

# How a Study Design could Impact on Recruitment and Enrollment Success: A Case Study

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## ABSTRACT

### Background.

Enrollment success is usually based on study Inclusion/exclusion criteria. However, as study designs are becoming more complex, how these designs could impact on recruitment and enrollment power?

### Methods.

Two similar clinical studies were executed with different study design complexities involving post menopausal females (PMF) in phase I trials. The M80 trial consists in a typical crossover design and the M06 consists in a partially sequential 3-arm crossover design. In order to assess the impact of the study design on recruitment and enrollment, several steps were monitored and quantified including quantification of overall impacts on divergent Inclusion/Exclusion as well as a deep assessment of recruitment and screening effort.

### Results.

A detailed comparison of Inclusion/Exclusion criteria revealed that a clear screening advantage was provided to the M06 trial based on the age, cardiac (PR, QRS, QTc), vital signs and body mass index restrictions. Interestingly, these advantages were not observed during recruitment and screening. Indeed, on the recruitment effort side, while both have generated the same amount of "request for information" inquiries from PMF, we observed a positively significant difference in the number of PMF actually deciding to register on M80 trial. This was transposed as well in the recruitment days required per PMF enrolled where M06 trial was requiring an additional 33% effort. The same trend was observed on the screening side where the M06 trial was requiring 44% additional work to enroll a PMF resulting, ultimately, in an additional 50% PMF to be screened compared to the M80 trial. The refusal rate obtained for M06 at screening was significantly supporting these observations.

### Conclusion.

Based on these observations, it appears clear that, the study design is affecting recruitment/enrollment power and that Inclusion/Exclusion criteria nor a punctual environmental factor might not be the only reasons.

## INTRODUCTION

The primary success of a clinical trial mainly depends on recruitment and enrollment of the appropriate study population in an adequate screening window. In early stage trials, we usually base the success of these steps on Inclusion and exclusion (I/E) criteria. However, as study designs are becoming more complex, how these designs could impact on recruitment and enrollment power?

The following poster intends to illustrate a case study, involving the same study population with similar inclusion and exclusion criteria, demonstrating the impact of a complex design on recruitment and enrollment.

## METHODOLOGY

Algorithmme Pharma recently performed two studies involving PMF for phase I trials: Trials M80 and M06.

### STUDY M80

This study consists in a Single center, randomized, single dose, laboratory-blinded, crossover design where 14 healthy PMF must be enrolled. In order to determine the impact of food on the pharmacokinetic while ensuring subject's safety, 3 subjects received the investigational product under Fed conditions while 11 received the same investigational product but fasted. If no safety concerns were observed, subjects will be asked to participate to the second period under a typical crossover approach. The study compensation was the same for all subjects completing the trial.

