Medical Grade CFC storage options to accompany a possible 2009/2010 manufacturing exit campaign

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**Definite Requirements**

Secure, legal storage for medical grade CFCs, that will not allow their leakage, contamination or degradation in any way, to enable CFCs made in 2009/10 to be stored through to the end of 2015.

**Optional requirements**

1. In country of final use
2. In familiar packages
3. Local destruction facilities for any surplus CFCs to avoid trans-border shipment of waste.

**Dimensions/scope**

Following on from the discussions on key points of medical CFCs final campaign productions and stockpile during the Regional Workshop on Phasing-out CFC-based Metered Dose Inhaler (MDI) during 13-15 March 2008 at Langkawi, Malaysia, it appears that there is a first cut need to store around 2,200 Tes of CFCs for use in Bangladesh, India, Iran and Pakistan (excluding China), and an as yet not fully quantified additional need by China. It is probable that whatever solutions to storage vs just in time manufacture are worked through in China, these will take care of needs by China, and will probably be only applied internally. So the rest of this discussion will focus mainly on the 2,200 Tes that are needed by 4 manufacturing countries in the region i.e. Bangladesh, India, Iran and Pakistan.

These figures are from 1 January 2010, and if we assume that a final campaign is taking place in perhaps the first six months, then CFCs needed to meet approved essential uses over that time and for a few months afterwards would be delivered directly, and not form part of the stock. As shown in the draft report from the Langkawi meeting, CFC demand for 2010 in Bangladesh, India, Iran and Pakistan will be around 700 Tes, so around 200 Tes of this may need to come from the stockpile. Therefore, storage requirement need to be considered in these countries would be around 1,700 Tes to cover the period 2010-15.

The CFC formulation technology that most MDI companies now use is pretty similar, so it is pretty safe to assume that roughly 2/3 of the CFC need will be for P12 (the propellant) and 1/3 for P11 (the carrier/solvent).

This allows us to start homing in on possible storage quantities. Applying this ratio to the quantities to be stored:

- CFC11: 570 Tes
- CFC12: 1,130 Tes
Options

The storage options are summarised in table 1 below, in the form of a risk/cost matrix.
At present by necessity most of the data is very sketchy but should give a rough ‘order of magnitude’ feel to the options.

<table>
<thead>
<tr>
<th>Option</th>
<th>Estimated Cost ($/ton/pa)</th>
<th>Risk score (0=no risk, 10=high risk)</th>
<th>cost x risk</th>
<th>Commentary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bulk storage in UK</td>
<td>190</td>
<td>1</td>
<td>190</td>
<td>Simon storage, Immingham. A purpose built medical CFCs storage facility, capacity 1250 Tes. In 5 tanks Used by Fisons, Glaxo, IVAX in the past. Perfect record. Whole site is normally rented, so the fixed fee has to be amortized across the tons stored. This example assumes full use to half use.</td>
</tr>
<tr>
<td>Bulk storage in user countries</td>
<td>170</td>
<td>5</td>
<td>850</td>
<td>Issue will be identifying suitable storage tanks - if any exist, modifying them, cleaning, validating and operating them in a way that will not compromise the products. Most tank facilities are linked to chemical plants, and there is a poor record of being able to successfully convert these for medical use. No definite costs exist, but as substantial conversion costs will be incurred, they are likely to be in a similar band to the UK storage.</td>
</tr>
<tr>
<td>Isotank storage in user countries</td>
<td>839.5</td>
<td>3</td>
<td>2518.5</td>
<td>Isocontainers are pretty secure, but quality of storage facilities an unknown at present. Also an issue that they need to be pressure tested (empty) every 5 years, so some problems might arise towards end of life - maybe some sort of extension?</td>
</tr>
<tr>
<td>P11 storage in disposable 280 Kg drums, temperate warehoused</td>
<td>730</td>
<td>2</td>
<td>1460</td>
<td>Note: Only STORAGE costs included. In addition there will be a drumming cost at the time of production that will not be less than 400$/Ton. Packages must be stored indoors, in a cool, dry, environment.</td>
</tr>
<tr>
<td>P11 storage in disposable 280 Kg drums, tropics warehoused</td>
<td>730</td>
<td>7</td>
<td>5110</td>
<td>The higher risk is due to the adverse storage conditions that may apply in the tropics. High RH% rots the drums, and temperatures &gt;30C will cause high pressures within the drums distending the ends and causing stacks to collapse.</td>
</tr>
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</table>

Table 1: Risk/cost matrix for CFC storage options

One important fact to be borne in mind when considering these options – or a mix of them – to meet CFC storage needs is that of the companies that traditionally take their CFC supply in smaller ‘non bulk’ deliveries. The P11 will be delivered in 280 Kg disposable sheet metal drums, the P12 in one tonne returnable ‘roll’ drums. A number of companies take a mixture, P12 in bulk, P11 in sheet metal drums.

