

ESTIV Congress 2026, 30 June 2026

Session 3 – Track A: International Standards as the Bridge to the Future of Safe Medical Devices

Literature

Ayehunie, S., Cannon, C., Lamore, S., Kubilus, J., Anderson, D. J., Pudney, J., & Klausner, M. (2006). Organotypic human vaginal-ectocervical tissue model for irritation studies of spermicides, microbicides, and feminine-care products. *Toxicology in Vitro*, 20(5), 689–698. <https://doi.org/10.1016/J.TIV.2005.10.002>

Ayehunie, S., Cannon, C., Larosa, K., Pudney, J., Anderson, D. J., & Klausner, M. (2011). Development of an in vitro alternative assay method for vaginal irritation. *Toxicology*, 279, 130–138. <https://doi.org/10.1016/j.tox.2010.10.001>

Bellentani L. (1982). Cyclic and chronobiological considerations when employing the rabbit fever test. *Progress in clinical and biological research*, 93, 329–342.

Beutler, B., Hoebe, K., Du, X., & Ulevitch, R. J. (2003). How we detect microbes and respond to them: the Toll-like receptors and their transducers. *Journal of Leukocyte Biology*, 74(4), 479–485. <https://doi.org/10.1189/JLB.0203082>

Borton, L., & Coleman, K. (2026). Material-mediated pyrogens in medical devices: Myth or reality? *ALTEX - Alternatives to Animal Experimentation*, 43(1), 78–97. <https://doi.org/10.14573/ALTEX.2504231>

Borton, L. K., & Coleman, K. P. (2018). Material-mediated pyrogens in medical devices: Applicability of the in vitro Monocyte Activation Test. *ALTEX - Alternatives to Animal Experimentation*, 35(4), 453–463. <https://doi.org/10.14573/ALTEX.1709221>

Cooper, J. F., Weary, M. E., & Jordan, F. T. (1997). The impact of non-endotoxin LAL-reactive materials on Limulus amebocyte lysate analyses. *PDA journal of pharmaceutical science and technology*, 51(1), 2–6. PMID: [9099058](https://pubmed.ncbi.nlm.nih.gov/9099058/)

Costin, G. E., Raabe, H. A., Priston, R., Evans, E., & Curren, R. D. (2011). Vaginal irritation models: the current status of available alternative and in vitro tests. *Alternatives to Laboratory Animals : ATLA*, 39(4), 317–337. <https://doi.org/10.1177/026119291103900403>

De Jong, W. H., Carraway, J. W., Liu, C., Fan, C., Liu, J., Turley, A. P., Rollins, T. S., & Coleman, K. P. (2020). The suitability of reconstructed human epidermis models for medical device irritation assessment: A comparison of In Vitro and In Vivo testing results. *Toxicology in Vitro*, 69. <https://doi.org/10.1016/j.tiv.2020.104995>

De Jong, W. H., Hoffmann, S., Lee, M., Kandárová, H., Pellevoisin, C., Haishima, Y., Rollins, B., Zdawczyk, A., Willoughby, J., Bachelor, M., Schatz, T., Skoog, S., Parker, S.,

Sawyer, A., Pescio, P., Fant, K., Kim, K. M., Kwon, J. S., Gehrke, H., ... Coleman, K. P. (2018). Round robin study to evaluate the reconstructed human epidermis (RhE) model as an in vitro skin irritation test for detection of irritant activity in medical device extracts. *Toxicology in Vitro*, 50, 439–449. <https://doi.org/10.1016/j.tiv.2018.01.001>

Dinarello, C. A. (2000). Proinflammatory cytokines. *Chest*, 118(2), 503–508. <https://doi.org/10.1378/chest.118.2.503>

Ding, J. L., & Ho, B. (2001). A new era in pyrogen testing. *Trends in Biotechnology*, 19(8), 277–281. [https://doi.org/10.1016/S0167-7799\(01\)01694-8](https://doi.org/10.1016/S0167-7799(01)01694-8)

Dover, S. E., Aroutcheva, A. A., Faro, S., & Chikindas, M. L. (2007). Safety study of an antimicrobial peptide lactocin 160, produced by the vaginal *Lactobacillus rhamnosus*. *Infectious Diseases in Obstetrics and Gynecology*, 2007. <https://doi.org/10.1155/2007/78248>

Dunér K. I. (1995). The importance of the quality of water in *Limulus* Amebocyte Lysate tests. *PDA journal of pharmaceutical science and technology*, 49(3), 119–121. PMID: [7613989](https://pubmed.ncbi.nlm.nih.gov/7613989/)

European Directorate for the Quality of Medicines & HealthCare (Ed.) *Ph. Eur.: Chapter 2.6.30 Monocyte-Activation Test*, 10th ed.; Council of Europe: Strasbourg, France, 2020.

European Directorate for the Quality of Medicines & HealthCare (Ed.) *Ph. Eur.: General Chapter 5.1.13 Pyrogenicity*, 11th ed.; Supplement 11.8; Council of Europe: Strasbourg, France, 2025.

