Atmospheric and watershed modelling of HFO-1234ze(E) emissions from

prospective pressurized metered-dose inhalers usage by Shivendra G. Tewari et al.

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This paper investigates the production of trifluoroacetic acid (TFA) from the atmospheric oxidation of a latest generation hydrofluoroolefin (HFO), HFO-1234ze(E), that is being used as a replacement for previous generation propellants in pressurized metered-dose inhalers (pMDI). The paper also investigates the subsequent TFA deposition within three separate river drainage basins, produced from the atmospheric oxidation of HFO-1234ze(E). The paper uses well-tested methods and models but I have several concerns (outlined below) with regards to the oxidation pathways, data used and conclusions made. The paper is interesting and scientifically valuable as not many studies have been done on pMDI emissions; therefore, once the following issues have been addressed, the paper merits publication in ACP.

Response: We thank the Reviewer for their positive feedback. In the revised manuscript, we have addressed all of their concerns. Below, we provide our point-by-point responses to each issue raised.

General comments

Based on the title of the paper, I would expect to see more information on other atmospheric oxidation routes of HFO-1234ze(E). Despite OH being the most probable oxidation pathway for this HFO due to the reaction rate, ozonolysis has been shown as a viable oxidation pathway to ultimately produce trifluoromethane (HFC-23; CHF3) with yields of 3.11 ± 0.05% (https://doi.org/10.1073/pnas.2312714120) despite the lower reaction rates. As pMDI emissions are likely to occur in the lower troposphere, un regionally polluted areas with high ozone, ozonolysis will play a role in the oxidation of HFC-1234ze(E). The authors allude to another oxidation process, i.e. photolysis, of trifluoroacetyl aldehyde (TFAA) that does not produce TFA; however, it does produce HFC-23. Considering the main focus of this paper is the atmospheric breakdown of HFO-1234ze(E), these mechanisms that produce other trace gases should be outlined at least in the introduction, irrespective of if the focus is only on TFA production.

Response: The Reviewer raises two points related to (1) the removal of HFO-1234ze(E) by reaction with ozone and (2) the photolysis of trifluoroacetaldehyde (TFAA), and the reported formation of HFC-23 from each of these routes.

1) Reaction of HFO-1234ze(E) with ozone

All tropospheric removal routes for HFO-1234ze(E) were considered in construction of the chemical mechanism. As the Reviewer indicates, removal by reaction with OH is the dominant removal route, the 298 K rate coefficient (k_{OH}) currently recommended by the IUPAC Task Group on Atmospheric Chemical Kinetic Data Evaluation being 7.0×10^{-13} cm^3 $molecule^{-1}$ s^{-1}. A widely-applied criterion for inclusion of the reaction of an organic compound with ozone in chemical mechanisms such as the MCM (e.g. Jenkin et al., 1997) is if its rate coefficient (k_{O3}) is greater than 10^{-8} k_{OH}, this being the threshold where about 1% of the organic compound is estimated to be removed by reaction with ozone. The currently recommended rate coefficient is $k_{O3} = 2.5 \times 10^{-21}$ cm^3 $molecule^{-1}$ s^{-1} (IUPAC Task Group on Atmospheric Chemical Kinetic Data Evaluation – Data Sheet oFOx129), such that $k_{O3} = 3.6 \times 10^{-9}$ k_{OH}. Reaction with ozone was therefore not represented.

The Reviewer comments on the relatively recent study of McGillen et al. (2023) which reports a small yield (about 3%) of HFC-23 from the slow reaction of HFO-1234ze(E) with ozone, and a resultant increase in the GWP calculated for HFO-1234ze(E) (i.e. from about 1 to about 12 on the 100-year horizon). Although this is an important result, it is possible that the impact has been overestimated. First, McGillen et al. (2023) report that about 3% of HFO-1234ze(E) is removed by reaction with ozone in their global modelling study, the highest fraction of all the HFOs considered. Based on the relative OH and ozone rate coefficients reported in their study, it seems likely that the highest fractional removal by ozone should be for HFO-1243zf, with that for HFO-1234ze(E) being somewhat lower (as discussed above). Secondly, McGillen et al. (2023) applied temperature independent rate coefficients for the HFO + ozone reactions in their model. In practice, these reactions are expected to possess strong temperature dependences. Based on the reaction of ozone with cis-dichloroethene (which is of comparable reactivity to HFO-1234ze(E)), the rate coefficient would be expected to fall by a factor of about 100 between 298K and an upper troposphere temperature of 220K (e.g. Leather et al. 2011, this study being from the same group as McGillen et al. (2023)). Representation of the likely temperature dependence would therefore further reduce the fractional loss of HFO-1234ze(E) by reaction with ozone, and the calculated HFC-23 yield from its global oxidation.

Regarding the possible increased removal by reaction with ozone in locally polluted regions where HFO-1234ze(E) is emitted, it should be noted that even at 100 ppb of ozone at ground level, the lifetime of HFO-1234ze(E) with respect to reaction with ozone is 5 years. Consequently, its removal is not influenced by local ozone hotspots, but by transport and the global distribution of oxidants (specifically OH radicals), with its oxidation mainly occurring in regions where the average OH radical concentrations are the highest.

