

Changes in Supply and Cost of Quick Release Medications

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Disclosure of Conflict of Interest Information

I have no existing conflict of information to disclose

Changes in Supply and Cost of Quick Release Medications

- Objective: Participants will receive the latest information on the changes in supply and cost of quick-relief short acting beta-2 agonists

Asthma Fast Facts

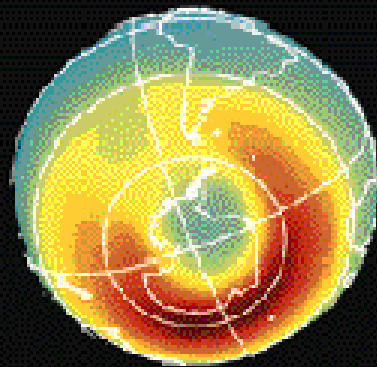
- Every day in America:
- 40,000 people miss school or work due to asthma.
- 30,000 people have an asthma attack.
- 5,000 people visit the emergency room due to asthma.
- 1,000 people are admitted to the hospital due to asthma.
- 14 people die from asthma.

Asthma Fast Facts

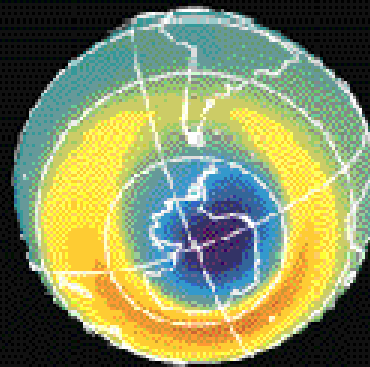
- Estimated 20 million Americans use MDI's for Asthma or COPD
- Estimated 70 million patients worldwide
- FDA GOAL:
 - To protect the environment without putting patients' health at risk