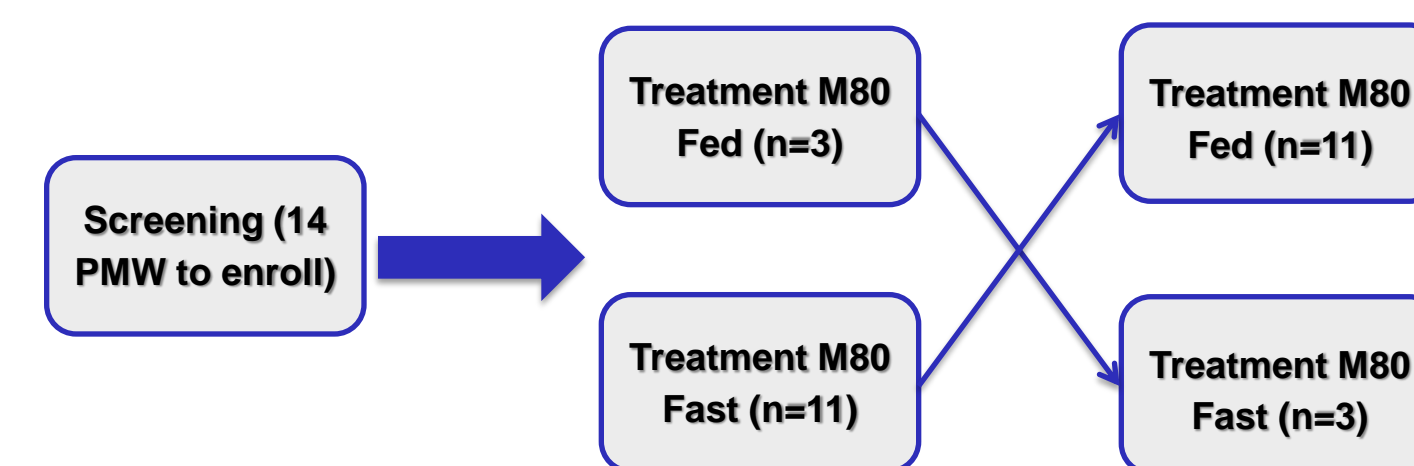
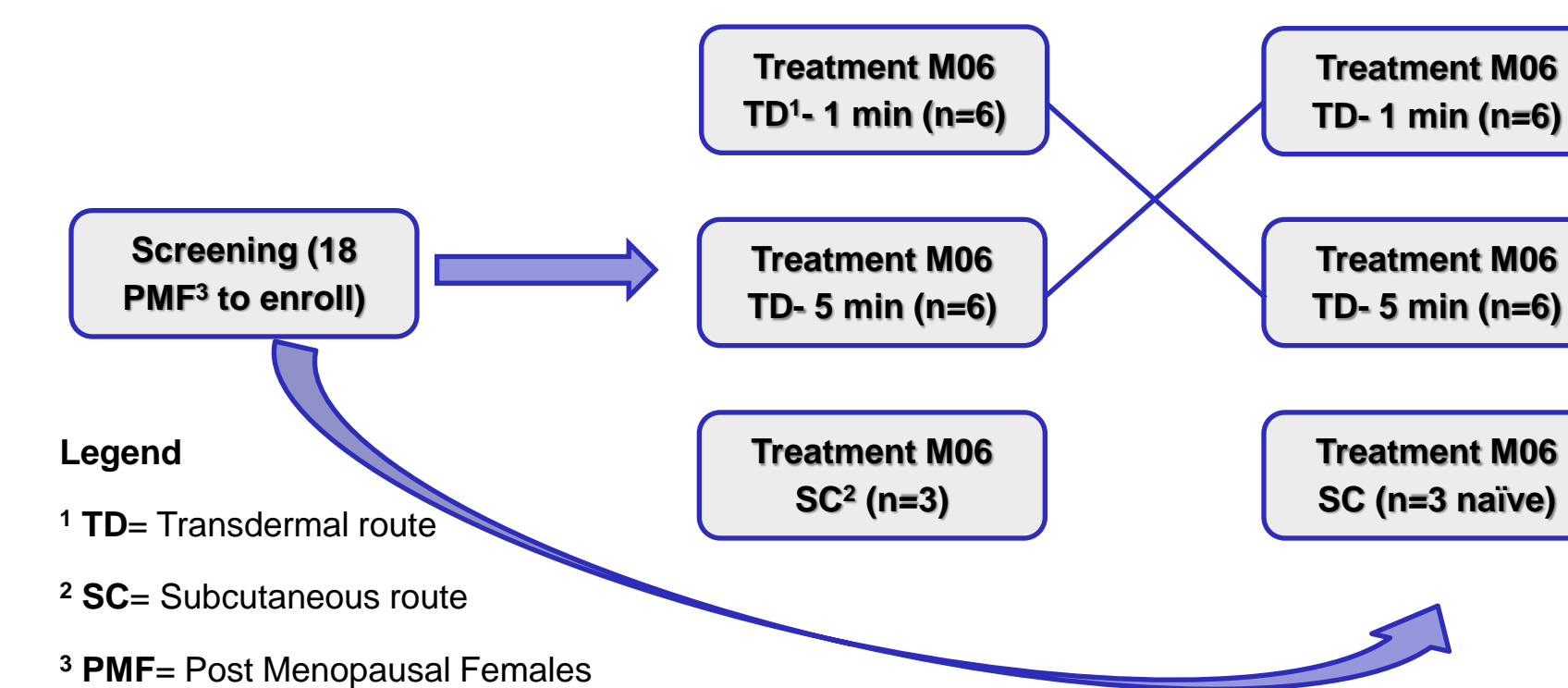


FIGURE 01: A SCHEMATIC PRESENTATION OF THE STUDY DESIGN OF STUDY M80

### STUDY M06

On the other side, trial M06 consists in a Single center, randomized, repeat dose, crossover design where 18 healthy PMF must be enrolled. All 18 subjects will be randomized on Day 0 (of period 1). As illustrated in figure 02, 12 subjects will be enrolled for potentially 2 periods and an additional 6 subjects will be enrolled but for only one period. It is important to note that all 18 subjects are enrolled during the same period without knowing exactly which treatment they will be enrolled in. Naturally, as healthy subjects are compensated for clinical commitment and travelling, we understand that the monetary compensation will be different between these two situations.