2) Photolysis of TFAA

The photolysis of TFAA is currently recommended to have only one significant channel under lower atmospheric conditions, namely by C-C bond scission to produce CF_3 and HCO (IUPAC Task Group on Atmospheric Chemical Kinetic Data Evaluation – Data Sheet IV PF3). The further oxidation of these products does not form TFA or HFC-23.

The Reviewer is correct that there is also a product channel forming CHF_3 (HFC-23) and CO. This has long been known to contribute at wavelengths shorter than the tropospheric range. The preliminary paper (not peer-reviewed) from 2021 highlighted by the Reviewer (https://doi.org/10.21203/rs.3.rs-199769/v1) reports a contribution from this channel at 308 nm (i.e. within the tropospheric range), but based on observation under low pressure collision-free conditions. A subsequent full paper from the same group (Thomson et al., 2024), confirms a quantum yield of 0.16 at 308 nm for formation of HFC-23 under collision-free conditions, but with this falling to 0.00023 at atmospheric pressure. In the interim Sulbaek-Andersen et al. (2022) and Sulbaek-Andersen et al. (2023) have found no evidence for HFC-23 formation under tropospheric conditions (in agreement with earlier studies, e.g. Chiappero et al., 2006). As a result the IUPAC Task Group recommends a quantum yield of < 0.003 at 308 nm (IUPAC Task Group on Atmospheric Chemical Kinetic Data Evaluation – Data Sheet IV PF3).

Because of the points discussed in 1) and 2), we did not consider HFC-23 formation in the MCM mechanism of HFO-1234ze(E). Although since 1) is an important result, in the revised manuscript, we have added a few sentences stating that formation of HFC-23 from atmospheric breakdown of HFO-1234ze(E) is possible.

The study uses nitric oxide (NO) emission estimates as a proxy for the spatial distribution of HFO-1234ze(E), which are then scaled based on the monthly pMDI sales from the top 51 countries to calculate total emissions per month per country. A significant limitation of this methodology does not account for biogenic NO emissions (i.e. partial denitrification), aircraft or ship emissions, which would not be associated with pMDI usage. Rather than using NO as a proxy, a priori information of population density or nighttime light could be used to better resolve emissions distributions. Furthermore, the full inclusion of information used to estimate emissions of HFO-1234ze(E) from the use of pMDI should be included. Currently no sales data are included in the paper or supplement, making it impossible for the reader to recreate the results given in the paper. Additionally, the limitation of only using sales data from one pharmaceutical company reduces the representativeness of the results. It would be better to use total global sales of pMDIs instead. If the latter has been used, it was not made clear within the paper.

Response: As specified in the manuscript, the NO emissions used as a spatial proxy for HFO-1234ze(E) emissions are from the residential and commercial sectors of the CEDS inventory. This was done intentionally, as these sectors are representative of population density and human activity and are therefore more likely to correlate with pMDI usage. Emissions from unrelated sources—such as biogenic, aircraft, or maritime—were not included in this proxy.

With the revised manuscript, we will include a new supplementary data which contains the country wise HFO-1234ze(E) emissions based pMDI volume sales data. Note that the pMDI data is for all manufacturers across all respiratory diseases. We have revised the relevant sections throughout to clarify this ambiguity.

The conclusion that even if HFO-1234ze(E) was the only propellant used in pMDIs, the continuous emission to the atmosphere would have negligible effects on surface water and soil TFA concentrations is misleading. Albeit that the results from this study might indicate that this is the case, they are based on a single emission rate of HFO-1234ze(E) that does not vary over time and on sales data from one single pharmaceutical company. Considering the total number of asthma and COPD diagnoses continue to increase globally (https://doi.org/10.1586/17476348.2016.1114417), a time varying emission estimate would be more representative, as well as using global sales data.

Response: We agree that there are limitations to this study, such as assuming pMDI sales do not increase over time. Note that the monthly pMDI sales data that we have used to calculate global HFO-1234ze(E) is from all manufacturers, i.e., not tied to a single pharmaceutical company. The Reviewer is further correct that numbers of COPD/Asthma patients are projected to increase by 23% in the next thirty years. However, without hard evidence, it is difficult understand what regions will see the most increase of such patients. Moreover, we cannot predict weather patterns for the next thirty years which should also affect TFA formation and deposition globally. Therefore, for relative simplicity, we used region-specific annual TFA deposition flux for calculating net accumulation of TFA in surface water, soil, and sediment over time.

Specific comments

Lines 1-2: As previously outlined in the general comments, the title is not representative of the true focus of the paper and is too broad. Greater specificity is needed so that a reader truly knows what the paper is about. A suggested title, based on the current scope, is "Atmospheric and watershed modelling of trifluoroacetic acid from the oxidation of HFO-1234ze(E) from pressurized metered-dose inhaler usage".