Ozone Depletion

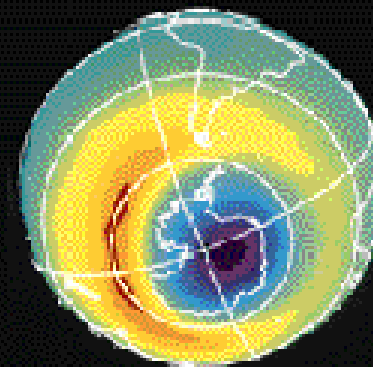
Depletion of the Ozone Layer



1979



1986



1996

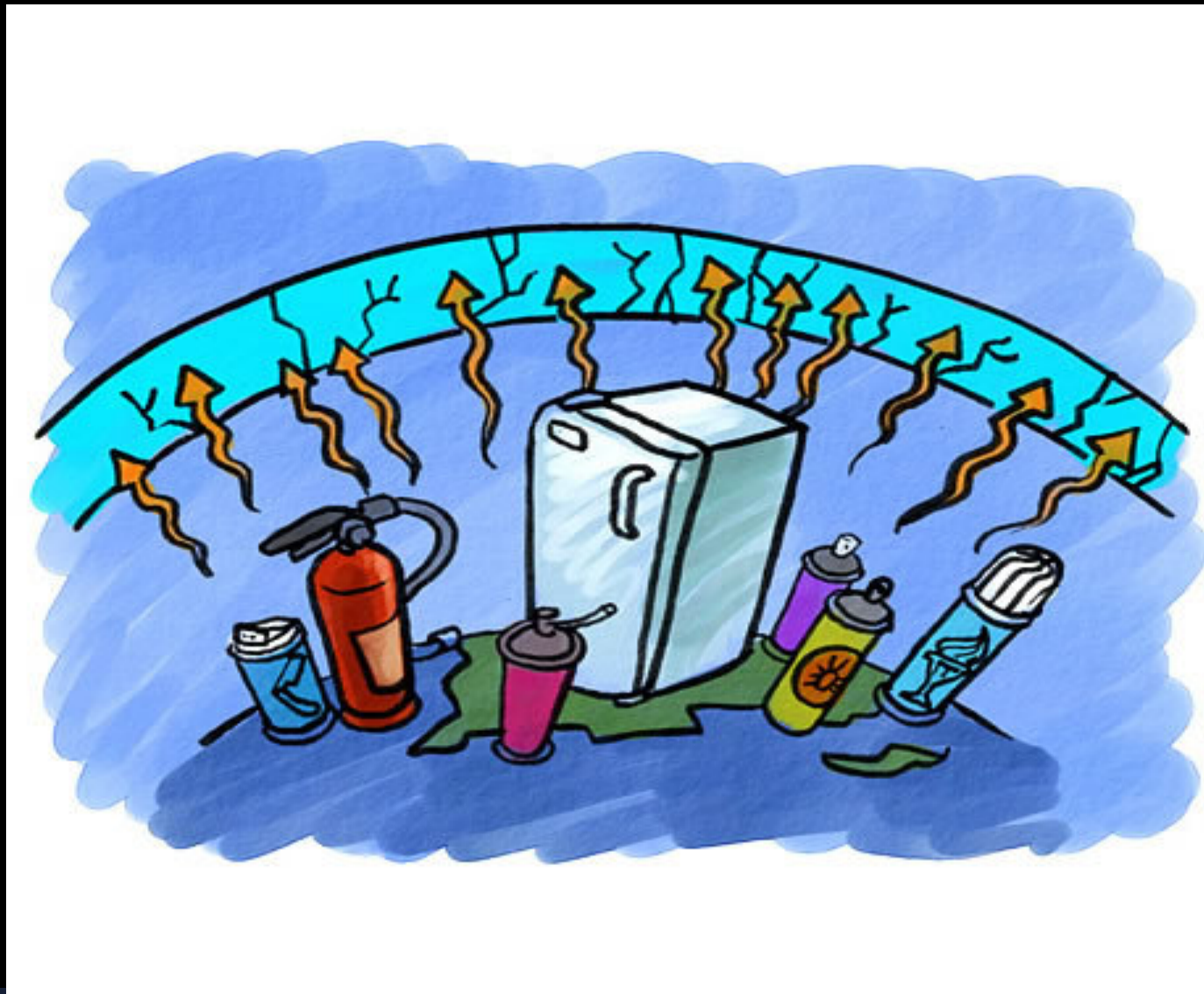


Total Ozone (DU)

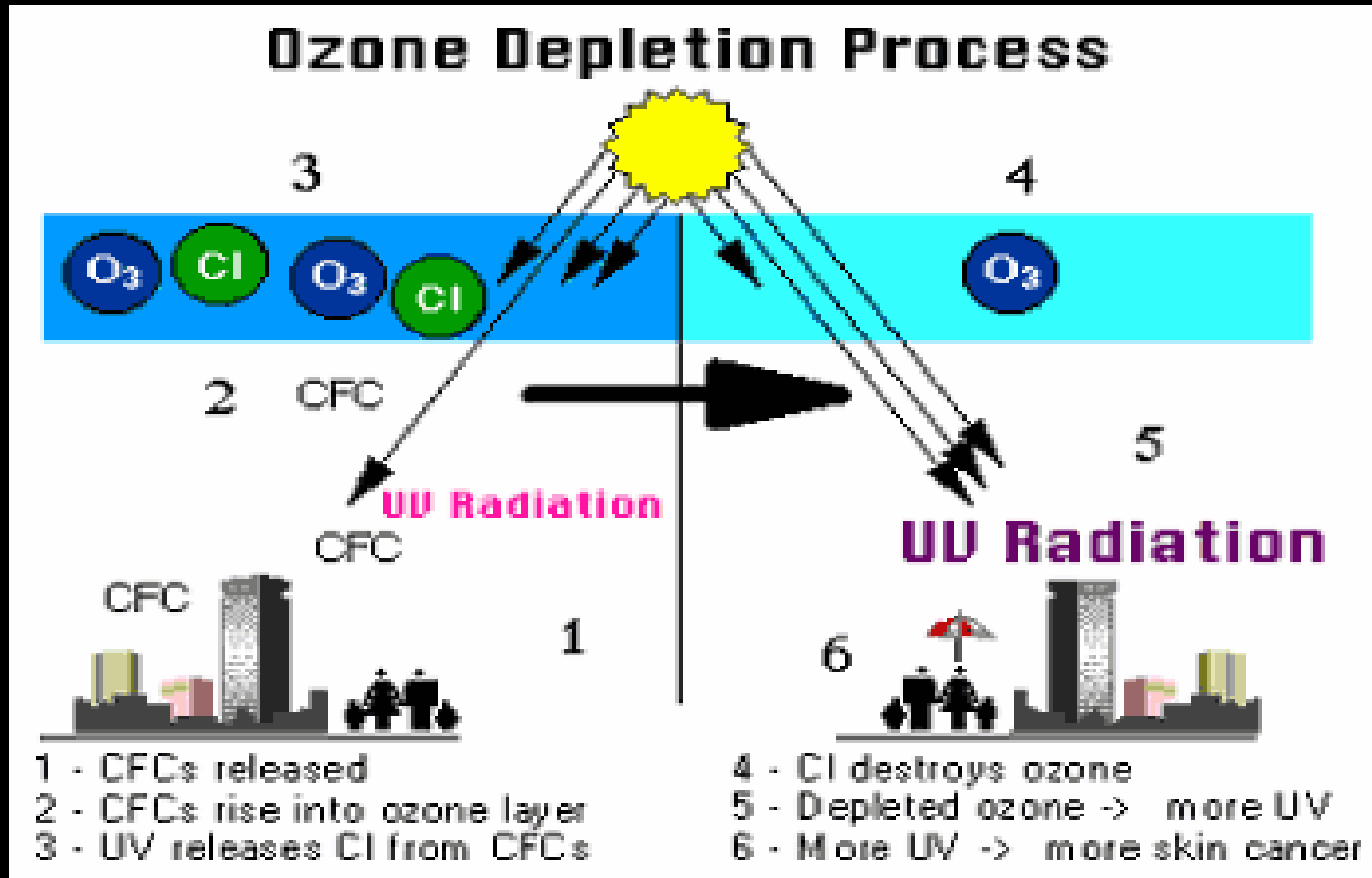
Since 1979, ozone levels have decreased over many parts of the world. The areas with the biggest ozone losses, like Antarctica (above), are purple. Normal ozone levels are usually around 300 Dobson Units (DU).

