**RISK ADJUSTED-TRIAL MANAGEMENT FOR LOW INTERVENTION/LOW RISK TRIALS IN THE PROPOSED CLINICAL TRIAL REGULATION**

**Position statement on behalf of the**

**European Society for Clinical Oncology (SIOP-E) and UKCRC Registered Clinical Trials Units Network**

The main focus of research conducted within the academic community is to contribute to the evidence-base which underpins standard treatments thereby improving patient outcomes and contributing positively to public health policy and practice. This is primarily achieved through trials optimising the use of currently available and licensed medicinal products and generally these trials do not provide information towards marketing authorisation or product labels.

Unless the definition of 'Low Intervention / Low Risk' defined with the new EU Clinical Trials Regulation (CTR) can be applied appropriately and is associated with risk-adjusted requirements for trial management there remains a real risk that clinical trials research in the academic setting, especially for rare diseases will continue to suffer.

We strongly advocate that the final version of the CTR is consistent with the following 2 key points:

1. **The following types of clinical trials must fall within the low intervention/low risk category:**

- Use of placebo where it does not increase the risk in the trial.
- Trials of an authorised medicinal product that does not involve a route of administration or dosage level or use in a patient population that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product [1] e.g. use of an authorised medicinal product outside the terms of the marketing authorisation, where its use is supported by standard treatment guidelines or sufficient published scientific literature and generally known clinical experience available in regard to its safety profile.
- Trials of food supplements and medicinal products that can be sold without prescription.

The risk of differences in interpretation of these or any agreed categories for low intervention / low risk must be mitigated by thorough guidance provided by the EU Commission or an agreement that the decision in regard to risk category is made by the Lead Investigator.

2. **Designation as a Low Intervention / Low Risk trial must confer all the following proportionate regulations:**

- Subject to shorter timelines for authorisation.
- No mandatory requirement for additional insurance cover over standard practice.
- In relation to pharmacovigilance:
    - Not required for auxiliary medicinal products.
    - Use of the Summary of Product Characteristics as the Reference Safety Information.
    - An option to define SAEs that do not need reporting to the Sponsor.
    - Trials with long term follow up for survival shall be granted the option to define a reporting period that ends prior to the End of Trial Notification.

1. US Department of Health and Human Services Food and Drug Administration. Guidance for Industry IND Exemptions for Studies of Lawfully Marketed Drug or Biological Products for the Treatment of Cancer 2004

    - No annual reporting of safety information.

- No additional procedures over and above that required by standard practice for labelling, handling and traceability of Investigational Medicinal Products (other than placebos) and auxiliary medicinal products.
- Conduct of the trial in terms of management and monitoring is in proportion and adapted to the trial specific risks (ICH-GCP guidelines are not mandated).
- A clinical professional other than a medically qualified person shall be appointable as Lead or Clinical Site Investigator, given that she/he is undertaking activities which are within the scope of their expertise and standard clinical practice.
- Simplified End of Clinical Trial Report.
- Subject to an inspection schedule that is planned and prioritised based on the risks of the trial, Sponsoring organisation and Lead Investigator.

The Sponsor or Investigator would be expected to include any additional processes necessary to protect patient safety or the robustness of the trial.

Responding UKCRC Registered CTUs:

Barts Clinical Trials Unit

Barts Pragmatic CTU

Birmingham Clinical Trials Unit

Bristol Clinical Trials Evaluation Unit

Bristol Randomised Trials Collaboration

CRUK Clinical Trials Unit, Birmingham

CRUK and UCL Cancer Trials Centre

CRUK Clinical Trials Unit, Glasgow

CTRC, University of Liverpool

CTSU, Oxford

Diabetes Trials Unit, University of Oxford

ICR – CTSU

Imperial Clinical Trials Unit

Leeds Institute of Clinical Trials Research

MRC Clinical Trials Unit at UCL

Northern Ireland CRSC

NWORTH, The Bangor Trials Unit

PRIMENT Clinical Trials Unit

University of Southampton Clinical Trials Unit

Wales Cancer Trials Unit

Warwick CTU

1. US Department of Health and Human Services Food and Drug Administration. Guidance for Industry IND Exemptions for Studies of Lawfully Marketed Drug or Biological Products for the Treatment of Cancer 2004