Response: Thank you for the feedback. We have revised the title of the manuscript to "Atmospheric and Watershed Modelling of Trifluoroacetic Acid from Oxidation of HFO-1234ze(E) Released by Prospective Pressurized Metered-Dose Inhaler Use."

Lines 13 – 15: Halogenated hydrocabons with a '—CF3' moiety also have the possibility to produce HFC-23. Despite this not being within the scope of the paper, this pathway should at least be acknowledged. Despite the ACP house style specifically stating that units must be written exponentially (i.e. Gg yr-1), the authors have not done this throughout the paper.

Response: As discussed under the "General comments," we have added a few sentences in the Introduction of the revised manuscript to address this comment. In the revised manuscript, we have also edited the units to match the exponential format of ACP journal.

Lines 20 - 22: The authors assume that the model-predicted TFA deposition rates, which are higher in tropical regions than northern-temperate regions despite higher sales of pMDI in the latter region, is based on photolysis of TFAA being the dominant process; however, this assumption does not seem to take into account atmospheric transport and the lifetime of HFO-1234ze(E). Moreover, this could be a function of the spatial distribution estimation using NO emissions (see General comments). Have the authors looked into a sensitivity analysis to verify if the photolysis reaction of TFAA is dominant in northern-temperate zones?

Response: We would like to clarify that the model-predicted TFA deposition is calculated using the GEOS-Chem chemical transport model, which explicitly accounts for atmospheric processes, including chemical transformation, transport, and both dry and wet deposition. Our conclusion that photolysis of TFAA is dominant is based on the short atmospheric lifetime of HFO-1234ze(E), approximately 20 days. This suggests that the transport of the propellant will have a smaller effect on distant regions compared to other intermediates, such as TFA itself. Since we did not perform a sensitivity analysis in deriving these conclusions, we have updated the relevant section to acknowledge that the impact of TFA transport cannot be completely ruled out.

Additionally, please note that while the spatial distribution of emissions is based on NO from residential and commercial sources, the resulting TFA deposition patterns are determined by the model's comprehensive treatment of atmospheric dynamics and chemistry. This means that although TFA deposition is influenced by NO emissions, the deposition patterns will not directly correlate with the NO emission patterns.

Watershed is a contentious word within hydrology as it can have different meanings depending on readers nationality (c.f. river drainage basin as a unit, line that separates neighbouring drainage basins, a time of day in broadcasting). To avoid confusion and increase readership beyond that of North America, it would be good to either change the word to a less contentious naming or have a definition of what is meant by watershed.

Response: In the revised manuscript, we have clarified that "watershed" means drainage basin or catchment area to establish a common understanding of how it is used throughout the paper. As used here, a watershed is an area that channels precipitation and runoff into a common body of water (also sometimes referred to as a drainage basin or catchment).

Lines 26 – 28: It might be that pMDI usage-based HFO-1234ze(E) emissions only do not pose a risk to human health based on the results and data used in this study but they contribute to other sources. It would be good to acknowledge that the culmination in other sources and growth in pMDI usage might change this, as well as contextualizing with the limitations of the paper.

Response: We agree with the Reviewer that TFA's effect on the environment are only beginning to be understood. To address these concerns, we have added a new section "Limitations of the Study" in the revised manuscript (see below).

"**Limitations of the Study**

One limitation of the current study is that HFO-1234ze(E) emissions used in the atmospheric modelling of TFA are based on pMDI volume sales data from a single year (2022), which does not account for the projected increase in respiratory disease patients in the future. Emissions of species other than HFO-1234ze(E) were also held constant over the 30-year period. Future trends, particularly in NOx emissions, are expected to influence the yield of TFA due to changes in gas-phase chemistry. The 0.1° × 0.1° spatial resolution of the emissions data may not capture fine-scale variations (<11 km). However, since the smallest sub-basin has an area of approximately 7,040 km², this grid cell size is appropriate for the study's needs. Additionally, the limited geographical coverage of the emissions data may result in an incomplete representation of global HFO-1234ze(E) emissions, potentially affecting the accuracy of TFA formation and transport predictions on a broader scale.

TFA deposition estimates made with GEOS-Chem are subject to uncertainties arising from both the meteorological input data and model configuration. The use of MERRA-2 meteorological inputs introduces uncertainty in projecting future scenarios, mainly due to the complexities of predicting future weather patterns associated with climate change. The chemical mechanism, implemented using KPP version 3.0 and including new chemical reactions for the MCM of HFO-1234ze(E), aims to represent our current understanding of complex atmospheric processes. Despite its detail, there are

still uncertainties regarding reaction rate constants, product yields, and possible reaction pathways. Furthermore, to improve computational efficiency, we did not dynamically simulate atmospheric concentrations of H_2O, OH, and HO_2; instead, the model reads these from the meteorological input (MERRA-2). As a result, omitting them from the reactions does not affect their concentrations in the model, though it may have a minor impact on the spatial pattern of oxidation products.
To estimate the effects of prospective pMDI usage on surface water TFA, we modelled three different watershed regions. In scenarios lacking site-specific data, we used default modelling parameters reflecting average watershed conditions; thus, these may not always accurately represent specific water bodies. However, the impact of these defaults is usually small or insignificant, and most parameter estimates are based on generally available sub-basin data. For example, the empirical intercept coefficient's default value, derived from studies of various watersheds, minimally affects model results but may slightly over- or underestimate TFA concentrations. Finally, our conclusions that model-predicted TFA levels do not pose a threat to human health or the environment are based on currently known safety thresholds. Since information related to TFA toxicity is still evolving, these conclusions may change in the future."