Source: NASA/Goddard Space Flight Center

Ozone Depleting Substances



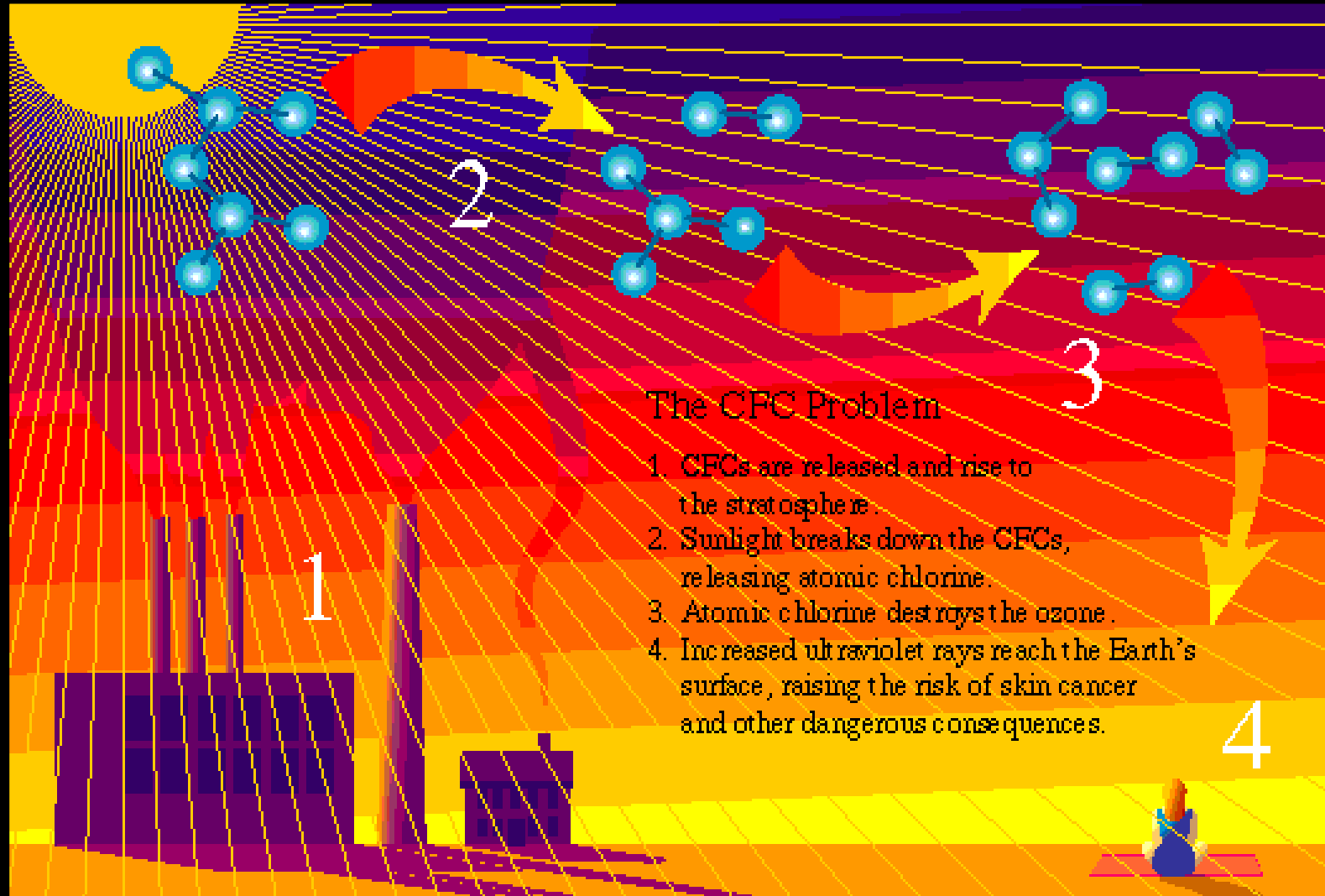
Ozone Depleting Substances



Ozone Depleting Substances

Compound	Formula	ODP	Atmospheric lifetime (years)
CFC-11	CFCl_3	1.0	60
CFC-12	CF_2Cl_2	1.0	120
CFC-113	$\text{CF}_2\text{ClCF}_2\text{Cl}$	0.8	90
CFC-114	$\text{CF}_2\text{ClF}_2\text{Cl}$	0.6-0.8	200
Halon-1211	$\text{CF}_2\text{Br}_2\text{Cl}$	2.2-3.5	25
Halon-1301	CBrF_3	7.8-16	80-110
Halon-2402	$\text{C}_2\text{F}_4\text{Br}_2$	5.0-6.2	23-28
HCFC-22	CHF_3Cl	0.04-0.06	15-20
HCFC-123	CF_2CHCl_2	0.02-0.16	1-2
HCFC-141b	CH_3CFCl_2	0.03-0.11	6-11
HCFC-124	CF_3CHFCl	0.016-0.024	5-10