#### Legend

<sup>1</sup> TD= Transdermal route

<sup>2</sup> SC= Subcutaneous route

<sup>3</sup> PMF= Post Menopausal Females

FIGURE 02: A SCHEMATIC PRESENTATION OF THE STUDY DESIGN OF STUDY M06

Therefore, despite a similar study population, the complexity brought by these study designs is slightly different.

- How this complexity would affect subject's interest and ultimately recruitment and enrollment parameters?
- How to quantify these intangible parameters?

In order to do so, several steps were monitored and quantified to demonstrate impacted parameters such as:

- Difference between I/E criteria and overall expected impact on recruitment power
- Recruitment efforts monitoring
  - Advertisement interests between studies
  - Active recruitment days per subject enrolled
- Screening efforts monitoring
  - Active screening days per subject enrolled
  - Number of PMF screened
  - Refusal rate at screening

## RESULTS

### DIFFERENCE BETWEEN INCLUSION AND EXCLUSION CRITERIA

As the I/E criteria may introduce an important bias in this analysis, it is crucial to assess if there is any major differences in this area between M80 and M06 that would considerably impact study enrollment.

Table 01 below indicates screening advantages based on level of flexibility provide by the main I/E.

TABLE 01: COMPARISON OF SCREENING ADVANTAGES BETWEEN TRIAL M06 AND M80

CRITERIA	SCREENING ADVANTAGES	
	M06	M80
Age restriction	X	
Cardiac restrictions (PR, QRS, QTc)	X	
Blood pressure restrictions	X	
BMI restrictions	X	
Delay required between clinical trial participations		X
Medical Laboratory restrictions		X*

\*Interestingly, despite M80 was clearly advantaged by the medical laboratory restrictions, internal screening failure reasons revealed that this specific criteria was 16% higher than the one obtained on M06 trial.

As seen in this table, based on I/E criteria the M06 trial demonstrate a clear screening advantage over trial M80. Therefore, screening process should be considered easier than the one for trial M80.

### RECRUITMENT EFFORTS

#### Advertisement interest between studies

One of the first technique to verify the interest in a given trial over volunteers would be to assess how this given trial was able to generate registrations in our database compared to the number of volunteers requesting information on this study. Based on Web 2.0 approach, we recorded the number of volunteers requesting information for each of these trials versus the number of volunteers deciding to apply online to these trials. Our first observation was that both studies obtained approximately the same number of volunteers requesting information about these trials. However, while 8% of all these persons asked to electronically register on M80 trial, none (0%) requested to register on M06 trial.

#### Active recruitment days per subject enrolled

Trial M80 was requiring 1.33 day per post-menopausal female enrolled while the more complex one (trial M06) was requiring 2 days. This difference consists in a 33% additional recruitment effort to get the same participant on the M06 study. Once again, as the M06 trial seems a more complex design it is clear that recruitment efforts must be adjusted consequently.

### SCREENING EFFORTS

#### Active screening days per subject enrolled

A similar trend, as above, was observed where the M06 trial required an additional 44% screening effort to complete the panel. Indeed, in terms of screening days per volunteers we obtained 0.87 vs 1.56 screening day per PMF enrolled for the M80 and M06 respectively.

#### Number of PMF screened & refusals

Curiously, we obtained a ratio screened/enrolled of 4.11 PMF for the M06 trial where only 3.33 PMF were required for the M80 trial; representing an additional 50% volunteers screened. Therefore, despite the fact that criteria are less stringent on enrolling, the M06 trial still required more volunteers to be screened to achieve that same result. Looking deeper into main reason explaining this situation we observed that the study design complexity might not be stranger to that observation. Indeed, we obtained a refusal rate at screening significantly higher with the M06 trial (6.8%) versus the M80 trial (0%).

## CONCLUSION

In addition to the typical I/E criteria impact, the study design might affect recruitment and enrollment power. This was observed at multiple steps suggesting that a punctual external environmental factor might not be the only reason. Data obtained also suggest that a synergic effect is caused between every single of these aspects described above, which is increasing considerably the global effort. In conclusion, while assessing project feasibility is usually mainly based on I/E criteria, the study design impact should not be minimized and, in fact, should be considered as well in the initial recruitment and screening feasibility assessment.