the duration of the spermatogenic cycle. For mice, the entire duration of spermatogenesis is approximately 42 days comprising the following stages: spermatogonial mitoses—6 days, spermatocytes—14 days, spermatids—9 days, testicular sperm—5.5 days, and epididymal sperm—7.5 days (*1*). Thus, matings within 3 weeks after single drug administration represent samplings of sperm exposed during post-meiotic stages, and matings from 4–8 weeks later represent samplings of sperm exposed during premeiotic and stem cells stages.

The classical form of the dominant lethal assay involves autopsy of females aproximately 13 days following timed matings, as determined by vaginal plugs in mice and vaginal cytology in rats, and enumeration of corpora lutea and total implants, as comprised by living fetuses, late fetal deaths, and early fetal deaths. The test can be considerably modified and simplified and hence made more suitable for routine practice by sacrificing the females at a fixed time, *e.g.*, 13 days in mice, following the midweek of their caging and presumptive mating. Additionally, this allows determination of effects of drugs on pregnancy rates. Similarly, corpora lutea counts, which are notoriously difficult, laborious, and inaccurate in mice and afford a measure of total fertilized zygotes, can be omitted and numbers of total implants in test animals can be related to those in controls, thus affording a simple measure of preimplantation losses. Using such modified procedures together with computerized data handling, large numbers of test agents can be simply and rapidly tested for mutagenic activity. The assay can also be conducted with drug administration to female mice, either before or in early pregnancy; however, this test has not yet been developed for routine purposes.

Dominant lethal mutations are directly measured by enumeration of early fetal deaths, and indirectly by preimplantation losses, as measured by reduction in the number of total implants in test compared with control females. Results are best expressed as early fetal deaths *per* pregnant female, rather than as the more conventional mutagenic index, early fetal deaths x 100 *per* total implants, as the latter index can be markedly altered by variation in the number of total implants (*11*). Preimplantation losses offer a presumptive index of mutagenic effects, but there is no precise parallelism between preimplantation losses and early fetal deaths. These should be regarded as concomitant and not alternate parameters. Furthermore, the use of the mutagenic index presupposes that the number of early deaths is proportional to the number of implants regardless of preimplantation losses; this would anticipate that absolute number of early deaths are lower in those animals with reduced numbers of total implants. This has been shown experimentally not to be so (*11*). Finally, an additional disadvantage of such ratios