Lines 38 – 40: As the scope of the paper is global, it would be good to include other non-USA regulations on the phase out of HFCs too, i.e. European F-gas regulation.

Response: In the revised manuscript, we have added that HFCs are being phased out in Europe under European F-gas regulation as well.

Line 80 – 81: Why were emissions calculate at 30-minute time steps as this must have made the running of the model computationally expensive? As the anthropogenic and biogenic emission estimates outlined in section 2.2 that are used in the model have a temporal resolution of one month, why was the 30-minute time step chosen?

Response: The 30-minute emissions time step refers to how frequently the emissions fields are read and updated within the GEOS-Chem model, and it aligns with the model's default configuration. While the anthropogenic and biogenic emissions used in this study are provided at monthly resolution, GEOS-Chem internally applies temporal scaling factors (e.g., diurnal, weekly) where available to generate more realistic sub-monthly variability. Since the model was run at a spatial resolution of 2° × 2.5° on a high-performance Linux system configured to handle parallel processing similarly to an HPC cluster, the computational cost associated with using a 30-minute emissions update frequency was minimal and did not present a significant burden.

Lines 95 – 112: How come the method for HFO-1234ze(E) emissions calculations are not outlined in this section? It would be a pertinent location to include it to help any reader find the necessary information to run GEOS-Chem to verify your results. It would also allow the authors to give more information on the sales data used (c.f. one company vs. global sales values) and how this was scaled. Currently very little information is given on how these emissions are calculated and this is crucial information to be able to replicate the results.

Response: We have now included the following description of emissions in Section 2 of the revised manuscript. Specifically, monthly pMDI sales data from all manufacturers for the top 51 countries were used to estimate emissions, assuming a daily dose of 4 puffs/day and ~14 g of HFO-1234ze(E) per pMDI. These emission estimates were converted to monthly totals and spatially distributed within each country using NO emissions from the residential and commercial sectors in the CEDS inventory as a proxy. This approach assumes that NO emissions in these sectors correlate with population density and, hence, pMDI usage. Consequently, the spatial resolution of the emissions follows that of the CEDS proxy data. With the revised manuscript, we will now provide a supplement data containing our estimates of global monthly HFO-1234ze emissions for the top 51 countries.

Lines 132 - 134: The exclusion of O2 and H2O from GEOS-Chem reactions is significant limitation in the study as atmospheric mole fractions of these vary spatially and temporally and will have an impact on the different reactions associated with the oxidation of HFO-1234ze(E). For example, O_2 is required in the $CF_3CH(OH)CHF(O\bullet)$ pathway to produce TFAA (see figure 5 in Behringer et al., 2021).

Response: O_2 is indeed involved in many tropospheric reactions, with a large number of organic radicals reacting rapidly and often exclusively with O_2. Because these reactions occur essentially instantaneously (owing to the high concentration of O_2), and there is no competing reaction in many cases, it is not necessary to represent the reaction explicitly in these cases, and the reaction is invariably combined into the preceding reaction in tropospheric chemical mechanisms for computational efficiency.

This is the case for many reactions in the HFO-1234ze(E) degradation mechanism. For example, the addition reaction of OH with HFO-1234ze(E) initially forms two possible organic radicals, each combining rapidly with O_2 to form a peroxy radical, e.g.,

$OH + CF_3CH{=}CHF \rightarrow CF_3CH(OH)\dot{C}HF$ (1)

$CF_3CH(OH)\dot{C}HF + O_2\ (+M) \rightarrow CF_3CH(OH)CH(O\dot{O})F\ (+M)$ (2)

Because of the high concentration of O_2, reactions of type (2) typically occur on the timescale of ≤ 25 ns in air at atmospheric pressure (i.e., instantaneously), such that reaction (1) is the rate-determining step – the timescale being several weeks. The reactions can therefore be combined, and it is not necessary to represent the involvement of O_2 (or M) explicitly, i.e.:

$OH + CF_3CH{=}CHF \rightarrow CF_3CH(OH)CH(O\dot{O})F$ (1) + (2)

In the example given by the reviewer, as illustrated in the report of Behringer et al. (2021), the subsequent reaction of this peroxy radical with NO forms an oxy radical, $CF_3CH(OH)CH(\dot{O})F$, which initially decomposes as follows:

$CF_3CH(OH)CH(O\dot{O})F + NO \rightarrow CF_3CH(OH)CH(\dot{O})F + NO_2$ (3)

$CF_3CH(OH)CH(\dot{O})F\ (+M) \rightarrow CF_3\dot{C}HOH + HC(O)F\ (+M)$ (4)

The radical product, $CF_3\dot{C}HOH$, then reacts rapidly and exclusively with O_2:

$CF_3\dot{C}HOH + O_2 \rightarrow CF_3CHO + HO_2$ (5)

(Note: the report of Behringer et al. (2021), and the source paper of Javadi et al. (2008), incorrectly show OH as the co-product of CF_3CHO).