Ozone Depleting Substances



The CFC Problem

1. CFCs are released and rise to the stratosphere.
2. Sunlight breaks down the CFCs, releasing atomic chlorine.
3. Atomic chlorine destroys the ozone.
4. Increased ultraviolet rays reach the Earth's surface, raising the risk of skin cancer and other dangerous consequences.

Ozone Depleting Substances

- Dangerous consequences include:
 - Skin cancers
 - A United Nations study estimated that a 1 percent decrease in the atmospheric ozone concentration translates into a 2 percent increase in the rate of non-melanoma skin cancer, which can be fatal
 - Cataracts
 - Damage to marine organisms
 - Damage to plants
 - Damage to plastics



The Montreal Protocol

- 1930's CFC's used commercially to replace sulfur dioxide and ammonia
 - used in refrigeration and deemed hazardous
 - Subsequently demonstrated potential for many uses including solvents and propellants in many aerosol products
- 1970'S – link between CFC's and damage to Earth's protective ozone layer was discovered

The Montreal Protocol

- 1978 – FDA & EPA ban use of CFC's as propellants in any food, drug, medical device, or cosmetic aerosol product
- “Essential uses” exempt from ban:
 - Metered-dose adrenergic bronchodilator human drugs for oral inhalation
 - Space shuttle
 - Laboratory analytical use

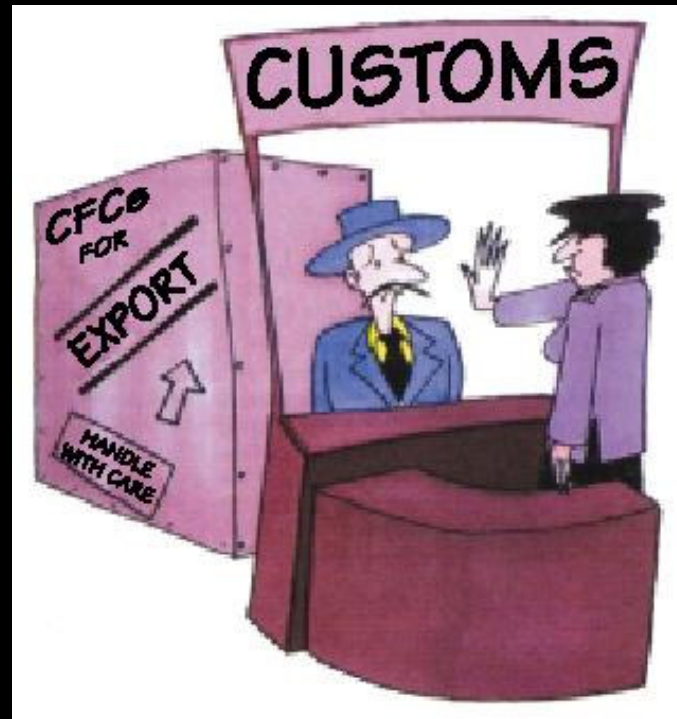
The Montreal Protocol

- 1981 – Albuterol MDI approved by the FDA
- 1987 – “Montreal Protocol on Substances that Deplete the Ozone Layer” established
 - Committed to reducing production and consumption of certain CFC’s to 50% of 1986 levels by 1998
 - Initiated by 27 nations
 - Over 180 parties involved today

The Montreal Protocol

- 1990 - Phase out date for CFC's slated for 2000
- 1992 – Increased evidence of ozone depletion, CFC phase out date moved up to end of 1995
- 1995 – Generic albuterol FDA approved
- 1996 – FDA approves NDA for Proventil HFA[®]

The Montreal Protocol



The Montreal Protocol

- 1996 - Montreal Protocol bans importation and production of CFC products
 - MDI's considered essential with no suitable alternatives are exempted from this ban
 - Parties in developed countries take action to promote industry's participation in smooth and efficient transition away from CFC MDI's

The Montreal Protocol

- 1997 – developed countries present initial national or regional transition strategy by January 31, 1999
- 2000 – indicated that any MDI for treatment of asthma or COPD approved for marketing after 2000 would not be “essential use” unless it met criteria:
 - No technically feasible alternative
 - Provide substantial (health, public, or environmental) benefit
 - Release of CFC small or justified

