From:	Rob Thomas
To:	Mark McCall
Cc:	Amit Chandra
Subject:	Rooster Bio
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Just spoke to Mark about this. We can catch up briefly on Tuesday as you suggest Amit, but I am comfortable with this. Logic as follows.

Population doublings are actually more informative than passage as proliferative state is what we are interested in to determine if we have 'original' material remaining.

Presuming that there is a statistical distribution that represents the time to first division for cells in the population.... this would have a mode somewhere between 12-48 hours.

If there are significant undivided cells left after a mean cell population doublings of 9, this would imply a very long positive skew tail in the above distribution for individual cells.

If such a heavy skew existed, it would be pretty much impossible to culture out such quiescent cells in any reasonable time.

As a matter of interest, we could work this out to lay down what a sensible PDs would be to reduce original material risk to a sufficiently low level (something that would not be possible with passage). This would be exponentially decreasing risk, and i suspect that we would come out with somewhere ~5 population doublings for a relatively homogenous population (this could be where the 5 passage rule of thumb comes from as in the absence of growth rate data 5 passages should pretty much guarantee 5PDs). After all, this is impossible to prove so has to be done on a probability/risk basis.

Rob.