

## **Current Status and Future Progress of Reproductive/Developmental Toxicity Tests**

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Currently, ECVAM (European Centre for the Validation of Alternative Methods) in the EU appears to be at the forefront of the development of alternative methods for developmental toxicity tests (reproductive/developmental toxicity tests). According to the 7th amendment of the EU Cosmetic Directive promulgated on March 11, 2003, the deadline for abolition of animal experiments is set at March 11, 2009 for many toxicity tests; however, it is set at March 11, 2013, 10 years after the promulgation of the directive, and further extension may be allowed for developmental toxicity tests. This implies that the establishing new methodology for developmental toxicity tests is very difficult.

Why is it difficult to develop alternative methods for developmental toxicity tests in comparison with other toxicity tests? In developmental toxicity tests, chemical substances first enter the blood stream and then reach the placenta *via* metabolism in the liver, and other organs. After further metabolism in the placenta, chemical substances finally reach to the fetuses where they affect fetal development. The difference in the *in vivo* route of chemical substances is an important reason for the difficulty in establishment of new methods for developmental toxicological tests in comparison with general toxicity tests.

According to the EU, the use of "*in silico*" techniques for developmental toxicity tests may be difficult, and I agree with this. The *in silico* technique is basically a method for prediction of toxicological effects from existing data, and can not predict new effects, because data obtained by developmental toxicological tests are too complex.

Three techniques are now being examined to overcome with the difficulty in changing the method of developmental toxicological tests. They are the technique utilizing ES cells (EST), the micromass culture technique (MM) and the whole embryonic culture technique (WEC).

In this symposium, the current status of developmental toxicity tests and the 3 techniques examined in the EU will be introduced, and opinions on future progress will be presented.