The Montreal Protocol

- 2002 – Standards developed to determine use of an ODS in a medical product is no longer “essential” of a medical product:
 - At least one non-ODS with the same active moiety is marketed, it must have the same indication, route, and the same level of convenience
 - Supplies and production for non-ODS product exists at levels sufficient to meet patient needs
 - At least one year of adequate post-marketing data available
 - Patients who require ODS product are adequately served by the non-ODS product

The Montreal Protocol

- 2002 – FDA approves Ventolin HFA[®]
- 2005 – FDA approves Xopenex HFA[®]
- 2005 – Final Ruling
 - December 31, 2008 is the date selected for removal of inhaled albuterol from the “essential-use” designation list

“Essential” CFC Inhaled MDI's

- Beta-agonists
 - Metaproterenol (Alupent®)
- ICS
 - Flunisolide (Aerobid®)
 - Triamcinolone (Azmacort®)
 - HFA product expected in 2008
- Cromones
 - Cromolyn (Intal®)
 - Nedocromil (Tilade®)
- Anticholinergics
 - Ipratropium/Albuterol (Combivent®)
 - HFA product in development

Approved Non-CFC Inhaled MDI's

- Beta-agonists
 - Albuterol (Proventil HFA[®], Ventolin HFA[®], ProAir[®])
 - Formoterol (Foradil DPI[®])
 - Levalbuterol (Xopenex HFA[®])
 - Pirbuterol (Maxair[®])
 - Salmeterol (Serevent Diskus[®])
- ICS
 - Beclomethasone (QVAR[®])
 - Budesonide (Pulmicort DPI[®])
 - Fluticasone (Flovent HFA[®], Flovent Diskus[®])
 - Mometasone (Asmanex[®])

Approved Non-CFC Inhaled MDI's

- Combination Products
 - Fluticasone/Salmeterol (Advair Diskus[®])
- Anticholinergics
 - Ipratropium (Atrovent HFA[®])
 - Tiotropium (Spiriva DPI[®])

The Montreal Protocol – Essential Use Criteria

1. At least two products with the same active moiety, same indication, route, and the level of convenience
 - Albuterol Inhaled for relief of bronchospasm
 - Proventil HFA®
 - Ventolin HFA®
 - ProAir HFA®
 - Albuterol HFA

The Montreal Protocol – Essential Use Criteria

2. At least one year of adequate post-marketing data available
 - Proventil HFA[®] marketed for 10 years
 - Ventolin HFA[®] marketed for 4 years
 - *ProAir HFA[®] marketed for 2 years*
 - *Just approved at the time of the final ruling, so limited data available at that time*

The Montreal Protocol – Essential Use Criteria

3. Supplies and production for non-ODS product exists at levels sufficient to meet patient needs
 - Manufacturers state increased production capacity can be achieved in 12-18 months, after final decision
 - Glaxo: 30-33 million albuterol HFA MDI units
 - Ivax: 50-60 million albuterol HFA MDI units
 - Schering: 50 million albuterol HFA MDI units

The Montreal Protocol – Essential Use Criteria

4. Patients who require ODS product are adequately served by the non-ODS product

- Albuterol CFC \$20-30
- Albuterol HFA \$37
- ProAir[®] \$37
- Proventil HFA[®] \$44
- Ventolin HFA[®] \$38
- Xopenex HFA[®] \$50
- Maxair[®] \$100 (400 doses per inhaler)

Cost Data: Amerisource Bergen AWP

Patient Assistance Programs

- Schering-Plough
 - SP Cares: 1-800-656-9485
 - Up to a three month supply is sent to provider
- GlaxoSmithKline
 - GKS for you: 1-866-GSK-4YOU
 - “small” co-pay for up to a 60-day supply, paid at the drugstore.
 - refills for most drugs by mail at no cost
- IVAX
 - Consumer Hotline 1-305-575-6000
 - Up to a three month supply is sent to provider

Stroger Hospital Cost Impact

Product	Price Increase	Additional Annual expenditures
Albuterol MDI	10-20 fold	\$1,000,000
Atrovent [®]	3.5 fold	\$400,000

FDA Drug Shortage Information

- **Albuterol Metered Dose Inhalers**

- Albuterol metered dose inhalers, both HFA and CFC inhalers, are made by multiple manufacturers. Beginning in early 2006, there have been temporary outages of albuterol inhaler products from some manufacturers. However other manufacturers continue to supply the market at previous or increased levels. Therefore, albuterol inhaler products continue to be available and additional supplies are anticipated over the next several weeks.

- 3/9/2006
- GSK updated 6/28/2006
- IVAX updated 7/12/2006

Information from FDA website 9/18/06

FDA Drug Shortage Information

The following firms are currently producing albuterol and levalbuterol metered dose inhalers. FDA considers all of these inhalers as options for patients who cannot otherwise get their preferred albuterol brand or product:

- Albuterol metered dose inhalers:
Schering Plough is not experiencing a shortage at this time. Schering Plough's products are as follows:
 - Proventil® (NDC 00085-0614-02)
 - Proventil HFA® (NDC 00085-1132-01)
 - Warrick - albuterol MDI (NDC 59930-1560-01).
 - Schering Customer Service: 1-877-432-7768.