Greisman, S. E., & Hornick, R. B. (1969). Comparative Pyrogenic Reactivity of Rabbit and Man to Bacterial Endotoxin. *Proceedings of the Society for Experimental Biology and Medicine*, 131(4), 1154–1158. <https://doi.org/10.3181/00379727-131-34059/PDF>

Hartung, T., Sauer, A., Hermann, C., Brockhaus, F., & Wendel, A. (1997). Overactivation of the Immune System by Translocated Bacteria and Bacterial Products. *Scandinavian Journal of Gastroenterology*, 32(222), 98–99. <https://doi.org/10.1080/00365521.1997.11720729>

Hasiwa, N., Daneshian, M., Bruegger, P., Fennrich, S., Hochadel, A., Hoffmann, S., Rivera-Mariani, F. E., Rockel, C., Schindler, S., Spreitzer, I., Stoppelkamp, S., Vysyaraju, K., & Hartung, T. (2013). Evidence for the detection of non-endotoxin pyrogens by the whole blood monocyte activation test. *ALTEX*, 30(2), 169–208. <https://doi.org/10.14573/ALTEX.2013.2.169>

ICCVAM. (2024). Validation, Qualification, and Regulatory Acceptance of New Approach Methodologies. <https://doi.org/10.22427/NICEATM-2>

ISO (2025). ISO 10993-1:2025, Biological evaluation of medical devices - Part 1: Requirements and general principles for the evaluation of biological safety within a risk management process. International Organization for Standardization.

ISO (2017). ISO 10993-11:2017, Biological evaluation of medical devices - Part 11: Tests for systemic toxicity. International Organization for Standardization.

ISO (2022). ISO 10993-2:2022, Biological evaluation of medical devices - Part 2: Animal welfare requirements. International Organization for Standardization.

ISO. (2021). ISO 10993-23:2021, Biological evaluation of medical devices - Part 23: Tests for irritation. International Organization for Standardization.

Jacobs, M. N., Colacci, A., Louekari, K., Luijten, M., Hakkert, B. C., Paparella, M., & Vasseur, P. (2016). International regulatory needs for development of an IATA for non-genotoxic carcinogenic chemical substances. *ALTEX*, 33(4), 359–392.

<https://doi.org/10.14573/altex.1601201>

Japan Center for the Validation of Alternative Methods (JaCVAM). (2024). *Round robin study report to evaluate LabCyte EPI-MODEL24 for medical device extracts*.

https://www.jacvam.go.jp/files/list/02/02_04_LabCyte_EPI-MODEL24_RRS_Report.pdf

Japanese Pharmacopoeia. Monocyte-Activation Test as an Alternative 1 Method for Pyrogen Test 〈G4-13-190〉, [Link](#)

Kim, J., Kang, N. H., Kim, J. S., Kim, I. S., & Kim, Y. (2024). Round Robin Study for Evaluation an in vitro skin irritation test for medical device extracts using KeraSkin™ in Korea. *Food and Chemical Toxicology*, 192. <https://doi.org/10.1016/j.fct.2024.114942>

Kluger, M. J. (1991). Fever: role of pyrogens and cryogens. *Physiological Reviews*, 71(1), 93–127. <https://doi.org/10.1152/PHYSREV.1991.71.1.93>

Mazzotti, F., Beuttler, J., Zeller, R., Fink, U., Schindler, S., Wendel, A., Harlung, T., & Von Aulock, S. (2007). In vitro pyrogen test—A new test method for solid medical devices. *Journal of Biomedical Materials Research Part A*, 80A(2), 276–282.

<https://doi.org/10.1002/JBM.A.30922>

Moltz, H. (1993). Fever: causes and consequences. *Neuroscience and Biobehavioral Reviews*, 17(3), 237–269. [https://doi.org/10.1016/S0149-7634\(05\)80009-0](https://doi.org/10.1016/S0149-7634(05)80009-0)

Morath, S., Geyer, A., Spreitzer, I., Hermann, C., & Hartung, T. (2002). Structural Decomposition and Heterogeneity of Commercial Lipoteichoic Acid Preparations. *Infection and Immunity*, 70(2), 938. <https://doi.org/10.1128/IAI.70.2.938-944.2002>

Nakagawa, Y., Maeda, H., & Murai, T. (2002). Evaluation of the in vitro pyrogen test system based on proinflammatory cytokine release from human monocytes: comparison with a human whole blood culture test system and with the rabbit pyrogen test. *Clinical and Diagnostic Laboratory Immunology*, 9(3), 588–597.

<https://doi.org/10.1128/CDLI.9.3.588-597.2002>

OECD (2025), *Guidance Document on Good In Vitro Method Practices (GIVIMP)*, Second Edition, OECD Series on Testing and Assessment, No. 421, OECD Publishing, Paris, <https://doi.org/10.1787/5ba6777b-en>.

