$25^{\text{th}}$  WHO Expert Committee on Selection and Use of Essential Medicines Expert review

C.6 Nitrous oxide – EML and EMLc					
Reviewer summary	⊠ Supportive of the proposal				
	☐ Not supportive of the proposal				
	Justification (based on considerations of the dimensions described below):				
	The proposed addition to the WHO Model List of Essential Medicines highlights the environmental harm of using centrally piped nitrous oxide ( $N_2O$ ) systems in healthcare. These systems are major contributors to greenhouse gas emissions due to widespread and often undetectable leaks, with studies from countries such as the UK, Australia, and the U.S. reporting losses of 70–95% of $N_2O$ before it reaches patients. $N_2O$ is a potent greenhouse gas—273 times stronger than $CO_2$ —and a leading ozone-depleting substance, with a lifespan exceeding 100 years.				
	Real-world experiences reinforce these findings. Facilities in the U.S. (NYC Health + Hospitals), Canada (Vancouver General), Australia (Westmead Hospital), Kenya (Aga Khan University Hospital), and India have decommissioned piped systems or detected severe inefficiencies, shifting instead to point-of-care cylinders. These changes have resulted in significant emission reductions and improved cost efficiency.				
	Professional bodies, including the Royal College of Anaesthetist Anesthesiologists, now recommend avoiding central piped $N_2O$ based delivery maintains clinical utility while enhancing enviror sustainability. The proposed statement aligns with global clima environmentally responsible healthcare. Its inclusion on the EN operationally feasible.	systems. nmental ai te targets	Transition nd health and WHO	ning to cylinder- system 's commitment to	
Does the EML and/or EMLc currently recommend alternative medicines for the		☐ Yes	□ No	⊠ Not applicable	
proposed indication that can be considered therapeutic alternatives?					
(https://list.essentialmeds.org/)					
Does adequate evidence exist for the efficacy/effectiveness of the medicine for the proposed indication?		☐ Yes	□ No	☑ Not applicable	
(e.g., evidence originating from multiple high-quality studies with sufficient follow up.  This may be evidence included in the application, and/or additional evidence identified during the review process;)					
Does adequate evidence exist for the safety/harms associated with the proposed medicine?		□ Yes	□ No		
(e.g., evidence originating from multiple high-quality studies with sufficient follow up. This may be evidence included in the application, and/or additional evidence identified during the review process;)					
Overall, does the proposed medicine have a favourable and meaningful balance of benefits to harms?		□ Yes	□ No	Not applicable	
Are there any special requirements for the safe, effective and appropriate use of the medicines?		□ Yes	□ No	⊠ Not applicable	
(e.g. laboratory diagnostic and/or monitoring tests, specialized training for health providers, etc)					
Are there any issues regarding price, cost-effectiveness and budget implications in different settings?		□ Yes	□ No	⊠ Not applicable	

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Is the medicine available and accessible across countries?	☐ Yes ☐ No ☒ Not applicable		
(e.g. shortages, generics and biosimilars, pooled procurement programmes, access programmes)			
Does the medicine have wide regulatory approval?	☐ Yes, for the proposed indication		
	<ul><li>☐ Yes, but only for other indications</li><li>(off-label for proposed indication)</li><li>☐ No</li><li>☑ Not applicable</li></ul>		
	_ net applicable		
In Additio:			
Justification for Inclusion  1. Environmental Impact and Climate Relevance Nitrous oxide (N <sub>2</sub> O) is a potent greenhouse gas with a global warming potential (GWP100) 273 times that of CO <sub>2</sub> , and an atmospheric lifetime of over 100 years N <sub>2</sub> O is currently the largest ozone-depleting substance emitted in the 21st century c.6. nitrous-oxide.  Healthcare facilities contribute 1–3% of global N <sub>2</sub> O emissions, with piped N <sub>2</sub> O systems being major culprits due to pervasive system leaks  2. Evidence of Systemic Leakage and Waste Multiple studies (Scotland, Australia, USA) have found that 70–95% of N <sub>2</sub> O in piped systems is lost through infrastructure leaks before clinical use This loss translates into unnecessary financial costs, occupational hazards, and avoidable environmental degradation. Infrastructure aging makes it difficult and often unfeasible to detect and fix all leak points  3. Global Expert and Institutional Support The Royal College of Anaesthetists (UK and Ireland) and the American Society of Anaesthesiologists recommend deactivating central piped systems in favor of point-of-care cylinders Point-of-care systems are already proving feasible and effective in facilities that have transitioned globally.  4. Practicality and System Resilience Portable cylinders reduce loss, simplify monitoring, and improve supply chain resilience.  Transitioning does not restrict clinical use but improves efficiency and sustainability.  There are multiple real-world reports from various countries that corroborate the environmental concerns associated with central piped nitrous oxide (N <sub>2</sub> O) systems in healthcare facilities. These reports highlight significant leakage issues, leading to environmental harm and prompting transitions to point-of-care cylinder systems.  International Case Studies on N <sub>2</sub> O Leakage and Mitigation  1. United States  • NYC Health + Hospitals: Deactivated central piped N <sub>2</sub> O systems across its network, resulting in over a 50% reduction in anesthesia-related carbon emissions. This move was part of a broa			

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supply system, the hospital achieved a reduction in greenhouse gas emissions equivalent to removing 57 cars from the road annually.

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## 3. Australia

- Children's Hospital at Westmead: Implemented custom-built flow meters to detect N₂O leaks, discovering that about 50% of the gas was lost due to system inefficiencies. This finding prompted initiatives to identify and rectify leakage points within the facility. PMC+1Agency for Clinical Innovation+1
- Australian Government Report: Released a practical guide outlining methods to detect and reduce N<sub>2</sub>O leaks in healthcare facilities. The report emphasizes the environmental impact of N<sub>2</sub>O and provides strategies for healthcare providers to mitigate emissions. Health.gov.au

## 4. Kenya

Aga Khan University Hospital, Nairobi: Decommissioned its piped N₂O system after recognizing that nitrous oxide accounted for over 95% of the hospital's anesthetic gas emissions. Transitioned to using portable Entonox cylinders in operating rooms, effectively reducing greenhouse gas emissions and improving supply chain resilience. <a href="healthprocanada.com+2Atach">healthprocanada.com+2Atach</a> Community+2BJA Anaesthesia+2

## 5. India

 Tertiary Healthcare Center: An observational study revealed that between 49% to 63% of N<sub>2</sub>O was lost due to leaks in the central piping system. The study highlighted the substantial environmental impact, with annual emissions equating to over 10,000 tons of CO<sub>2</sub> equivalents. PMC