Information from FDA website 9/18/06

FDA Drug Shortage Information

- GlaxoSmithKline
 - Ventolin HFA® (NDC# 0173-0682-20) - additional supplies anticipated to be available mid 2006.
 - Customer service number 1-888-825-5249 (updated 6/28/2006)
- IVAX Laboratories, Inc.
 - ProAir HFA® (Albuterol Sulfate HFA): NDC 59310-579-20.
 - For questions, call 1-888-482-9522. (updated 7/12/2006)
- Armstrong Pharmaceuticals
 - albuterol metered dose inhalers (NDC 17270-0721-01).
 - Customer service - 1 (800) 423-4136

Information from FDA website 9/18/06

FDA Drug Shortage Information

- Levalbuterol metered dose inhalers:
Sepracor
 - Xopenex HFA[®] (levalbuterol tartrate) Inhalation Aerosol metered dose inhalers (NDC 63402-510-01).
 - Customer service 1-888-394-7377

FDA will continue to closely monitor this situation and will continue to work with the manufacturers on issues related to increasing supplies.

Information from FDA website 9/18/06

ASHP Drug Shortage Information

Albuterol metered dose inhalers (MDIs) are in short supply.

Armstrong, Andrx, GlaxoSmithKline, and IVAX Laboratories will not provide a reason for the shortage

IVAX Pharmaceuticals has discontinued their CFC inhalers due to a lack of raw materials.

Schering states that increased demand for product is limiting supplies of the Proventil® products and Warrick albuterol CFC MDI. To decrease depletion of the ozone layer, the Food and Drug Administration (FDA) announced that all albuterol MDIs containing CFC propellant must be withdrawn from the market by December 31, 2008

Information from ASHP website 9/18/06

ASHP Drug Shortage Information

- Armstrong manufactures albuterol metered dose inhalers (MDIs) for Andrx. Both companies have limited supplies. Armstrong is shipping product to wholesalers as it is available.
 - Andrx inhalers are not available at wholesalers. Customers who have an account with Anda may obtain limited quantities of Andrx inhalers only if they purchase additional products sold by Anda.

Information from ASHP website 9/18/06

ASHP Drug Shortage Information

- IVAX Pharmaceuticals has discontinued their albuterol CFC MDIs. The company has no remaining supplies.
- IVAX Laboratories is shipping the albuterol HFA (ProAir[®]) MDI to wholesalers. The company states they have good supplies available.

Information from ASHP website 9/18/06

ASHP Drug Shortage Information

- GlaxoSmithKline has available Ventolin HFA[®] with a dose-counter. The new NDC number is 00173-0682-20. GlaxoSmithKline discontinued production of Ventolin[®] CFC products in 2003.
- Schering is allocating supplies of the Proventil[®] CFC and Warrick brand albuterol MDIs to wholesalers. The company has good supplies of the Proventil HFA[®] MDIs

Information from ASHP website 9/18/06

Short-acting Beta 2 inhaled products

	Maxair [®] Autohaler	ProAir [®]	Proventil HFA [®]	Ventolin HFA [®]	Xopenex HFA [®]
Ages	≥12 yrs	≥12 yrs	≥4 yrs	≥4 yrs	≥4 yrs
Prime	2 sprays	3 sprays	4 sprays	4 sprays	4 sprays
Prime if not used in:	48 hrs	2 wks	2 wks	2 wks	3 days
Dose	2 sprays q 4-6 hrs	2 sprays q 4-6 hrs	2 sprays q 4-6 hrs	1-2 spray q 4-6 hrs	2 sprays q 4-6 hrs
# doses	400	200	200	200	200

