

**OPTIMAL INHALER SELECTION: ENVIRONMENTAL CONSIDERATIONS AND PATIENT PREFERENCES**

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Big Sky Pulmonary Conference  
Friday, March 1, 2024

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**OBJECTIVES**

<b>01</b> Differentiate between inhaler propellants' role on ozone depletion and green house gas production	<b>02</b> Describe the history of inhaler propellant including new propellants to be ready in 2025	<b>03</b> Use patient preferences to identify optimal devices for their condition
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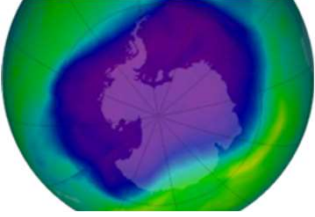
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**CFC WAS USED AS INHALER PROPELLANT UNTIL 2009**

**Montreal Protocol on Substances that Deplete the Ozone Layer**

- UN treaty
- Universally ratified in 1987, 14 years after hole discovered

**Goal: Protect the ozone layer by phasing out ozone depleting substances (ODS)**

- Chlorofluorocarbon (CFC) Phase-out

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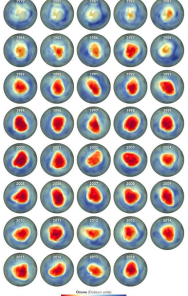
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**OZONE HOLE THROUGH THE YEARS**

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**HFC/A PROPELLANTS REPLACED CFC**

Development costs for the transition of pMDIs from CFCs to HFCs estimated at more than USD2 billion

Phase-out of CFC pMDIs took over 20 years to complete

Pharmaceutical companies replaced CFCs with HFCs propellants in pMDI

- HFC-134a and HFC-227ea
- Not ozone depleting substances (ODS) but are potent greenhouse gases (GHG)

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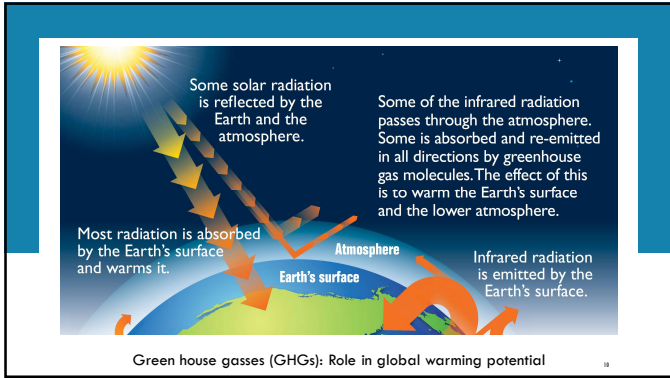
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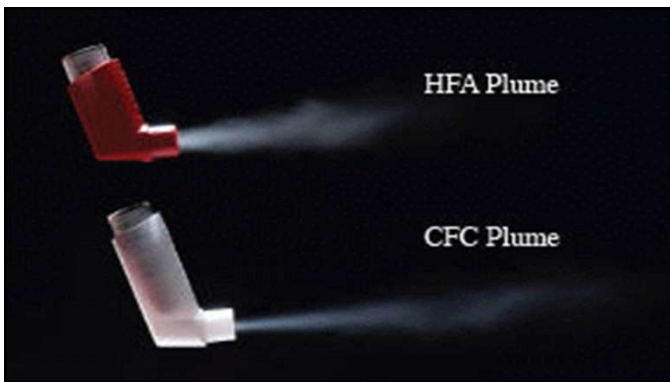
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### KIGALI AMENDMENT: HFC/A PHASE DOWN

HFAs have significant global warming potential (GWP)

Two low-GWP chemicals are under development as potential replacements for HFC-134a and HFC-227ea propellants  
HFC-152a and HFO-1234ze(E)

Introduce to market in 2025; complete phase out ~2030

Risks of supply chain interruptions place patients at risk  
HFAs phased down before adequate supply of lower GWP pMDIs is available

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The amount of CO<sub>2</sub> and other carbon compounds emitted by a product

