The Montreal Protocol and the Phase-out of CFC-based Metered Dose Inhalers

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The Montreal Protocol

- Binding international agreement for the preservation and recovery of the ozone layer
- The Protocol establishes commitments for the Parties to phase-out ozone depleting substances (ODS)
- Among international environmental agreements only the Montreal Protocol has achieved universal ratification
- First international agreement that applied the precautionary principle
- The first agreement where financial cooperation between developed and developing countries has been demonstrated successful (common but differentiated responsibilities)
- Several amendments and adjustments to reflect scientific progress and to add further commitments

The Montreal Protocol

- Objective: protecting the ozone layer by phasing out the production and consumption of Ozone Depleting Substances.
  - ✓ Production of ODS
  - ✓ Refrigerants
  - ✓ Foam-blowing agents
  - ✓ Aerosols
  - ✓ Solvents
  - ✓ Fumigants

- Funding
  - Multilateral Fund
  - Bilateral Funding (Italy, Japan, Spain, Canada, Sweden)

- Implementing Agencies
  - UNIDO
  - UNEP
  - UNDP
  - World Bank
  - Bilateral Agencies: GTZ (Germany), Environment Canada, Agence Française de Developpement, METI (Japan), US Environmental Protection Agency, Swedish Environmental Protection Agency.

Chemicals listed in the Montreal Protocol

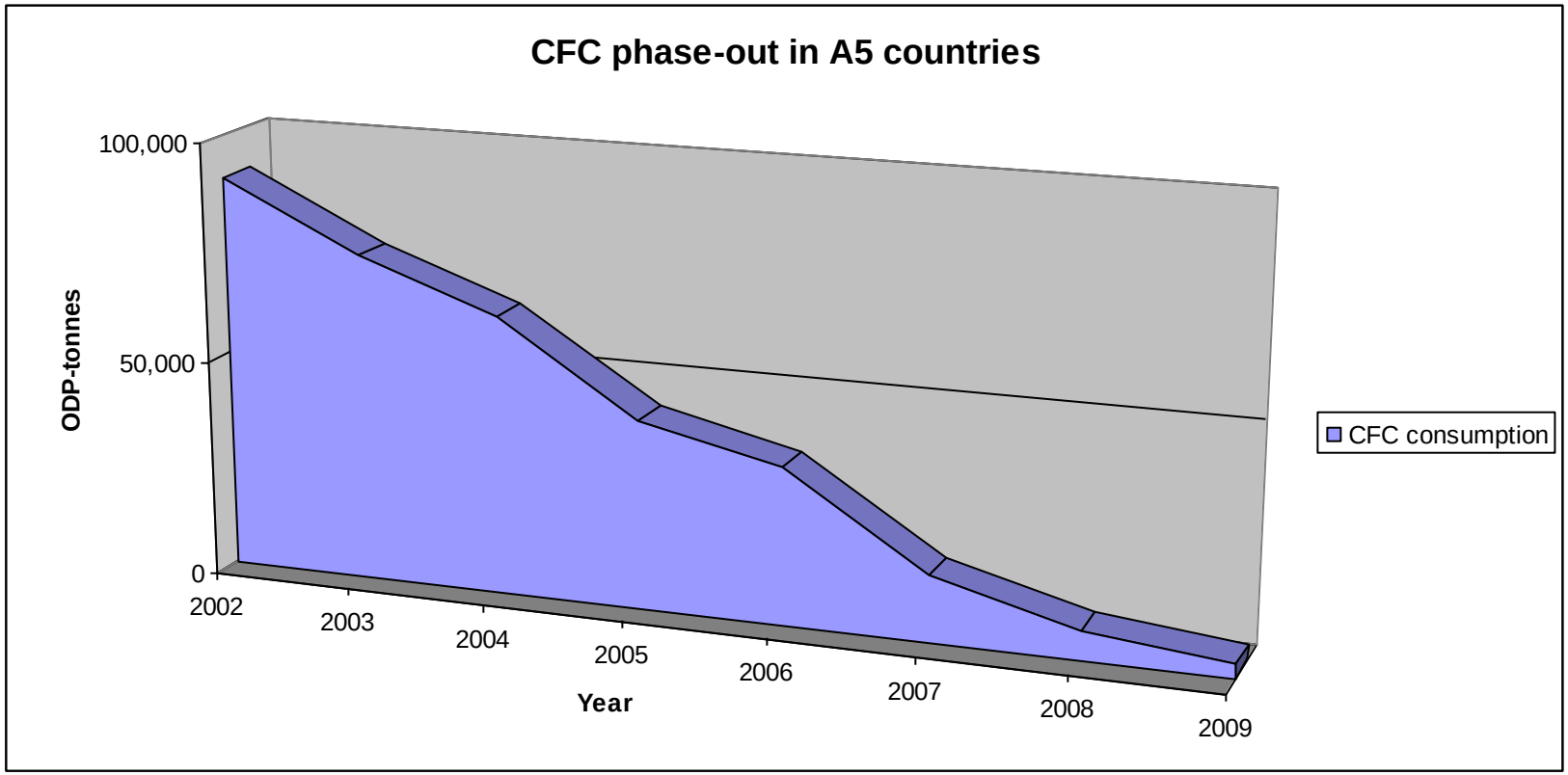
- Chlorofluorocarbons (CFCs)
- Halons
- Carbontetrachloride
- 1,1,1-Trichloroethane
- Methyl bromide
- Hydrobromofluorocarbons (HBFC)
- Hydrochlorofluorocarbons (HCFC)