In this reaction sequence, reaction (3) is the rate determining step, and neither reaction (4) nor reaction (5) needs to be represented because they occur very rapidly and have no competing processes. The combined reaction does not then contain O_2 explicitly, although its involvement is included:

$CF_3CH(OH)CH(O\dot{O})F + NO \rightarrow HC(O)F + CF_3CHO + HO_2 + NO_2$ (3)+(4)+(5) *(note this is Reaction R2 in the manuscript)*

Methods like those described above are commonly used to make tropospheric chemical mechanisms more computationally efficient, as the involvement of O_2 is intrinsically incorporated into many reactions represented in the applied mechanism. Moreover, both O_2 and H_2O are included in the core GEOS-Chem model, provided by the meteorological input data (MERRA2), and are not dynamically simulated within the chemical mechanism itself. Consequently, although O_2 and H_2O were not explicitly added to the TFA chemical mechanism (as in the O_2 example above), their concentrations in the model are unaffected. Thus, omitting them from the TFA mechanism reactions does not impact their modelled concentrations. However, this omission could have a minor influence on the spatial distribution of oxidation products as noted in the new "Limitations of the study" section. For completeness, in the revised manuscript and supplement, we have updated the HFO-1234ze(E) MCM reactions to include O_2 and H_2O wherever these species are necessary to balance the reactions.

Lines 226 – 229: What was the rationale for choosing the southern Indian drainage basin? India is an Article 5 party under the Montreal Protocol and its Amendments; therefore, it has a delayed phase-down of HFCs compared to non-article 5 countries (i.e. western countries such as USA or Europe). As such, the use of HFCs in pMDI would be expected to continue on longer in India than the USA or Europe.

Response: The Reviewer correctly notes that the phasedown of HFCs in India will take longer than in the US or Europe. In this study, we planned to investigate TFA levels in the surface waters of three watersheds. We chose the Rhine watershed in Europe as the primary location due to the availability of numerous TFA-related literature references for comparison. The US was selected because it has the highest pMDI sales/usage globally. India was chosen as the third watershed because it ranks as the third-largest pMDI market in the world, after the US and the UK. Since we were already considering the Rhine watershed (Europe), we decided to include India instead of the UK as the third location. In the revised manuscript, we have briefly added this rationale for selecting three watersheds.

Lines 232 – 235: How do you account for the granularity in GEOS-Chem spatial resolution and the resultant TFA deposition rates (model resolution of 2° x 2.5°) on the deposition rates put into the drainage basin model?

Response: The modeled deposition dataset was superimposed onto basin boundaries in GIS to estimate TFA deposition flux in each subbasin of each basin. The TFA deposition flux for each subbasin was calculated using the gridded dataset by computing a weighted average that accounts for the overlapping area of each grid cell with the subbasin. The 2° x 2.5° resolution of the TFA deposition data does not fully capture granularity, specifically in smaller subbasins, but this resolution is necessary considering the global scale of the modeling and is typical of such modeling.

Lines 256 – 268: How does the model account for infiltration and percolation rates across the river drainage basins, as these will vary spatially based on soil and bedrock types.

Response: The infiltration and percolation rates are primarily affected by precipitation, irrigation, run-off, and evapotranspiration in this model. This study is a conceptual level study and does not account for micro-scale variations such as soil types and bedrock types which could be specific for a local area. Modeling parameters such has precipitation was estimated for each sub-basin and accounted for spatial variation. When sub-basin specific data were not readily available for parameters such as irrigation, run-off, and evapotranspiration, they were based on as average values across the entire Rhine River basin. Using average values for the entire basin could have some impact on the modeling results for each sub-basin but should not have significant impact on the results (i.e., changing the order of magnitude of the results).

Lines 271 – 281: The results and discussion section should not be where the method of distributing HFO-1234ze(E) emissions from pMDI usage I located. Instead, it should be included in section 2.2. Furthermore, the monthly pMDI sales data used within the paper should be included, either in figure or tabulated form, so that readers of the paper can use the data along with other methods outlined in the paper to verify the results presented in the paper.