- CFCs have a large carbon footprint
- HFC pMDIs have a far greater carbon footprint than DPIs or SMIs
- 88–98% of the carbon footprint of pMDIs is due to propellant release during use or end of life
- DPIs and SMIs are propellant-free
- Reusable SMIs or single-dose DPIs have the smallest carbon footprints

**CARBON FOOTPRINT**

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### PHARMAS ROLE

PHARMACEUTICAL COMPANIES HAVE COMMITTED TO BEING CARBON-NEUTRAL BY 2030

PMDI CONSTITUTE UP TO 45% OF SOME COMPANY'S CARBON FOOTPRINT

3 PHARMACEUTICAL COMPANIES AND 1 CDMO HAVE ANNOUNCED PLANS TO REFORMULATE INHALERS. THEY ACCOUNT FOR OVER 70% OF THE PMDI MARKET IN THE US AND EUROPE

GSK, 2021, Our position on: respiratory products and global warming, October 2021. <https://www.gsk.com/media/2962/respiratory-products-and-global-warming-policy.pdf>.

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BBC

### Asthma carbon footprint 'as big as eating meat'

© 2019 BBC

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## TOTAL INHALED RESPIRATORY MARKET

Grown in volume by ~ 30% over the past decade

In 2021

- 800–825 million HFC pMDIs manufactured annually
- 450 million DPIs manufactured annually




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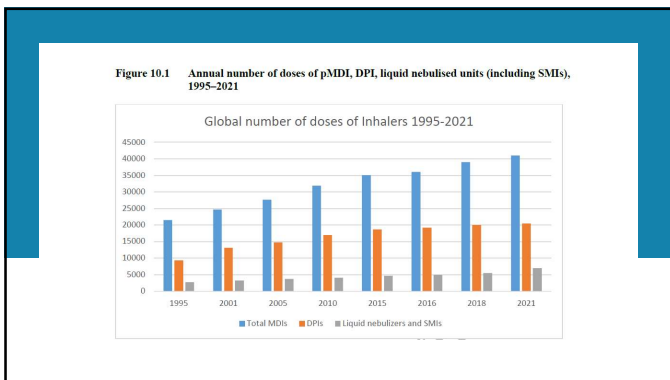
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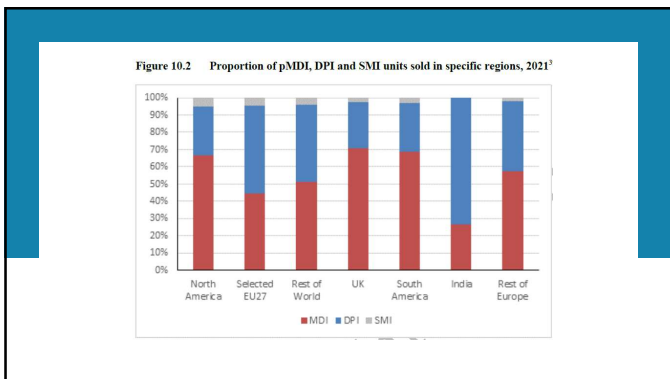
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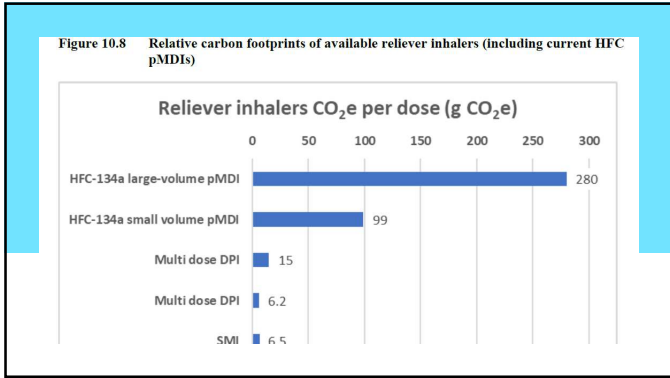
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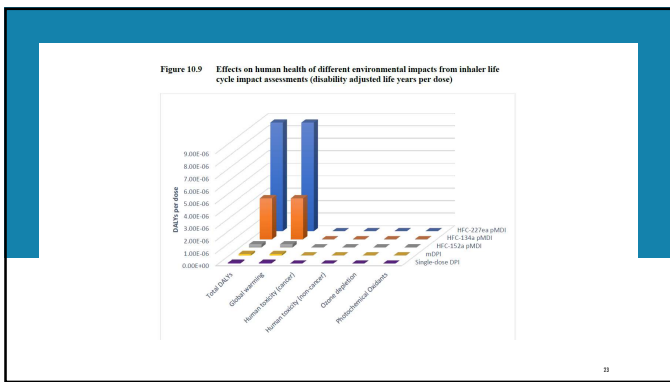
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**PATIENT PREFERENCES** | Optimal devices for their condition

