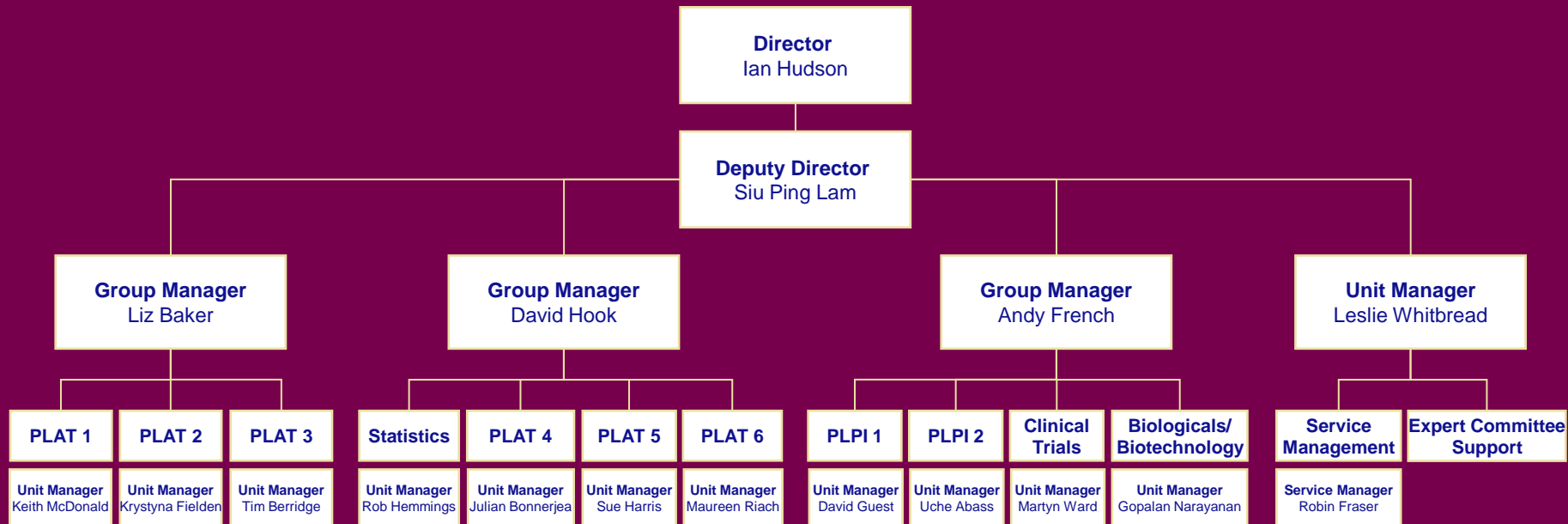
MHRA

- The Medicines and Healthcare products Regulatory Agency (MHRA) is the government agency responsible for drug and device approval/regulation
 - **10 Divisions**
 - Licensing
 - Vigilance
 - Device Technology and Safety
 - Devices, Clinical
 - Inspection, Enforcement & Standards
 - Information Management
 - Human Resources
 - Operations and Finance
 - Policy
 - Communications

MHRA: Executive Board



MHRA: Licensing Division



PLAT (Product Lifecycle Assessment Team) Therapeutic Groupings:

PLAT 1: Cardiovascular; diabetes
 PLAT 2: Respiratory; ear, nose & throat (ENT); endocrine; dermatology
 PLAT 3: Central nervous system (CNS); anaesthetics
 PLAT 4: Gastrointestinal (GI) & nutrition; blood
 PLAT 5: Anti-infective; obstetrics & gynaecology; genitourinary tract
 PLAT 6: Musculoskeletal; malignant disease

PLAT: Risk Management, scientific advice, application assessment

UK Regulatory Framework and the CTA

- Integrated into the International Conference on Harmonisation (ICH)
 - Conforms to EMEA and ICH Guidance/Regulation
- Obtaining a Clinical Trial Authorisation (CTA)
 - All trials of an IMP must have a CTA approved MHRA prior to study start
 - EudraCT application
 - Review timeline up to 60 days
 - MHRA is currently providing 14-21 day review for Phase I studies
 - Timeline for amendment review 35 days
 - Associated fees
 - Phase I NHV £2322
 - Phase I, Phase II or Phase III patient trial, unknown product £4202
 - Phase I, Phase II or Phase III patient trial known product £3414
 - Phase IV trial Protocol £262
 - Additional protocol [same sponsor and same product (s)] £262