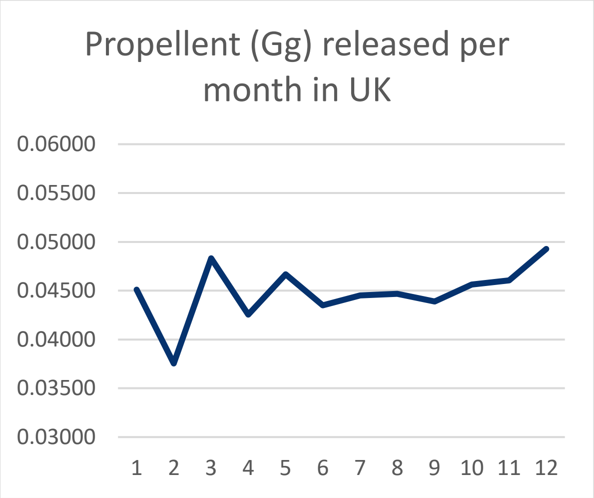
Response: The Reviewer raises a valid point regarding the placement of emission information in the Methods section. However, we believe that our global pMDI emission calculations are novel and also merits inclusion in the Results section. To ensure proper flow of information, we have added a few sentences to outline how the emissions were calculated and have provided an indication for readers that further details are available in the Results section. We will include the global, monthly propellant emission data as a supplement of the revised manuscript.

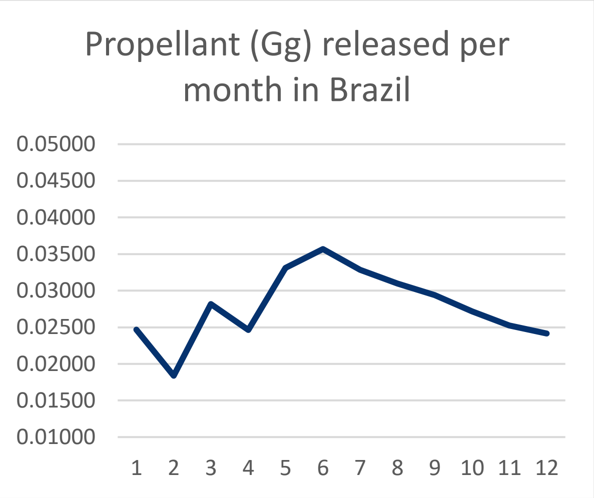
Lines 287 – 291: Considering that NO is used as a proxy and often total emissions of this gas do not vary significantly temporally, would one not expect to see the same in the HFO-1234ze(E) emissions considering NO is used as an emissions proxy? Furthermore, based on your methodology, I don’t believe you can current definitively state that there are sustained demand of pMDIs in the respiratory disease community without temporal variations.

Response: We thank the Reviewer for raising this important point. Our conclusion that pMDI-based HFO emissions do not vary seasonally is based on the global monthly average of propellant emissions (Fig. S2), which shows only minimal changes in pMDI-based HFO emissions over time.

Following the Reviewer's suggestion, we examined region-specific global, monthly propellant emission (pMDI sales) data. We observed that propellant emissions do indeed vary in some regions—for example, in the UK and Brazil, as shown in the new supplemental data show estimated propellant emissions (also, see below). However, the timing of peak emissions (pMDI sales) differs between regions. When these region-specific differences are averaged globally (as in Fig. S2), the variations are largely offset and thus not apparent at the global level.

We have clarified this reason, in the revised manuscript, explaining why minimal variation in pMDI-based HFO emissions is observed over time.


Propellent (Gg) released per month in UK


Propellant (Gg) released per month in Brazil

Lines 301 – 302: How does TFA deposition flux vary seasonally? It would be good to describe it here in the main text, despite not requiring the figures in the main text.

Response: TFA tends to have higher deposition rates in the summer as refrigerants are more commonly used in warmer months and more oxidants are present in summer, although precipitation is also a factor as it allows for more wet deposition. Wang et al. (2018) noted that maximum wet and dry TFA deposition occurred during the summer, accounting for 71% of global yearly deposition, followed by autumn with 12% global yearly deposition. Wang et al. (2018) also stated that although HFO-1234yf emissions are the dominant factor for TFA deposition, convective mass flux and precipitation also have an effect.

Lines 302 – 206: See Specific Comment for Lines 20 – 22, regarding transport of TFA and the subsequent dry deposition.

Response: In the revised manuscript, we have added that higher deposition of TFA around the tropical region can also be due to transport of TFA from other regions.

Lines 334 – 336: The description of the model and compartmentalisation should be included in the methods section.

Response: We have used the HHRAP model for simulating TFA fate and transport. This has been briefly described between Lines 253-260 of the (submitted) manuscript under the methods section.

Figure 6: The GEOS-Chem gridded TFA deposition over the selected river drainage basins often bridge both the drainage basin and the surrounding area. How are these deposition rates accounted for in the sections where the gridded deposition has both regions contained within it?

Response: As described in the comment response for lines 232-235, to account for a grid cell overlapping a basin and an area outside the subbasin, a weighted average calculation was used to provide a more appropriate estimation of the TFA deposition within the basin boundaries. The TFA deposition flux for each subbasin was calculated using the gridded dataset by computing a weighted average that accounts for the overlapping area of each grid cell with the subbasin.

