Taking the adversity out of suffering

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Objectives

- Nature of adverse effects and how to reduce them
- Implementation of study plans
- Reduction in suffering and sharing of knowledge

Adverse effects for severe protocols

- ASPA define severe protocols as *"Procedures on animals as a result of which the animals are likely to experience severe pain, suffering or distress or long-lasting moderate pain, suffering or distress, as well as procedures that are likely to cause severe impairment of the well-being or general condition of the animals shall be classified as severe."*

When are Standard Condition 18's needed?

Project Licence Standard Condition 18 requires the PPL holder to notify the Secretary of State if constraints on severity or observance of other controls described in the PPL have been breached or are likely to be

Situations resulting in SC18s range from mild behavioural abnormalities to death

Study plans

Introduction of study plans department wide in 2020

Protocol steps listed

Adverse effects

Personal licence: Standard Conditions

- **Condition 3**
- The licence holder must not apply a regulated procedure to an animal if the procedure may cause the animal severe pain, suffering or distress that is likely to be long-lasting and cannot be ameliorated.
- **Condition 4**
- The licence holder must not apply a regulated procedure to an animal unless the holder has taken precautions to prevent or reduce to the minimum consistent with the purposes of the procedure any pain, suffering, distress or discomfort that may be caused to the animal.
- **Condition 5**
- Where the licence holder is applying a regulated procedure to an animal the holder must ensure that any unnecessary pain, suffering, distress or lasting harm that is being caused to the animal is stopped.
- **Condition 6**
- Where the licence holder is applying or has applied a regulated procedure which is causing the animal severe pain, suffering or distress the holder must take steps to ameliorate that pain, suffering or distress.

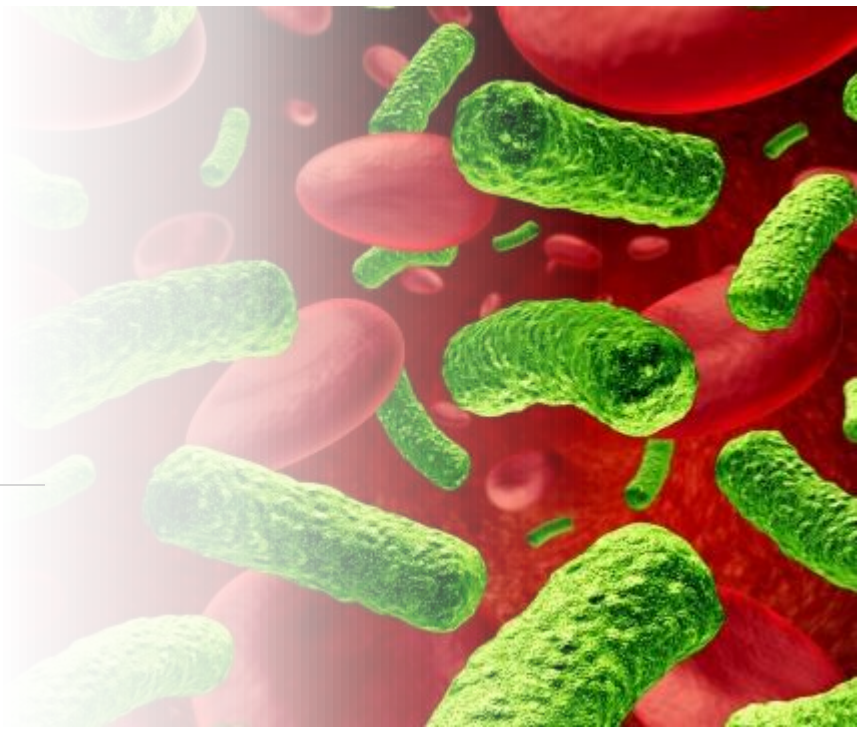
What did we do before the implementation of study plans?

- Unexpected deaths
- Standard condition 18 report outcomes
- Reviewing PPLs

Reducing suffering

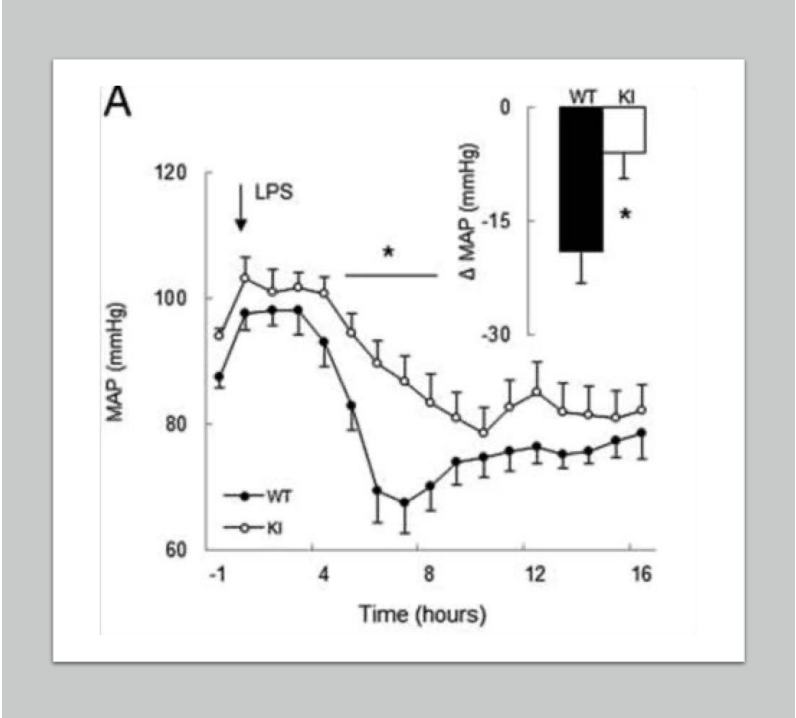
How do study plans work at KCL?