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### MDI PRESCRIPTIONS PER YEAR



800 million HFA MDIs manufactured annually



2% of global GWP-weighted total HFA emissions  
8% of NHS total carbon footprint



Use of HFA MDIs is projected to increase

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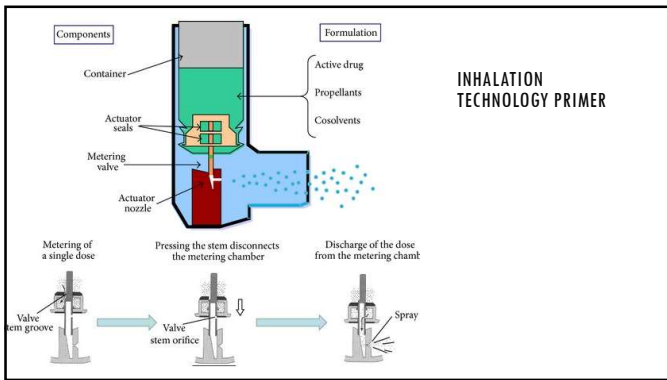
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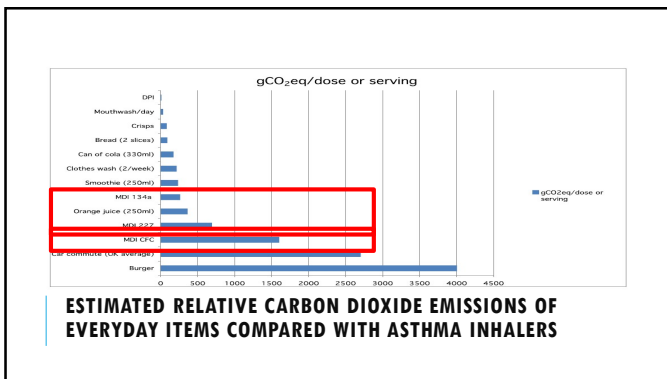
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## PATIENT PREFERENCES FOR PRESSURIZED MDI

### Pros

Can match same administration technique of rescue and controller  
Forgiving of low inspiratory flow  
Generally covered by insurance

### Cons

Most difficult to coordinate activation and inhalation  
• May require a spacer  
Requires priming and cleaning  
Most require shaking before and between puffs  
Environmental considerations  
• Higher GWP impact than other devices

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## HF(A)-MDIs

- HFC-134a
- HFC-227ea

## DPIs

## SIMs

## Nebulizers

## INHALED DELIVERY DEVICE OPTIONS

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175 miles – London to Sheffield



shutterstock.com • 289918949



4 miles – London to... another bit of London



shutterstock.com • 289918949

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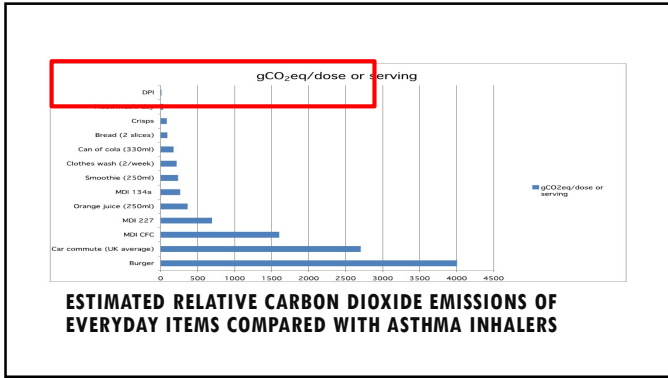
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### PATIENT PREFERENCES FOR PRESSURIZED DPI