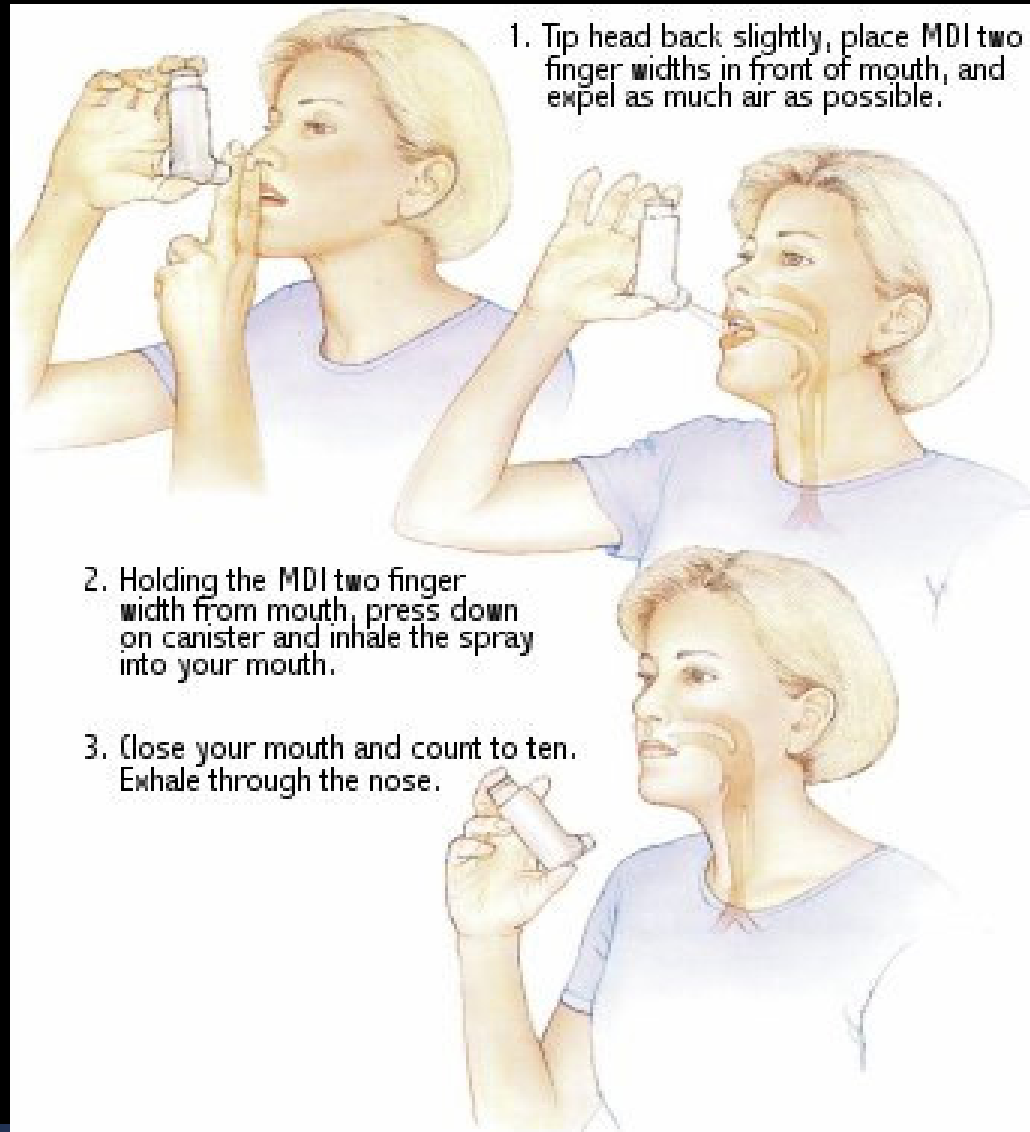
CFC vs. HFA products

	CFC inhalers	HFA inhalers
Spray Force	Greater	Less
Technique	See next slides	See next slides
Clean	Thoroughly and frequently	Weekly

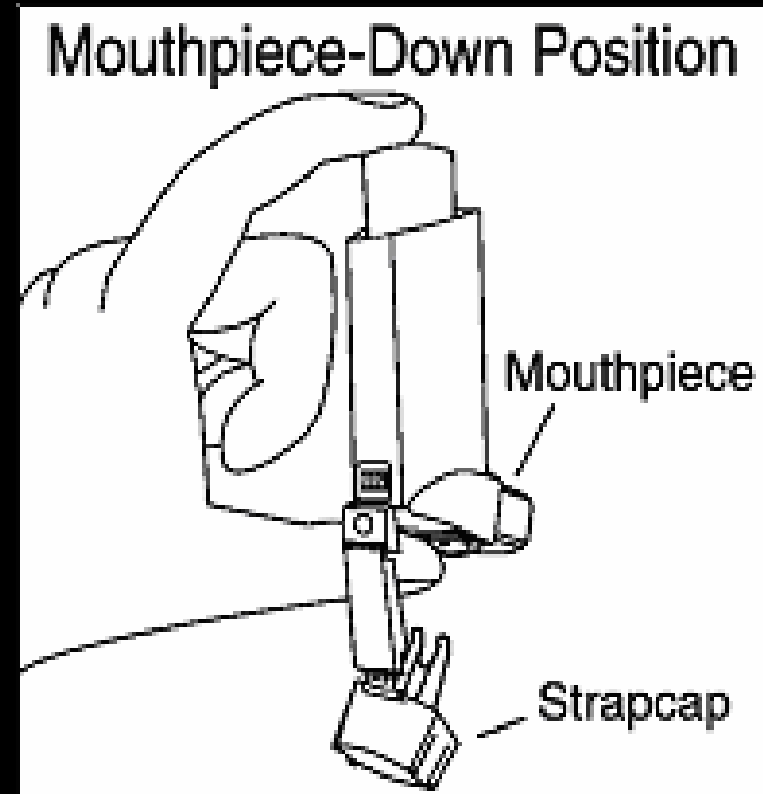
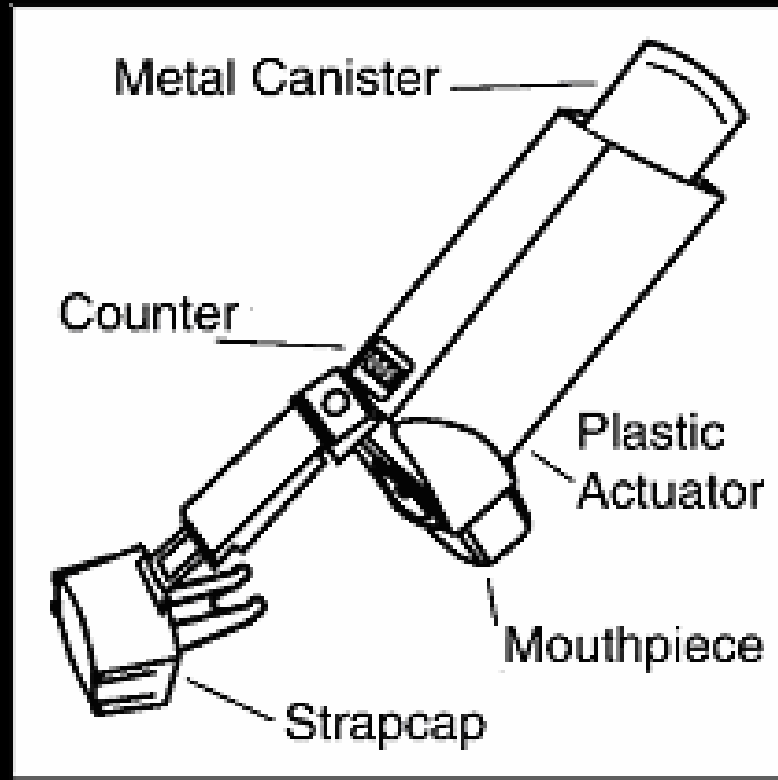
MDI Technique (CFC product)