Pellevoisin, C., Coleman, K. P., & Hoffmann, S. (2022). ISO 10993-23 In vitro irritation testing for medical devices: Substantiating applicability to mild irritants and non-extractables. *Toxicology in Vitro*, 82, 105371. <https://doi.org/10.1016/J.TIV.2022.105371>

Perrin, J., Costin, G.-E., Ayehunie, S., Kandárová, H., Landry, T., Brown, J., & Clippinger, A. J. (2026). Using a reconstructed human vaginal epithelium to assess irritation: A proof-of-concept study supporting regulatory qualification of the method for use with personal lubricants. *Toxicology in Vitro*, 112, 106198. <https://doi.org/10.1016/j.tiv.2026.106198>

Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC (Text with EEA relevance.), ELI: <http://data.europa.eu/eli/reg/2017/745/oj>, Current consolidated version: [01/01/2026](https://eur-lex.europa.eu/eli/reg/2017/745/oj/consolidated)

Roslansky, P. F., Dawson, M. E., & Novitsky, T. J. (1991). Plastics, endotoxins, and the Limulus amebocyte lysate test. *Journal of parenteral science and technology : a publication of the Parenteral Drug Association*, 45(2), 83–87. PMID: [2051261](https://pubmed.ncbi.nlm.nih.gov/2051261/)

Ross, V. C., & Bruch, C. W. (1982). Endotoxin testing of medical devices with LAL: FDA requirements. *Progress in clinical and biological research*, 93, 39–48. PMID: [6750646](https://pubmed.ncbi.nlm.nih.gov/6750646/)

Rudloe, A. (1983). The effect of heavy bleeding on mortality of the horseshoe crab, *Limulus polyphemus*, in the natural environment. *Journal of Invertebrate Pathology*, 42(2), 167–176. [https://doi.org/10.1016/0022-2011\(83\)90059-9](https://doi.org/10.1016/0022-2011(83)90059-9)

Schindler, S., Bristow, A., Cartmell, T., Hartung, T., & Fennrich, S. (2003). Comparison of the reactivity of human and rabbit blood towards pyrogenic stimuli. *ALTEX*, 20(2), 59–63. PMID: [12764541](https://pubmed.ncbi.nlm.nih.gov/12764541/)

Schindler, S., Von Aulock, S., Daneshian, M., & Hartung, T. (2009). Development, validation and applications of the monocyte activation test for pyrogens based on human whole blood. *ALTEX*, 26(4), 265–277. <https://doi.org/10.14573/ALTEX.2009.4.265>

Sica, V. P., Friberg, M. A., Teufel, A. G., Streicher-Scott, J. L., Hu, P., Sauer, U. G., Krivos, K. L., Price, J. M., Baker, T. R., Abbinante-Nissen, J. M., & Woeller, K. E. (2022). Safety assessment scheme for menstrual cups and application for the evaluation of a menstrual cup comprised of medical grade silicone. *EBioMedicine*, 86. <https://doi.org/10.1016/j.ebiom.2022.104339>

Spreitzer, I., Fischer, M., Hartzsch, K., Lüderitz-Püchel, U., & Montag, T. (2002). Comparative study of rabbit pyrogen test and human whole blood assay on human serum albumin. *ALTEX*, 19 Suppl 1, 73–75. PMID: [12096333](https://pubmed.ncbi.nlm.nih.gov/12096333/)

Szczepaniak, J., Cieřlik, W., Romanowicz, A., Musioł, R., & Krasowska, A. (2017). Blocking and dislocation of *Candida albicans* Cdr1p transporter by styrylquinolines. *International Journal of Antimicrobial Agents*, 50(2), 171–176.
<https://doi.org/10.1016/j.ijantimicag.2017.01.044>

U.S. Department of Health and Human Services Food and Drug Administration (2026) GUIDANCE DOCUMENT Pyrogen and Endotoxins Testing: Questions and Answers, Guidance for Industry, <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/pyrogen-and-endotoxins-testing-questions-and-answers>

United States Pharmacopeia (2017). *General Chapter, (151) Pyrogen Test*. USP-NF. Rockville, MD: United States Pharmacopeia
DOI: https://doi.org/10.31003/USPNF_M98900_01_01

United States Pharmacopeia (2017). *General Chapter, (1225) Validation of Compendial Procedures*. USP-NF. Rockville, MD: United States Pharmacopeia.
DOI: https://doi.org/10.31003/USPNF_M99945_04_01

Weary, M. E., Donohue, G., Pearson, F. C., & Story, K. (1980). Relative potencies of four reference endotoxin standards as measured by the *Limulus amoebocyte lysate* and USP rabbit pyrogen tests. *Applied and Environmental Microbiology*, 40(6), 1148–1151.
<https://doi.org/10.1128/AEM.40.6.1148-1151.1980>

Williams, K. L., & Pearson, F. C. (2007). *Endotoxins : pyrogens, LAL testing and depyrogenation*. (3rd ed. / edited by Kevin L. Williams.). Informa Healthcare.
<https://doi.org/10.3109/9781420020595>

Resources

Some examples of national standard bodies which are [member bodies](#) of the International Organization for Standardization (ISO)

France: [AFNOR – Association française de normalisation](#)

Germany: [DIN – Deutsche Institut für Normung e.V.](#)

Netherlands: [NEN – Royal Netherlands Standardization Institute](#)

Slovakia: [UNMS SR – Slovak Office of Standards, Metrology and Testing](#)