Lines 340 – 343: Why are the authors assuming the TFA deposition fluxes do not change temporally? Does Fig. S3 and S4 not show that these do vary both temporally and spatially for dry and wet deposition, respectively.

Response: We agree that Figures S3 and S4 show temporal and spatial variability in deposition fluxes. However, for the purpose of estimating long-term (30-year) cumulative TFA accumulation in surface water, soil, and sediment, we assumed no inter-annual variability in annual TFA deposition fluxes, and we used annual deposition (rather than seasonal deposition) in the surface fate and transport modeling. This simplification was made to enable a first-order estimate of long-term accumulation, given the absence of multi-year model simulations. Also, it is unknown how the seasonality itself would vary over the 30-year period. For clarity, we have rewritten the concerning section in the revised manuscript as follows,

“Assuming no inter-annual variability in the annual TFA deposition fluxes (Table 3), we estimated net TFA accumulations in the surface water, soil, and sediment of the three watersheds over a 30-year period. While TFA deposition varies seasonally, the focus here is on the accumulation of TFA over the 30-year period. Also, it is unknown how the seasonality itself would vary over the 30-year period. So the surface fate and transport modeling was based on the mean annual deposition flux.”

Lines 404 – 414: I find these three points hard to read and believe that they should be rewritten. Additionally, I find the language used to be quite emotive and political. Rather than pushing an agenda, results should be presented scientifically and then contextualised, but taking the assumptions and limitations of the study into account.

Response: We agree that those three points are hard to read. In the revised manuscript, we have revised them to the following,

“Atmospheric and watershed modeling predicts that future use of pMDIs may lead to TFA concentrations between 0.8 and 19.3 ng L^{-1} in surface waters, 2.3 and 8.8 ng kg^{-1} in surface soils, and 0.2 and 4.8 ng kg^{-1} in surface sediments across the three studied watersheds. These variations reflect local factors such as water flow, region-specific deposition rates, pMDI usage patterns, and weather conditions. The predicted TFA levels can be put into context by comparing them with established reference values below:

i) The German EPA’s precautionary threshold for TFA in drinking water is 10,000 ng L^{-1} (Arp et al., 2024). The modeled TFA concentrations attributed to pMDI use are over 500 times below this limit.

ii) The REACH dossier establishes a long-term no-observed effect concentration (NOEC) for TFA in soil at 830,000 ng kg^{-1} (Arp et al., 2024). The predicted soil levels from pMDI emissions are at least 90,000 times lower than concentrations known to affect plant shoot growth.

iii) Given the lowest reported concentration of TFA in Rhine surface water—400 ng L^{-1} (Sturm et al., 2023)—the results indicate that prospective NGP emissions from pMDI use would contribute less than 1% of the total TFA in the Rhine.

Overall, these results indicate that, even if HFO-1234ze(E) were to become the sole medical propellant in future pMDIs, its continuous atmospheric emissions would result in only very low quantities of TFA in surface water and surface soil—several orders of magnitude below concentrations associated with human or crop toxicity. In addition, the near-zero global warming potential of HFO-1234ze(E) supports its consideration as a potential long-term alternative to existing medical propellants."

Lines 416 – 420: As for the previous point, this whole paragraph is pushing an agenda, whereas it would be better to outline that these results are from sales figures from a single pharmaceutical company and that emissions of HFO-1234ze(E) are not limited to this one source or company. Instead, it contributes to total emissions.

Response: Note that the pMDI sales data that we have used for HFO-1234ze emission calculations is from all manufacturers, i.e., not tied to one company. We concede that in ideal scenarios we should have considered scaled the pMDI emission rate to match the predicted increase in COPD/Asthma population. We have mentioned this drawback of our study in the new "Limitations of the Study" section. In the revised manuscript, we have also revised the concerning paragraph, which states the suitability of HFO-1234ze(E) as a long-term medical propellant, to have a neutral tone.

Technical corrections

Line 13: HFO is not defined prior to its first use.

Response: The full name of HFO-1234ze(E) has been included in the Abstract of the revised manuscript. As ACP abstracts are limited to 250 words, in the revised manuscript, we have now edited the entire abstract to accommodate this change (see below).

"**Abstract.** Trans-1,3,3,3-tetrafluoroprop-1-ene (the E-isomer), written as E-$CF_3CH=CHF$ or HFO-1234ze(E), is a hydrofluoroolefin (HFO) compound developed for use in pressurised metered-dose inhalers (pMDIs) as a next-generation medical propellant (NGP). This compound has a '$-CF_3$' moiety, which makes formation of trifluoroacetic acid (TFA) possible in the atmosphere. To quantify the contribution of these prospective pMDIs in forming TFA, we performed an extensive study using a global atmospheric model coupled with detailed watershed modelling. Our approach incorporated the master chemical mechanism of HFO-1234ze(E), considering all known atmospheric pathways for TFA formation, and assumed pMDI usage as the sole emission source of HFO-1234ze(E). Based on global pMDI volume sales data, we estimate HFO-1234ze(E) emission rates to be 4.736 Gg yr^{-1}. Although emissions are higher in northern-temperate regions, our model predicts that the highest TFA deposition rates occur in the tropics, which is likely due to more intensive photolysis of trifluoroacetic aldehyde in temperate zones, which favours non-TFA products and/or transport of TFA into the tropical zone from nearby regions. Using predicted TFA deposition around the Hudson, Cauvery, and Rhine rivers, we applied a fate-and-transport model to estimate TFA concentrations in surface water, soil, and sediments within these watersheds. Our watershed modelling results indicate that surface water TFA concentrations would vary between 0.8–19.3 ng L^{-1}, corresponding to a margin of exposure exceeding 500-fold for drinking water. These findings suggest that TFA formation resulting from pMDI-related HFO-1234ze(E) emissions is minimal and does not present a risk to human health or the environment."