As will be seen as the options are discussed, it will not be really possible to maintain a P12 ‘roll’ drum traffic from the stock, as repacking is difficult without the presence of a chemical plant, and in any event the numbers of these roll drums are very limited. Therefore pharmaceutical companies that currently use these drums will have to make provision to receive the CFC in bulk isocontainers, most probably connecting directly up to the container and running from it, or possibly offloading the container into a new stock tank.

In contrast, CFC 11 can still be delivered in the traditional way, in 280 Kg disposable drums.

The main options will now be discussed in a little more detail.
1. **Fixed Bulk (UK)**

In the early 1990’s Fisons commissioned Simon Storage, a leading UK chemical storage company, to provide them with secure, FDA standard, storage for a CFC stockpile, as their current supplier (ICI) was due to cease manufacture by 1993/4. In all 2,200 tons of storage capacity was arranged, around 1,000 tons on one site, and 1,200 tons on a second site (Seal Sands) in the form of 5 x 250 ton bulk stock tanks, set up for loading and unloading isotanks.

By the late 1990’s Fisons had used the stored CFCs, and Simon Storage looked for other users for these facilities. Since then both GSK and IVAX have used the Seal Sands complex for storing medical CFCs, and GSK have now taken a long term lease on the other complex to store medical HFAs.

At present, the Seal Sands complex is empty (last used ~ 12 months ago) and available to rent.

Pro: Secure, very low risk, economical. Well understood.
Con: Can only fill isotanks. Product not held in final user country.

2. **Fixed bulk (user country)**

There are no other facilities like the Simon Storage complex as far as I am aware, so any other bulk storage in the world will either have to be new build or conversion of existing chemical storage stock tanks, probably at a CFC producer.

New build is not really an option at this stage, as both cost and timescales militate against it.

Stock tanks to hold P12 have to be constructed to the appropriate pressure rating, and as such they are rather uncommon, and most likely found associated with a refrigerant gases plant of some description. For example, the INEOS site in the UK has 5 x 400 Tes tanks on it that from a pressure perspective would be suitable. However, there are numerous issues associated with this.

a. Only countries with refrigerant gas manufacturing would have such an option (i.e. India only (China is not applicable in this report)).

b. These tanks are usually in heavy use supporting manufacturing taking place on the site, and would not be normally available to hold such stocks.

c. Significant work would need to be done to:
   i. Isolate them from the other plants and provide dedicated loading/unloading facilities
   ii. Clean them to a medical standard
iii. Validate that process

d. To illustrate the difficulties, it is worth considering the experience of Atofina that attempted to store CFCs for GSK at one of their facilities (Pierre-Benite). Despite the precautions that were taken when laying the stock down, it was cross contaminated and had, in the end, to be replaced.

The message in this is that establishing such stocks on working chemical plants is tricky, and not a game for amateurs.

Pro: Can be used in India. Fairly economical.

Con: Risk of loss or contamination. Only useful in India. No certainty suitable facilities exist.

3. *Isotank storage in user countries*

Isotanks are readily available, and with sufficient notice enough could be hired to hold the Bulk P12 stock and as much of the P11 stock that needs to be held in bulk. They are robust vessels normally capable of holding around 20Tcs of product, and can be fairly easily cleaned to a medical standard. The valves are reliable and with small modification can be sealed shut with strong security seals.

They are moved internationally to all countries, having the same physical dimensions as 20’ containers, and can be moved by the same types of lifting equipment.

Propellant stockpiles have been held in isotanks before (GSK held both CFCs and HFA 134a in them) and facilities to store them exist in most countries, although some careful searching is sometimes needed to find a yard with the right permits.

The only real drawback is one of cost. Isotanks rentals have increased over the last few years, and typically are in the order of 30-40$/day. In addition wherever they are stored will have additional charges, usually around 6-8$/day. This compares very unfavourably with the cost of bulk storage.