Pros	Cons
<ul style="list-style-type: none"> <li>Less difficult to coordinate activation and inhalation</li> <li>Cannot use a spacer</li> </ul>	<ul style="list-style-type: none"> <li>Most difficult to coordinate activation and inhalation</li> <li>May require a spacer</li> </ul>
<ul style="list-style-type: none"> <li>Does not require priming</li> </ul>	<ul style="list-style-type: none"> <li>Cannot match administration technique of rescue and controller</li> </ul>
<ul style="list-style-type: none"> <li>Generally covered by insurance if equivalent molecule in an MDI is not available</li> </ul>	<ul style="list-style-type: none"> <li>Each device has a different technique for loading a dose</li> </ul>
<ul style="list-style-type: none"> <li>Environmental considerations</li> <li>Lower GWP impact than other devices</li> </ul>	<ul style="list-style-type: none"> <li>Unforgiving of low inspiratory flow</li> <li>Requires cleaning</li> </ul>

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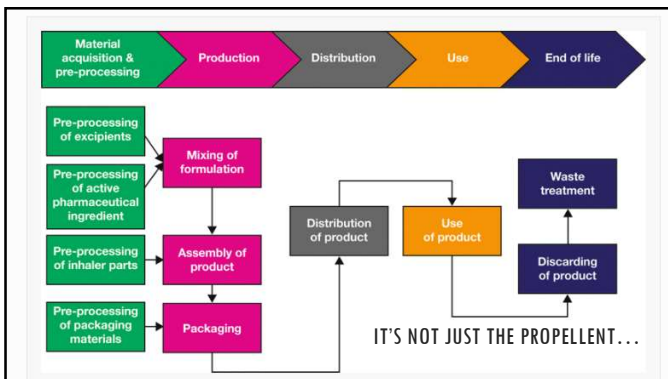
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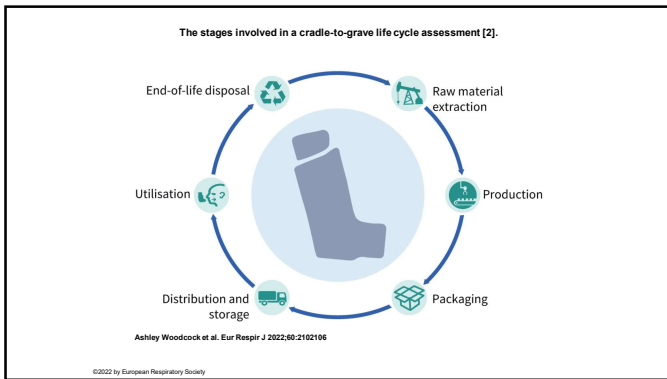
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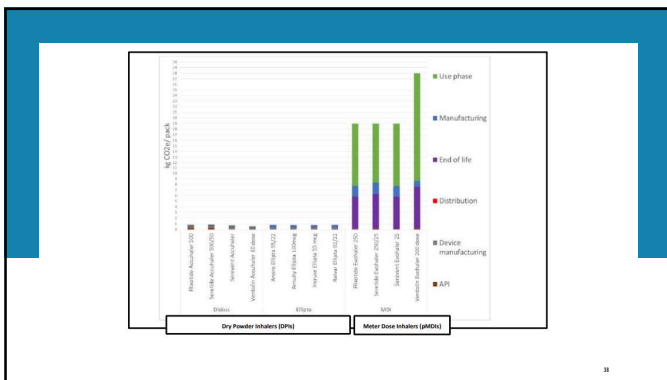
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**HF(A)-MDIs**

