

United and empowering anaesthesiologists around the world to improve patient care

Dr Lorenzo Moja World Health Organization

Via email: mojal@who.int

12 November 2024

Dear Lorenzo,

Re: Recommendation for the Discontinuation of Halothane from the 2027 WHO EML

I am writing to you on behalf of the World Federation of Societies of Anaesthesiologists (WFSA), a Non-State Actor in Official Relations with WHO, to formally recommend the discontinuation of Halothane from the 2027 EML.

Halothane, once a staple in anaesthetic practice, has been overshadowed by the advent of newer, safer, and more efficacious inhalational agents¹. Despite its historical significance, the continued use of Halothane is no longer justifiable, primarily due to the following critical concerns:

- 1. **Sensitization of the Heart to Catecholamines:** Halothane sensitizes the myocardium to catecholamines, increasing the risk of cardiac arrhythmias^{2,3}. Some studies found the incidence of significant arrythmias to exceed 20% of patients. In today's clinical settings, where patients often present with complex comorbidities, the risk of inducing cardiac complications is a critical concern.
- 2. **High Blood Solubility:** Halothane's high blood solubility leads to slower induction and recovery times compared to other agents^{2,4}. This may affect the efficiency of surgical operations but also impacts patient throughput and resource utilization in surgical units.
- 3. **Hepatotoxicity:** Halothane is significantly associated with the risk of hepatotoxicity, ranging from mild elevation of liver enzymes to severe and potentially fatal fulminant hepatitis^{2,5,6}. This risk, albeit rare, poses a significant safety concern, especially when safer alternatives are available.
- 4. **Environmental Impact:** Halothane is a potent greenhouse gas with a substantial environmental impact. The anaesthetic community has been moving towards more environmentally friendly options that align with global sustainability goals⁷.

5. **Availability of Safer Alternatives:** The development and availability of newer anaesthetic agents, such as sevoflurane, which is less hepatotoxic and has a more favorable pharmacokinetic profile, render the continued use of Halothane unnecessary and outdated⁸.

Given these points, we strongly advocate for the phasing out of Halothane in clinical practice. This action would not only enhance the safety profile of anaesthetic care but also align with current standards and expectations for patient safety and care efficacy. Further, the low cost, inflationary impacts on production, and the shrinking global market are resulting in progressively fewer manufacturers⁹.

We are aware of the complexities involved in changing clinical practice and the phased removal of any medication. However, we believe that the safety benefits clearly justify this move.

While Halothane is no longer available in upper-middle and high-income countries, the reasons why Halothane continues to be used in low-resource settings are its relatively lower cost and that poorly trained anaesthesia providers especially are familiar with it¹⁰. Transitioning to a new agent will require initiatives targeted to these providers.

A crucial aspect will be sufficient time for the Ministries of Health and Finance to make the appropriate budgetary allocations followed by the operational aspects of purchase and implementation. It's highly likely that in many lower-resourced countries, such activity will need to wait for the 2026 budget cycle.

WFSA envisions the following actions to be necessary, thereby justifying the delay to 2027:

- Informing and Sensitizing our 141 Member National Societies of Anaesthesiologists on the impending removal of Halothane. This will be done through targeted outreach at regional and global conferences and meetings, including through specific online events.
- Targeted communication with those of our Member Societies still using Halothane to provide guidance and advice on the safe changeover to another anaesthetic agent.
- Engagement with relevant stakeholders within industry and manufacturing both relating to anaesthetic equipment that needs to change and the vapours themselves to ensure they provide the most appropriate and relevant information to aid the changeover. We will encourage them to provide relevant patient safety information as part of the transition. We also plan to raise our concerns that this is not seen as an opportunity for price gouging but rather an opportunity whereby appropriate pricing or discounts would result in a larger market share and greater safety for patients.
- Template letters we will develop template letters in a range of languages for use at the local and national level that can be sent to hospital pharmacies, hospital leadership, and regional and national health authorities, including Ministries of Health and Ministries of Finance.

Given the global scope and magnitude of the above work, it will not be possible to finish this by 2025.

We are willing to participate in discussions with you and your committees to facilitate this transition and to assist in developing guidelines or protocols that may be required for the same. Similarly, we welcome your engagement for our development of relevant documents.

Thank you for considering this significant aspect of patient care improvement. We look forward to your continued support and to working collaboratively on implementing this change effectively.

Yours sincerely,

Professor Adrian Gelb

Adrian Jel

WFSA Past President, WHO Liaison

References:

- 1. Yunus A, Odigbo M, Tasiu S, Babangida SM, Yunusa Y, Kabiru AM, Yusuf MM. Comparison of the Qualities of Sevoflurane and Halothane in Paediatric Anaesthesia. Nigerian Journal of Medicine. 2023;32:23-27. doi:10.4103/njm.njm_126_22
- 2. Huang L, Sang C, Desai MS. Beyond Ether and Chloroform-A Major Breakthrough With Halothane. J Anesth Hist. 2017;3(3):87-102. doi:10.1016/j.janh.2017.05.003
- 3. MacLeod BA, McGroarty R, Morton RH, Walker MJ. Effects of halothane on arrhythmias induced by myocardial ischaemia. Can J Anaesth. 1989;36(3 Pt 1):289-294. doi:10.1007/BF03010767
- 4. Kangralkar G, Jamale P. Sevoflurane versus halothane for induction of anesthesia in pediatric and adult patients. Med Gas Res. 2021;11:53-57. doi:10.4103/2045-9912.311489
- 5. Böttiger LE, Dalén E, Hallén B. Halothane-induced liver damage: an analysis of the material reported to the Swedish Adverse Drug Reaction Committee, 1966-1973. Acta Anaesthesiol Scand. 1976;20(1):40-46. doi:10.1111/j.1399-6576.1976.tb05007.x
- 6. Black GW. A review of the pharmacology of halothane. Br J Anaesth. 1965;37:688-705. doi:10.1093/bja/37.9.688
- 7. Varughese S, Ahmed R. Environmental and Occupational Considerations of Anesthesia: A Narrative Review and Update. Anesth Analg. 2021;133(4):826-835. doi:10.1213/ANE.000000000005504
- 8. Baki MA, Ahmed K, Akter R, Barman NK, Hossein M, Sharma A, Shil S. Comparison of Sevoflurane and Halothane Anesthesia Cognitive Function in Adult. Glob Acad J Med Sci. 2023. doi:10.36348/gajms.2023.v05i03.006
- 9. Gelb AW, Vreede E. Availability of halothane is still important in some parts of the world. Can J Anaesth. 2024;71(10):1427-1428. doi:10.1007/s12630-024-02836-9
- 10. Mueller L. Medicating Anaesthesiology: Pharmaceutical Change, Specialisation and Healthcare Reform in Post-War Britain. Soc Hist Med. 2021. doi:10.1093/SHM/HKAA101