CTA Format

- Components
 - Cover letter
 - Allocation of EudraCT Number
 - Application Form
 - Clinical Protocol
 - Investigator Brochure
 - Investigational Medical Product Dossier (IMPD)
 - Format follows Directive 2001/20/EC

MHRA Interaction

- Pre-Application Meetings:
 - MHRA offers pre CTA application meetings:
 - Quality
 - Safety
 - Clinical
 - Paediatric forms and uses
 - Additional meetings during development are available
 - Sponsor submits request form and provides background and questions
 - MHRA will assess package prior to the meeting
 - Meetings last ~90 min
 - Sponsor sends meeting notes to MHRA with 15 days
 - MHRA written response with 30 days of the meeting
- MHRA ; <http://www.mhra.gov.uk>

Multi-Regional Ethical Committee (MREC)

- Application is sent to a central regional EC specific for the Principal Investigator
- If more ECs are involved then the central EC becomes the MREC (Multi-Regional EC) which has overall responsibility for the approval process
 - MREC approval is required when ≥ 5 or NHS organisations are involved in a study
- Application to the MHRA can be performed in parallel with the MREC
- Clinical trial may commence following receipt of MHRA 'no objection' letter and MREC approval
- Notification of MREC approval is sent to the local EC

Local Research Ethical Committee (LREC)

- For multi-centre studies notification of the MREC approval is sent to the Local Research EC (LREC)
- For single centre studies an application is made directly to the LREC
- All applications to LRECs in the UK are made using the Integrated Research Application system (IRAS)
- Timeline for approval 60 days
- No Fee applicable
- Additional information on MREC and LREC available at
 - <http://www.nres.npsa.nhs.uk>

Additional Approvals

- Research & Development (R&D) Approval
 - All NHS organisations must have R&D approval before any research involving human participants, their organs, tissue or data commences
 - All applications for R&D approval are made using IRAS
 - No Fee applicable
- Financial agreement
 - The model Clinical Trial Agreement (mCTA) is used by all NHS Trust sites for all clinical trials

Clinical Trial Insurance

- Sponsor must provide evidence of insurance coverage
 - Level of coverage appropriate to risks posed, OR
 - If self-insured evidence of financial capacity to do so
 - Usually judged on the basis of the latest Annual Report produced by the Sponsor
 - Multiple providers capable for issuing coverage for the UK
 - First in man, 30 subjects, multiple dose ~£6,000
 - Phase II/III dependent on risks, patient numbers etc
- Study Sponsorship under EU Directive requires negligence claims are dealt with using standard procedures in the individual hospital where the patient concerned is treated
- Insurance and Idemnification recommendations are available from the ABPI
 - <http://www.abpi.org.uk/publications>

UK Pharmaceutical Market

- One of the world's largest pharmaceutical markets
- In 2009, the NHS budget is £98.2 billion
 - Estimated to be £102.3 billion in 2010
- Between 2004-2008 the number of prescriptions
 - increased by 22.1% (1,025.7 million)
 - Prescription value increased by 3.4% (£10.3 billion)
- In 2008 the leading therapeutic areas
 - cardiovascular system (# prescriptions written)
 - central nervous system (in terms of value)

Population Information

- Under a single CA approval, access to large patient number
- UK Resident Population Estimate mid 2008*
 - 61,383,000
 - Median age overall: 39
 - Even distribution up to 71 year, then F>M
 - < 16 years old: 3,100,000 (19%)
 - > 65 years old: 2,600,000 (16%)
 - Race/Ethnicity
 - White British: 50,366,497 (85.67%)
 - White (other): 3,096,169 (5.27%)
 - Indian: 1,053,411 (1.8%)
 - Pakistani: 747,285 (1.3%)
 - White Irish: 691,232 (1.2%)
 - Mixed race: 677,117 (1.2%)
 - All other ≤1%

Geographic Factors

- Small country
 - 245,000 km²
- Population dense
- Metropolitan areas
 - London, Manchester,
 - Birmingham,
 - Leeds-Bradford



Number of People



Summary

- Large commercial pharmaceutical market
- Relatively High Population Density
- Single CA approval provides relatively large capacity
 - Clinical Trial Centres
 - Experienced investigators
 - Patient Population
 - Medical conditions
 - Enrollment contingencies
- Mature regulatory environment
 - Scientific advice
 - Strong history of drug development
 - Extensive early phase knowledge