

Evaluation report on the *in vitro* PBMC (peripheral blood mononucleated cell) test method as an alternative to pyrogen testing

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Summary

We consider the proposed *in vitro* PBMC (peripheral blood mononucleated cell) test method to be useful in reducing the number of rabbits necessary for testing, to be worthy of consideration as a novel test method for detecting pyrogenic substances based on mechanism of action, and to have satisfied acceptable criteria for the handling of validating data. In spite of this, however, there are a number of issues that must be clarified before this test method can be accepted as equivalent to and therefore a suitable alternative for pyrogen tests that use rabbits. In Japan, there are some issues that remain in the transition from rabbit pyrogen testing to endotoxin testing. Given this situation, the PBMC test can only be recommended for use in combination with rabbit pyrogen testing for specific situations in which the use of endotoxin testing is prohibited or in which significant discrepancies in pyrogenic potency between humans and rabbits are anticipated. We look forward to expanded application of the *in vitro* PBMC test based on further scientific research.