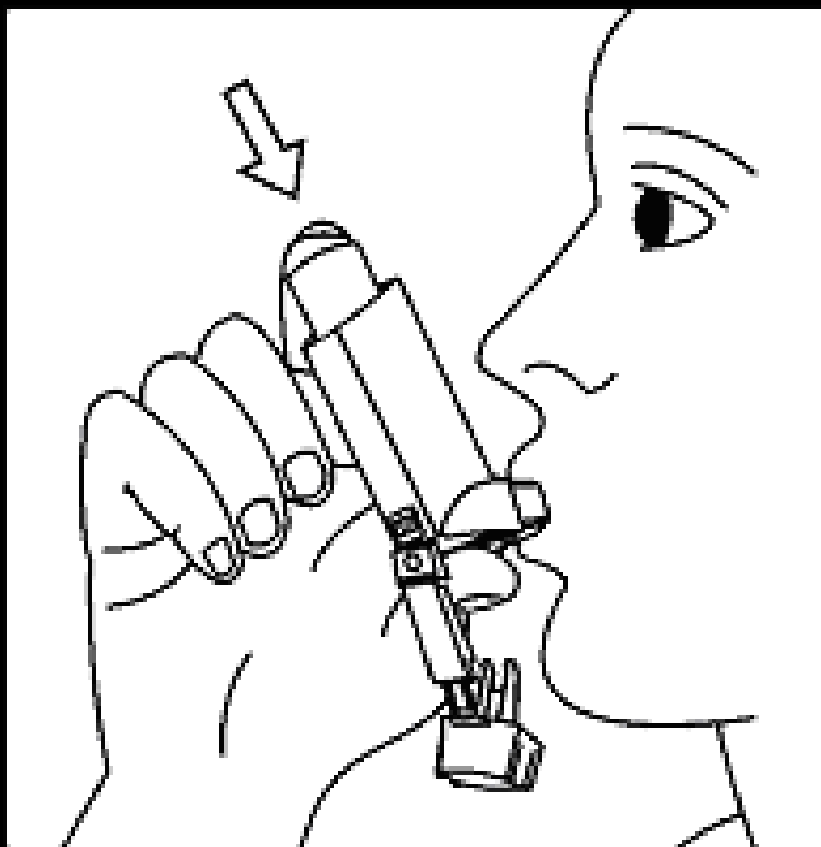
MDI Technique (CFC product)



MDI Technique (HFA product)



MDI Technique (HFA product)



Positive Outlook

- HFA inhaler products offer same device with similar technique
- Shortages appear to be resolving
- Shortages may have contributed to greater inhaled corticosteroid use??

Summary

- CFC have demonstrated damage to the ozone
- The Montreal Protocol has mandated the elimination of CFC products by December 31, 2008
- Inhaled Albuterol has met the criteria deeming it no longer “essential” beginning December 31, 2008
- Shortages have arisen, but presently appear to have adequate supply of HFA formulations
- New formulations may contribute to greater health care costs

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