- HFC-134a
- HFC-227ea

**DPIs**

**SIMs**

**Nebulizers**

**INHALED DELIVERY DEVICE OPTIONS**

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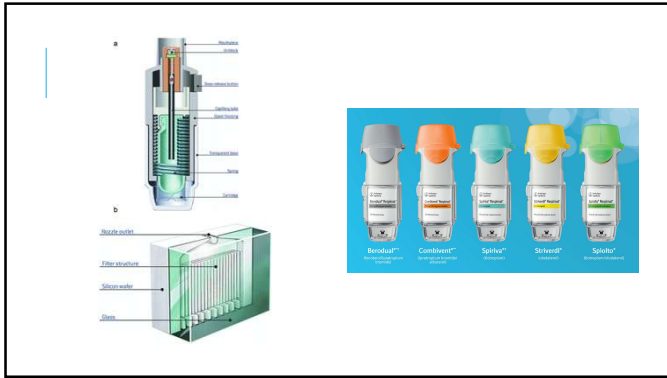
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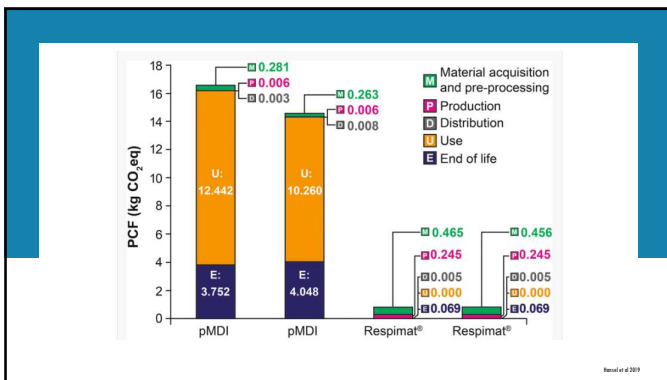
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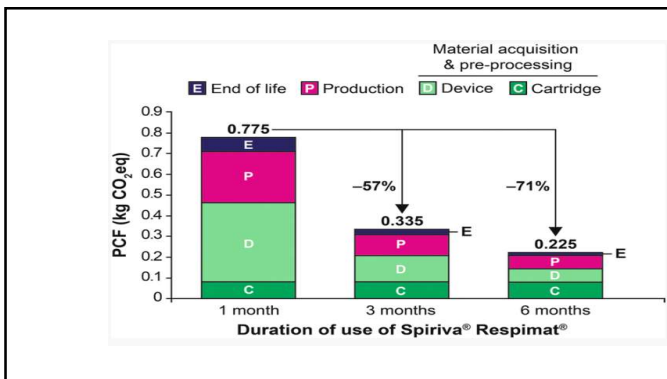
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### PATIENT PREFERENCES FOR SMI

#### Pros

Least difficult to coordinate activation and inhalation

- Cannot use a spacer

Does not require priming

Forgiving of low inspiratory flow

Generally covered by insurance because equivalent formulations are not available in an MDI

Environmental considerations

- Lowest GWP impact than other devices

#### Cons

Some individuals have difficulty loading the cartridges

Cannot match administration technique of rescue and controller

Require priming and cleaning

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- HFC-134a
  - HFC-227ea
- DPIs
- Nebulizers

### INHALED DELIVERY DEVICE OPTIONS

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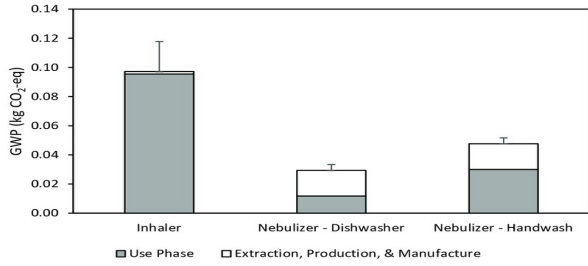
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Goulet, B., Olson, L., Mayer, B.K., A comparative life cycle assessment between a metered dose inhaler and electric nebulizer, Sustainability, 2017, 9(10), 1725. <https://doi.org/10.3390/su9101725>

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## PATIENT PREFERENCES FOR NEBS

### Pros

- Least difficult to coordinate activation and inhalation
  - Cannot use a spacer
- Does not require priming
- Forgiving of low inspiratory flow
- Generally covered by insurance
- Environmental considerations
  - Lower GWP impact than other devices?