Pro: high quality. Robust and secure. Can be in all the user countries.

Con: Cost.

4. *P11*(only) storage in disposable 280 Kg *sheet metal drums, temperate climate*.

Neither option 4 or 5 are full storage options, but they contrast options available for the storage of drummed P11 product. (NOTE: Warehousing costs are unchecked estimates only…may be greater than shown.)

Sheet metal drums are readily available, and are routinely used to deliver
medical grade P11 to tropical countries. Due to the fact that the drum closures are on the upper surface (when stood on end in their correct position) and the thin nature of the metal, they should only be stored indoors to avoid the risk of water getting in, or corrosion with P11 getting out.

We have regularly warehoused this product in the UK in this way with no problems whatsoever. As ever, the problem is cost, as covered warehousing is at a premium. The same comment applies through much of the EU.

Pro: Proven. Fairly robust and secure.
Con: Cost, not in final country.

5. P11(only) storage in disposable 280 Kg sheet metal drums, tropical climate

The key difference with the European storage option is the one of conditions. Sheet metal drums of P11 should not be stored at temperatures > 30C for long periods of time, otherwise the ends can dish out as the drum tries to become spherical rather than cylindrical. This leads to stacks collapsing, leaks, etc.

Furthermore, the high relative humidity in many tropical storage locations would be a severe problem, as the drums would tend to corrode at the seams and again there would be a risk of leakage. Both of these problems would be overcome with air conditioned warehousing, but this is likely to be scarce and costly.

Pro: In final country of use
Con: Risk of loss or cost of a/c warehousing.
Practical details and timings regarding some of the options

1. Fixed bulk in the UK, plus UK warehousing of drummed P11

There is a close working relationship between Arkema, INEOS Fluor and Simon Storage, and in reality if this bulk option were to be used it would be simplest if this group worked together to achieve it.

One point that must be appreciated is that Simon Storage tend to lease out the whole Seal Sands Storage complex, so the cost of storage is pretty near fixed (it will need to be negotiated, but is likely to be in the area of UKP70,000 pa.). So if the complex is used fully, the annual storage cost is around 100$/ton/pa, but as it becomes emptier it will go up. So if – say – India decides to do her own internal thing, and this option were only used for Iran, Pakistan, and Bangladesh, the cost per ton could easily treble.

   a. Capacities.

   On the other hand, earlier calculation shows that total storage needs in Bangladesh, India, Iran and Pakistan (excluding China) are in the order of:

   CFC 11: 570 Tes  
   CFC 12: 1,130 Tes

This exceeds the capacity of Seal Sands of 1250 Tes, but:

i) Maybe 200 Tes of the P11 will need to be stored as drummed product anyway (see below)

ii) the balance of the excess would be stored in ‘use first’ isos

iii) It would leave some space for limited country of use storage if some sort of compromise on location was useful.

iv) Of course, it is possible that India, with it’s own CFC manufacturing assets, may decide to either go the fixed local stock route, or attempt continued manufacture. In this case, the total volume to be stored would decrease (although it should be remembered that any S American needs are not yet known or accounted for) and the unit cost of storage at Seal Sands would tend to rise. At some point (< 40% usage at a rough guess) storage in isotanks might start to become cheaper.

   b. Logistics.

   The way it would work, for either bulk P11 or Bulk P12 would be that medically commissioned isotanks would load at Arkema, with CFC from Arkema stock tanks that had been pre-approved by sample analysis by INEOS Fluor. (If they were not in medical CFC traffic already, there would be additional commissioning steps for them to go through).
The isotanks would deliver to the Seal Sands terminal, and offload to one of the stock tanks. As there are 5 tanks, we would probably have 3 or 4 CFC 12 tanks, and 1 or 2 CFC 11 tanks. Once the tanks is full, it would be recirculated, sampled for analysis, and then sealed until needed. It is normal routine to take a sample every 6 months to demonstrate that no change is occurring in the product. (This may seem strange as we know the product will store with no problems having done this before, but this is done to meet medical regulatory expectations – a sort of regulatory insurance policy!)

As the product is required, it would then be loaded into isotanks for export to the destination country. Export would be with all valves sealed with uniquely numbered seals, for traceability purposes. A fine matter of detail would be whether the Certificate of Analysis provided would be from the bulk tank, or from re-analysis of the isotank. For cost saving reasons I would normally opt for the first option, but that can be debated nearing the time.