Reduction and phase-out plans

- CFCs, carbontetrachloride and halons – complete phase-out of production and consumption by 2010
  - Exemptions (essential uses, i.e. metered dose inhalers and laboratory uses) have to be approved by the Meeting of the Parties to the Montreal Protocol
- Methyl bromide and trichloroethane – complete phase-out by 2015
- Phase-out schedule for HCFCs:

- 2009-2010 – Baseline
- 2013 – Freeze
- 2015 – 10% reduction
- 2020 – 35% reduction
- 2025 – 67.5% reduction
- 2030 – 97.5% reduction
- 2040 – Total Phase-out

Typical Phase-down scenario during the past decade (example CFCs)



Essential use exemptions:

Estimated CFC usage for MDI manufacture by nominating Parties, 2010-2014

Country	2010	2011	2012	2013	2014	Total
Algeria	11	8	0	0	0	19.0
Argentina	178	107	3	0	0	288.2
Bangladesh	156.7	57	27	0	0	240.7
China	652.0	741.2	650	400	345	2,788.2
Egypt	227.4	0	0	0	0	227.4
India	344	0	0	0	0	343.6
Iran	2.2	0	0	0	0	2.2
Mexico	-	-	-	-	-	0.0
Pakistan	35	39.6	10	0	0	84.5
Russian Federation	212	212	30	0	0	454.0
Syria	44.7	0	0	0	0	44.7
United States	92.0	-	-	-	-	92.0
Total	1,954.6	1,165.0	720.0	400.0	345.0	4,584.5

Replacement of CFCs in metered dose inhalers (MDIs)

- Purpose of MDIs
  - Treatment of asthma and chronic obstructive pulmonary disease
- Alternative technologies
  - Hydrofluorocarbons (HFCs)
  - Dry powder inhalers
  - Nebulisers and soft mist inhalers

All alternatives are “ozone friendly”, the ozone depleting potential (ODP) is zero!

Evaluation of alternative technologies

Type of inhaler	Advantages	Disadvantages
Metered dose inhalers (MDI)	-Simple actuation system -Reliable accurate dose -Compact and portable -Easy to use -Economically viable solution -Good resistance to moisture	-Dosage accuracy may be dependant on the formulation -Coordination between actuation and breathing required (except breath-actuated systems) -Complex manufacturing process
Dry Power Inhalers (DPI)	-No propellant used	-Drug release depends on the breathing capacity -Inhaled fraction is reduced if patient breathes into the system -Relatively expensive
Nebulizers	-No special breathing coordination required -Useful for new or rarely used drugs	-Not portable -Power supply necessary -Expensive -Operation takes a long time -Requires preservatives to reduce risk of bacterial contamination