### Cons

- Length of treatment
- Lack of portability
- Require cleaning

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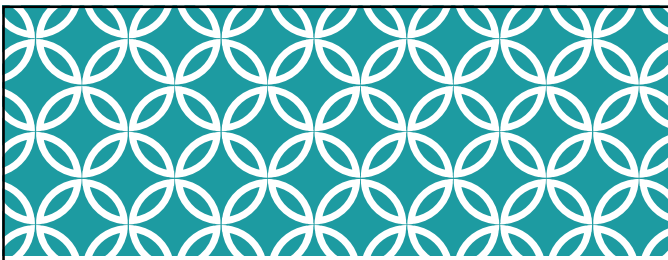
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## ENVIRONMENTAL IMPACT | Summary

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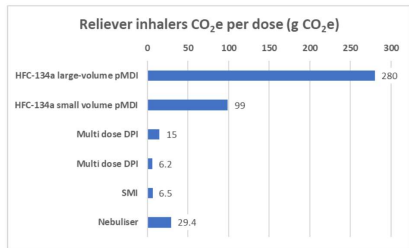
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Figure 10.8 Relative carbon footprints of available reliever inhalers (including current HFC pMDIs)




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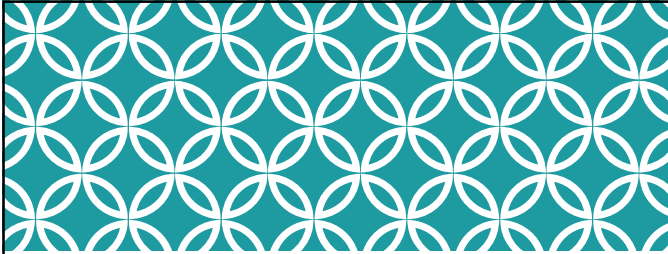
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### LAST THOUGHTS

MDIs with lower GWPs  
What to do when inhalers aren't recycled

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Looking to decrease size of metering chamber by 25-50%

50/50 goals

- 50% of all inhaler prescriptions will be low GWP
- 50% of all inhalers are recycled

PHARMAS OTHER GREEN GOALS

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### MDIs with lower GWP

**Formulations w/alcohol (ethanol) as a cosolvent have half the GWP as MDIs w/only HFA/Cs**

Ventolin has no ethanol  
Proair and Proventil do

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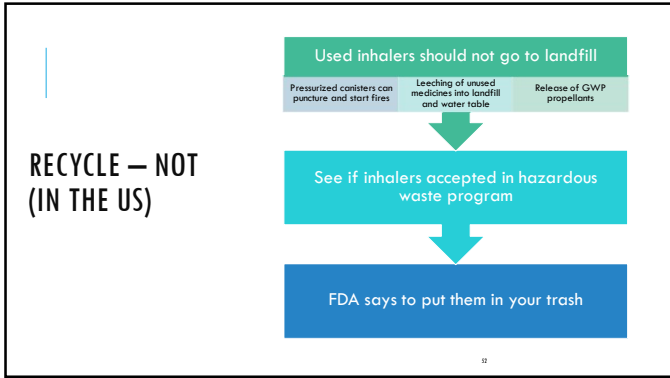
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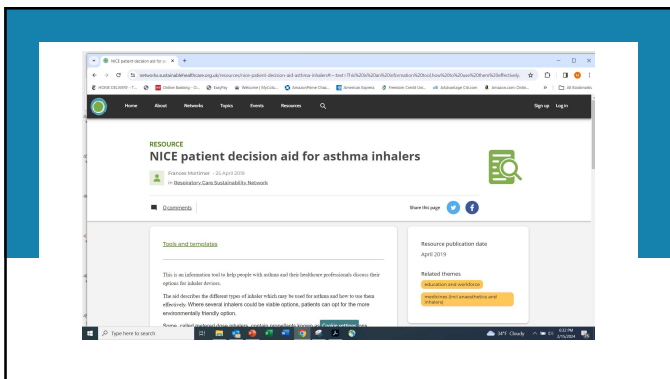
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TAKEAWAYS...  
UNTIL THE  
SWITCH

01 Prescribe more DPIs and SMIs	02 Prescribe fewer inhalers — MART	03 Use MDIs with lower GWP
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