Exercise 3 - Method development

Name..... .....

Matrikel No: .....Date: **.....**

For this task you need the documents available in the download under 'Module 3'

Your method development was successful. Now you want to proceed to a **validation covering all of the FDA, ICH and EMA guidelines**. Design the accuracy and precision experiment compare the recovery requirements and the acceptance criteria of the runs:

Task	Your answer/decision/comment
How many non-zero calibrators must be foreseen if you want to be able to exclude two?	All: 6 non zero, Answer = 8
Design the accuracy and precision experiment (samples and days)	EMA: within-run 5 per level, 4 levels (LLOQ, <3xLLOQ, 30-50%ULOQ, 75-100%ULOQ), between-run 3 days at least two different days FDA: within-run 5 per level, 4 levels as above, at least three independent runs, no mention of days ICH: dito, at least three runs on at least two days, at least one day with fresh calibrators => 3 days, 4 Levels of QC's, 5 replicates = 15 QC's per level 2 sets of calibrants plus one to be prepared fresh on day 3 Each day, analyze 1 set of calibrants and 5 sets of QC's
Describe the requirements for the recovery experiment in the three documents	EMA: not mentioned FDA: three concentration levels - L, M and H QC's compared to post-extraction spiking ICH: L, M and H QC's, dito => prepare spiking solutions for spiking L,M and H QC samples spike three replicates of each level, extract along with nine blank plasma samples, spike the blank extracts after extraction and the sample extracts with blank solvent
Compare the acceptance criteria for analytical runs between the various guidances	All: >75% and >=6 calibrators <±15% or 20% at LLOQ 5% or >=6 QC samples at >=3 levels and >=2 replicates, >=67% of QC's within ±15% and >=50% of QC's per level within ±15% (EMAp.11/12, FDA p.20/21, ICH p.17ff)