*Drummed P11.* This would be filled into 280 Kg sheet metal drums at Arkema’s facility, then moved as full container loads to a suitable warehouse, probably in the EU. Certificate of Analysis would be based upon the INEOS Flour analysis of the Arkema stock tank at the time of filling.

At the time of supply the P11 drums would be loaded to a container for export. As with the P12, part of the management activity that would be provided by INEOS Flour.

c. Commercial and Regulatory (Montreal Protocol) arrangements

This is a complex area, and though it may have a lot of common features with other options, I’ll discuss it here and then maybe refer back from other sections to avoid repetition.

i. Commercial Arrangements

The simplest way of running this would be for the Arkema/INEOS Fluor alliance that has supplied CFCs to a number of the member countries (Iran, India), to simply treat the stockbuild as a new customer in the UK.

This would mean a negotiated commercial transaction between the stock owners (MLF?) and INEOS Fluor (IF), with internal subsequent transactions between INEOS Flour and Arkema. INEOS Flour could contract to:

1. Supply fully qualified CFCs to Simon Storage site.
   Wrapped up in this cost would be an estimate of the amount of out of specification (OOS) CFC that Arkema
might have to destroy in 2010 as part of the production campaign.

2. subcontract and manage Simon storage.

3. Provide all the export logistics to deliver the CFCs to the final user destinations.

4. Provide advice to user destinations, where needed, in converting to receive isotank based deliveries.

5. Provide a general propellants handling ‘help desk.’

ii. Regulatory Arrangements

1. Necessary Permissions to allow manufacture of CFCs and internal EU movement to Seal Sands. This is beyond my area of expertise, but manufacture in either late 2009 or 2010 for the MLF as a customer sounds like something outside the original concept of BDN or EUA, so I assume a special process would need to be sanctioned by the Parties. The Campaign Quantity would need to be agreed – see later.

2. Necessary Export / Import Permissions. Arrangements would need to be put in place – possibly linked to EUAs granted to user countries. This would need to be very clearly laid out to give user countries confidence in having their key strategic stocks held overseas. iPIC would be useful to control export / import among these countries.

iii. Determination and Management of the Campaign Quantity (CQ).

This is a complex issue that encompasses both regulatory and commercial areas. I would propose that EUAs will need to be granted for the period 2010-15 up front FOR CFCS THAT ARE TO BE STOCKED, and the pharmaceutical companies left to determine in what pattern they will consume their approved, stocked, CFCs. Any just in time (JIT) manufacture that does take place (China, India) should be controlled by annual EUAs.

The reason for the up front approval is that the alternative – allow a stockbuild and then have a separate process to determine how much of it really needs to be used, is not viable.

The CQ would therefore be determined by a robust challenging of CFC phaseout plans through the established EUA granting processes, until a final requirement (FR) is determined for each
user country. These figures would then be aggregated to provide the CQ.

Whilst the MLF would then provide the funds to make and store (plus incidentals like transport to store), the companies in the user countries would be responsible to the MLF for the total value and all costs associated with providing the CFCs to their premises. If they did not eventually consume all their FR (this seems unlikely in this type of scenario) they would still be liable for all costs associated with manufacture and storage, plus additional destruction costs.

d. Timings.

i. Manufacturing campaign
Arkema can manufacture this type of material at the rate of around 100-200 tons per week, although there are many factors that can impact this. This would therefore suggest that a 1,600 Tes campaign would take in the region of 8-16 weeks.

ii. Readyng Seal Sands
A programme of pressure vessel inspections, recommissioning, confirming the validated status would need to be carried out before product could flow into the facility. A safe estimate would be that the process should start 9 months before imports to the facility are planned.

However, it is probably important to engage with Simon Storage as soon as possible if it is determined we will go this way, for fear that the facility might otherwise be either irreversibly decommissioned or used for another product (eg GSK HFAs)

iii. Engaging with Arkema
So far, INEOS Flour had not had any conversations with Arkema regarding this possibility, but for the same reasons as given above, I would like to do this earliest if there is a good possibility that we go this way, to ensure they are fully aware and get it in their outline planning.