Sepsis Studies

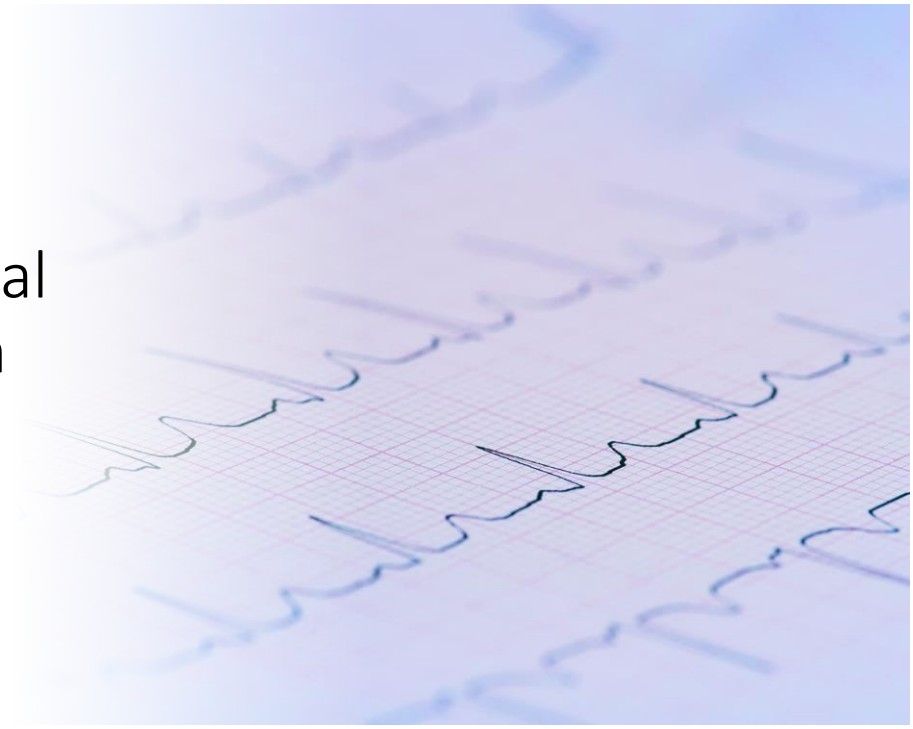


Study Improvements

- Prior to study plan:
  - 48 hour time course with sub-lethal dose of lipopolysaccharide (LPS).
  - Moderate level of suffering but over a prolonged period of time.
  - Study plan review:
    - Discussion on scientific requirements.
    - Time course reduced to 12 hours.
    - Better monitoring regime.



Myocardial Infarction Studies



Study Improvements

- Prior to study plan:
  - Severe model in the PPL.
  - Study plan review:
    - Discussion with scientists and Home Office Inspector.
    - Series of early time points to be investigated using a non-recovery model.
    - Severe end-points avoided.

Parkinson's Disease Studies

Study Improvements

- Prior to Study plan:
  - Moderate severity banding
  - Animals to be anaesthetized and stereotaxic injections carried out on a non-recovery protocol
  - Study plan review:
    - Animals culled by schedule 1 method
    - Stereotaxic injections performed to confirm accuracy of co-ordinates

Manager study plan feedback

- We have used the information in study plans to get more detail on adverse effects which has lead to amendments in PPLs . These have lead to greater monitoring regimes to ensure adverse effects are avoided or picked up a very early stages.
- When the study plans are approved, we are aware of when the study starts and are able to monitor right from the start. Before researchers would come in and start studies without our knowledge.
- Drug doses modified as a result of reading the study plan.
- Refinement of studies before they start has been an important part of the study plan approval process. An example was an experiment involving myocardial infarction that was going to be done as a recovery model (severe protocol) and the study plan led to it being done as non-recovery.
- The change of the duration of the time-course for mice on a severe protocol, reducing the time that the mice would have potentially be suffering due to the administration of drug

Continuing to move forward

- Study plans
- Adverse effect repository
- Standard Condition 18 notifications
- AWERBs

Thank you for listening.

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