Selected technology

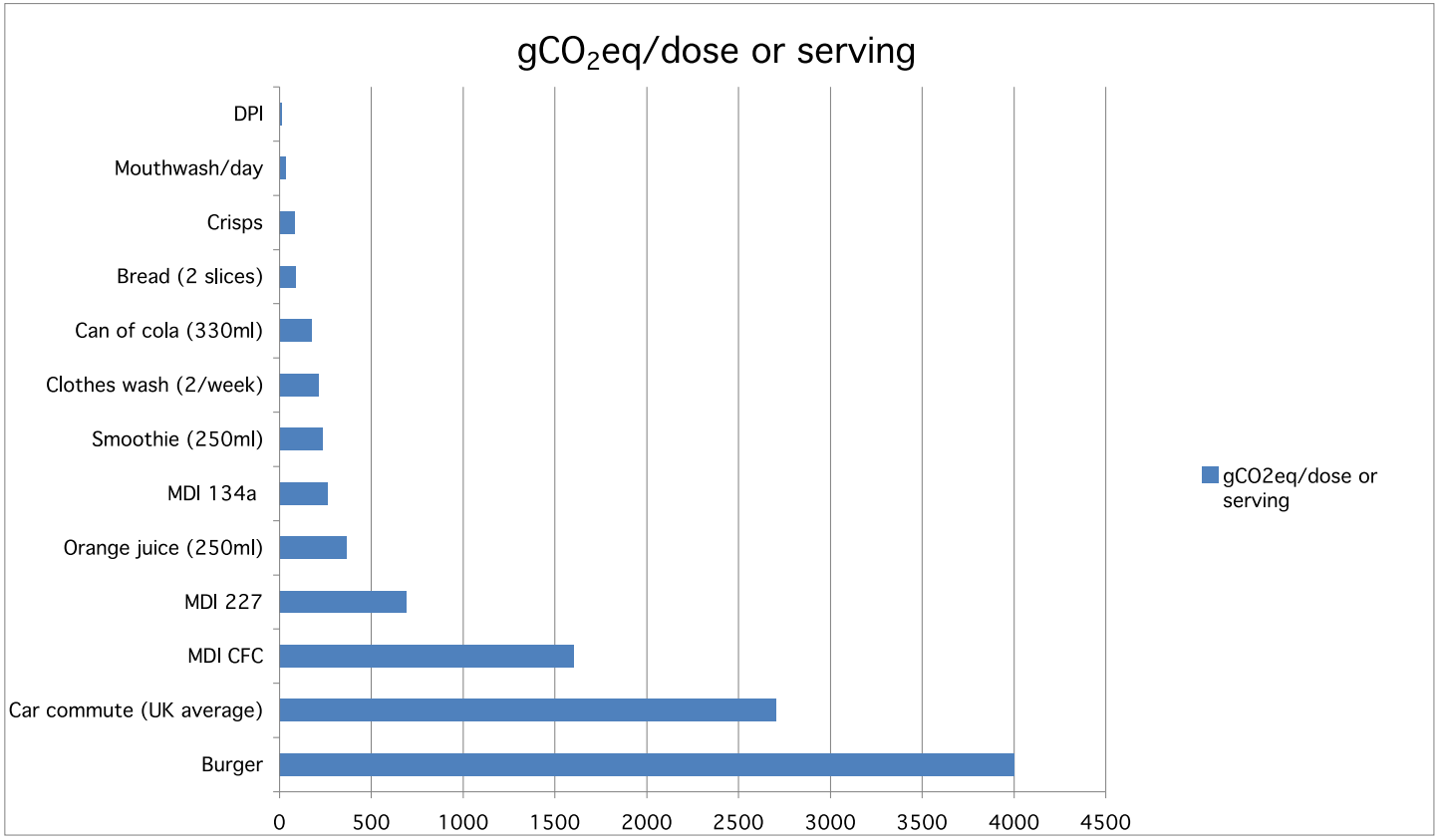
Other environmental considerations, in particular climate impact

Carbon footprints of respiratory devices and treatment methods

Respiratory devices and treatment methods	Carbon footprint Per 200 doses (Kilograms CO_2eq.)	Carbon footprint Per 2 puffs (Grams CO_2eq.)
CFC MDI	150-200	1,500-2,000
HFC-134a MDI	20-30	200-300
HFC-227 MDI	60-80	600-800
Dry Powder Inhaler	1.5-6.0	<20
Tablets	1.5-5.0	<20

Source: MTOC assessment report 2010

Estimated relative carbon dioxide emissions of everyday items compared with asthma inhalers



Source: MTOC assessment report 2010

General objectives of the project

- Phase-out of chlorofluorocarbons (CFCs) in the manufacture of metered dose inhalers (MDIs)
- Conversion of production facilities to CFC-free technology
- Technology transfer
- Introduction of more advanced pharmaceutical products

MDI market in Mexico

- National Companies
  - Eligible to receive funding from the Multilateral Fund (MLF)
- Laboratorios Salus

- Multi-national Companies
  - Not eligible for MLF support
- Glaxo-Smithkline
- Ivax
- Astra - Zeneca
- Boehringer Ingelheim

Outline of the strategy - principles

- Patients' health has highest priority in the transition period. The patient is at the core of the transition.
- All parties involved should actively manage the transition to ensure the patient's access to needed treatments is not interrupted.
- Transparency and efficacy in the authorization and follow-up of new products in the market is required.
- Awareness activities with the active participation of all stakeholders, health professionals, Ministries, pharmaceutical companies, and the community.

Criteria to consider for the selection of alternatives (1)

- Specific needs of the patients
- Relatively high incidence of asthma, allergic respiratory diseases, and chronic obstructive pulmonary disease (COPD) in all ages of the Mexican population
- Familiarity of patients with the existing MDI design as a device for delivery of the required medication
- Patient acceptance of CFC-free MDIs
- Resistance of the market to accept a significant increase in the cost of treating patients

Criteria to consider for the selection of alternatives (2)

- The maturity and established commercialization of alternative MDI technology
- Price of an alternative propellant, product availability, and cost-effectiveness of the new MDI formulation
- Properties CFC-MDI products manufactured by Laboratorios Salus
- Existing experience and skills of the personnel

Products converted (by active ingredient)

- Salbutamol — registered 1st April 2011
- Beclamethasone — registration submitted

Thank you!