

## **OHRS Information Sheet Implementing Dose Escalation Changes in PHASE I Approved Research**

The following describes how to implement a dose escalation change in an approved Phase I or Phase I/II protocol that is actively enrolling to the Phase I portion of the protocol. This does not apply to non-Phase I research.

### **When Study Teams May Proceed Directly to QACT:**

If the dose escalation change is **predefined** in the protocol (excluding percentage-based escalations) and **COE has already been built for all dose levels** (or COE is not being used), the study team may go directly to the Quality Assurance for Clinical Trials Office (QACT) if one of the following criteria is met:

1. PI-Initiated Trials where the QACT monitors Phase I Dose Escalation: As set out in DF/HCC SOP QA-708, the QACT notifies the PI and the Research Nurse when the last subject to a cohort has been registered; the PI submits a verification of the significant toxicities noted and states the next dose level is open for enrollment. The QACT form entitled "Phase I Dose Escalation Form" sets out the issues that must be addressed by the PI.  
[http://www.dfcc.harvard.edu/fileadmin/DFHCC\\_Admin/Clinical\\_Trials/CRO/Policies\\_and\\_Procedures-SOPs/QA-708\\_Monitoring\\_Phase\\_I\\_Dose\\_Escalation\\_for\\_PI-Initiated\\_Protocols.pdf](http://www.dfcc.harvard.edu/fileadmin/DFHCC_Admin/Clinical_Trials/CRO/Policies_and_Procedures-SOPs/QA-708_Monitoring_Phase_I_Dose_Escalation_for_PI-Initiated_Protocols.pdf)
2. Industry-Initiated Trials where the Sponsor Manages the Phase I Dose Escalation: The Industry sponsor is responsible for communicating the current dose level to the PI and the study team; and the PI and study team are responsible for indicating the appropriate dose level on the eligibility checklist submitted to QACT at the time of participant registration.

### **When Study Teams Must Submit an Amendment to OHRS:**

If the dose escalation change is **NOT predefined** in the protocol or **for any reason COE must be changed**, including where the sponsor wants to make any variation to pre-defined doses, then it must come to OHRS as a dose escalation amendment.

### **Alert Pages:**

When Study Teams are permitted to implement a dose escalation change directly with the QACT **an Alert Page is not required**. The dose level information is displayed for clinicians to see in the subject's registration banner and in the COE order set. However, if COE is not utilized by a participating site and there is no other mechanism in place for the study team to know the current dose level subjects are on, an Alert Page may need to be submitted to OHRS as an amendment. Please also refer to the OHRS Guidance on Alert Pages posted on the OHRS website.

Please contact OHRS at (617) 632-3029 or QACT at (617) 632-3761 if you have any additional questions.