WHITE PAPER

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# Med Devices: PMS/PMCF When AE Reporting is Low

Sample size estimation is an important step before undertaking any clinical study. However, the entire process depends upon the number of patients to be included for the proposed study. The purpose of this paper is to provide a reference table containing sample size required for a post marketing clinical trial when there is no background incidence of adverse events in the general population. The table provides sample size for various options such as the expected incidence rate of adverse reactions and the number of occurrence of a particular adverse reaction along with various statistical powers.

## Sample size Estimation when there is no background incidence of Adverse Events

If the expected incidence rate of adverse reactions is λ, the expected number of occurrences of a particular adverse reaction is a and the number of patients required to be studied is N. This N needs to be estimated. If the incidence of adverse reactions is reasonably low and for a given statistical power (1-ß ), N satisfies the following method.

$$\sum_{x=0}^{a-1} \frac{(N\lambda)^x e^{-N\lambda}}{x!} = \beta$$

When a = 1 (i.e., when adverse reaction expected to occur only in one patient) then the above equation simplifies to

$$N = \frac{-\log \beta}{\lambda}$$

For a > 1 there is no simple expression for the solution for the above equation but the same can be solved by using simulation methods. Thus the required sample size could be estimated from the above equations.

The following table gives required sample size for various options such as expected incidence rate of adverse reactions (λ), the number of occurrence of a particular adverse reaction (a) and statistical power (1-ß).

Table 1: Sample sizes required to observe a total of a adverse reactions with a given probability 1-ß and anticipated incidence λ.

| λ | a | Statistical Power | | | | | |
|---|---|---|---|---|---|---|---|
| | | 50% | 60% | 70% | 80% | 90% | 95% |
| | | 96688 | 104757 | 113873 | 125188 | 142060 | 157053 |
| 0.001 | 1 | 694 | 917 | 1204 | 1610 | 2303 | 2996 |
| | 2 | 1679 | 2023 | 2440 | 2995 | 3890 | 4744 |
| | 3 | 2675 | 3106 | 3616 | 4280 | 5323 | 6296 |
| | 4 | 3673 | 4176 | 4763 | 5516 | 6681 | 7754 |
| | 5 | 4671 | 5237 | 5891 | 6721 | 7994 | 9154 |
| | 6 | 5671 | 6292 | 7006 | 7906 | 9275 | 10514 |
| | 7 | 6670 | 7343 | 8112 | 9076 | 10533 | 11843 |
| | 8 | 7670 | 8390 | 9209 | 10233 | 11771 | 13149 |
| | 9 | 8669 | 9434 | 10301 | 11380 | 12995 | 14435 |
| | 10 | 9669 | 10476 | 11388 | 12519 | 14206 | 15706 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **0.005** | **1** | 139 | 184 | 241 | 322 | 461 | 600 |
| | **2** | 336 | 405 | 488 | 599 | 778 | 949 |
| | **3** | 535 | 622 | 724 | 856 | 1065 | 1260 |
| | **4** | 735 | 836 | 953 | 1104 | 1337 | 1551 |
| | **5** | 935 | 1048 | 1179 | 1345 | 1599 | 1831 |
| | **6** | 1135 | 1259 | 1402 | 1582 | 1855 | 2103 |
| | **7** | 1334 | 1469 | 1623 | 1816 | 2107 | 2369 |
| | **8** | 1534 | 1678 | 1842 | 2047 | 2355 | 2630 |
| | **9** | 1734 | 1887 | 2061 | 2276 | 2599 | 2887 |
| | **10** | 1934 | 2096 | 2278 | 2504 | 2842 | 3142 |
| **0.01** | **1** | 70 | 92 | 121 | 161 | 231 | 300 |
| | **2** | 168 | 203 | 244 | 300 | 389 | 475 |
| | **3** | 268 | 311 | 362 | 428 | 533 | 630 |
| | **4** | 368 | 418 | 477 | 552 | 669 | 776 |
| | **5** | 468 | 524 | 590 | 673 | 800 | 916 |
| | **6** | 568 | 630 | 701 | 791 | 928 | 1052 |
| | **7** | 667 | 735 | 812 | 908 | 1054 | 1185 |
| | **8** | 767 | 839 | 921 | 1024 | 1178 | 1315 |
| | **9** | 867 | 944 | 1031 | 1138 | 1300 | 1444 |
| | **10** | 967 | 1048 | 1139 | 1252 | 1421 | 1571 |

Sample size estimation is an important step in the planning of a post marketing clinical trial especially when there is no background incidence of adverse events in general population. The information provided above would certainly help clinical teams to simplify calculations to estimate sample size for the proposed study. Thus the table could be used as a ready reckoner for any post marketing clinical research to estimate the adverse events.

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