Line 16: What is environmental TFA? Suggest removing "environmental" as it is unnecessary.

Response: Corrected.

Line 36: Please use a more up-to-date GWP100 value for HFC-134a. The Annex to the WMO Scientific Assessment of Ozone Depletion 2022 has a more recent value of 1,470.

Response: Updated the GWP100 of HFC-134a to 1,470.

Line 41: HFO-1234ze(E) wasn't purely developed by the pharmaceutical industry as a propellant and is currently being used as a refrigerant and foam blowing agent. Emissions are already observed globally by the AGAGE network (see https://doi.org/10.1021/es505123x). Please reword this sentence.

Response: The Reviewer is correct that HFO-1234ze(E) was not developed exclusively by the pharmaceutical industry. Its development involved a partnership with Honeywell, which developed and patented the medical-grade version of HFO-1234ze(E). It is important to note that there are several differences between the medical-grade and industrial-grade versions of HFO-1234ze(E), which is used as a foam-blowing agent. The most significant being that the medical-grade version must be approved by regulatory agencies such as the FDA for use in human inhalation.

Lines 49 – 52: As far as I am aware, the PFAS regulation was passed in the EU and should be coming into law soon. Please update this sentence to reflect this.

Response: This is not accurate, particularly regarding the medical sector. Discussions on this sector only began this month, as indicated in the following document: link. Furthermore, we have not yet received an opinion from ECHA, which is required before the Commission can draft any legislative proposal.

Lines 62 – 65: Please outline the other TFAA degradation pathways that have been suggested in the literature. From the literature cited, it looks like the authors are mostly suggesting the photolysis of TFAA to produce HFC-23 but it is not entirely clear. There are pathways of TFAA oxidation through hydrolysis that can produce TFA – see Figure 8 in Berhringer et al (2021; https://www.umweltbundesamt.de/sites/default/files/medien/5750/publikationen/2021-05-06_texte_73-2021_persistent_degradation_products.pdf) for more information.

Response: Figure 1 shows the MCM of HFO-1234ze(E), with TFAA hydrolysis represented by dotted lines. As this is an important pathway, we are currently conducting experiments to determine the fate of the TFAA hydrate. However, since the rate constants for this pathway are not well established, it has not been included in our mechanism. A brief note regarding this is also provided in the figure caption.

Line 65 – 66: The assertion that no prior work has explored TFA production from HFO-1234ze(E) is slightly misleading. The authors have produced a similar study using a boxmodel with chemical degradation mechanisms included (see https://doi.org/10.3389/fenvs.2023.1297920).

Response: In the revised manuscript, we have clarified that except box-modeling of HFO-1234ze(E), no other work has addressed formation of TFA from HFO-1234ze(E)

Lines 75 – 81: Please include that GEOS-Chem is a Eularian model.

Response: While the phrase "global three-dimensional chemical transport model" used on line 75 inherently refers to a Eulerian modeling framework, we appreciate the opportunity to improve clarity and have updated the manuscript to explicitly refer to GEOS-Chem as a "global three-dimensional Eulerian chemical transport model."

Line 119: If stating the authors name in the text, it does not then need to be included in the citation in parenthesis – "… in GEOS-Chem by Mao et al. (2010) for the …". See the ACP house style for more information (https://www.atmospheric-chemistry-andphysics.net/submission.html#references)

Response: Thank you for the feedback. In the revised manuscript, we have updated in-line references to match ACP house style.

Lines 139 - 140: This sentence is not complete.

Response: Thank you for the feedback. We have fixed this formatting issue.

Line 375: Replace "Alphine" with "Alpine".

Response: Corrected.

Line 389: state what the GWP100 For HFO-1234ze(E) is.

Response: In the revised manuscript, the direct GWP100 of HFO-1234ze(E) has been mentioned in the introduction.

Fig. S6: Correlation values are usually stated as an R value in statistics, whereas pvalues are the statistical significance of each test. Both should be reported.

Response: In Fig. S6, we have computed Spearman's correlation, which is denote by the Greek symbol rho (ρ). In the revised manuscript, we have explicitly stated to make the reader aware because mentioning values for both rho (ρ) and p may be even more confusing for the reader.

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