Considering all these factors, the timing of manufacturing medical grade CFCs should be in early or middle 2009 and the Essential Use Nomination should be approved by the Meeting of the Parties at its 2008 Meeting rather than at the 2009 Meeting.
2. **Bulk Storage in another Country**

At present, the only option I can imagine here (as discussed earlier) is associated with storage tanks at the site of one of the Indian CFC producers (Navine, SRF). As I have no knowledge of what exists the following points are general rather than specific, but they hopefully will give a feeling for the practical issues.

a. **Suitability**

Tanks to store medical CFCs should have the following characteristics:

i. **Correct pressure ratings**

   Minimum 12 bar(g) for CFC 12, a lower figure of ~ 3bar(g) will suffice for CFC 11.

ii. **Size**

   To be worth the effort, the tank should be capable of holding at least 150 T (Tes) of CFC – otherwise an isotank option would probably turn out cheaper.

iii. **Recirculation**

   The tank must be configured such that its contents can be properly recirculated and mixed. This may involve engineering.

b. **Preparation**

A LOT of preparation work is required – even to tanks that have held CFCs – before they could be considered suitable for holding strategic medical grade stocks. (Hence the comment about size). The process would need to be overseen by expert consultants. This list is not comprehensive, but some items would be:

i. **Isolation from all mechanical connections other than those directly needed for loading/unloading**

   History abounds in this industry of propellant being contaminated with another product by a leaking valve, or traces of something left inside the spool of a valve. Bitter experience has shown that total segregation is the only way. This will probably involve significant engineering.

ii. **New loading/unloading terminal and hoses**

iii. **Entry to tanks, de-scaling and cleaning to grey steel**

   Probably the largest part of the job. Old tanks on a chemical plant are invariably pretty disgusting inside, with various deposits and substantial amounts of rusting. The tanks would
need to be shot blasted down to grey steel, then carefully cleaned and vacuumed so that no dust was left inside, then carefully re-commissioned (we have done this numerous times, it’s a pain).

c. **CFC 11 drums**

Storage of CFC 11 drums in the tropics is risky (see earlier discussion). So a tropical storage of CFC 11 would need to be in bulk and either:

- **i.** Delivered by isotank at the users inconvenience or
- **ii.** Repacked to drums shortly before delivery. If the stock tank is associated with an old CFC plant it is possible that such repacking facilities would exist and could be used, although a very thorough upgrading would be needed!

d. **Operation**

Operation would not be dissimilar to the UK based option, but obviously without the involvement of INEOS Flour.

e. **Regulatory/commercial matters**

Many of the points made regarding the UK stockpile apply here as well. Again, a multi-year process would be needed, but there would need to be absolute clarity that the company involved was not also involved in JIT manufacture, otherwise segregation and control could become very difficult, and the system might be open to abuse.
3. **Storage in Isotanks in country of use**

This is a simple, robust, flexible but expensive option. The isotanks can be filled by any suitable medical CFC manufacturer, as they are totally portable. A few key points:

a. **Commissioning of Isotanks**

Most industrial isotanks are also a little dubious inside, and like the tanks described in section 2 will need thorough cleaning and vacuuming, followed by filling with a small amount of CFC and proving by analysis that the tank has not put the CFC OOS. This therefore means that the validated analytical expertise of the CFC supplier has to be employed to achieve this.

b. **Suitable tanks**

Isotanks commonly come with the following inner surfaces: carbon steel, zinc, stainless steel. Zinc lined are very common but are NOT suitable, so care must be taken in the selection of the right type of tanks.

c. **Storage of tanks**

All countries will have a number of locations where these tanks can be lifted on/off ships, road and rail transport. Unfortunately, these locations are usually so busy that the tanks cannot be kept there for more than a few days, otherwise costs rise too high. There are usually a number of yards that will have the necessary hazardous goods permissions to allow storage, but most of these yards will not have the lifting equipment to take the isotank off a lorry or lorry trailer and place it on the ground or stack. Options are:

i. **Find one that can**

The most economical option. In the EU storage rates are typically 8$/day at such a location.

ii. **Leave the isotank on the trailer**

Only an option in countries that use the detachable trailer and tractor unit option. Many developing countries still only used fixed lorries. If this option is possible, it will be more costly, perhaps 20$/day upwards.
4. Quality Requirements

*It cannot be overstated* that the storage and handling of stockpile CFCs has to be conducted to rigorous GMP standards. We can police the manufacture, and reject any CFCs that we are unhappy with, but once they are stockpiled and the source decommissioned, *they are irreplaceable.*

It is also a sad fact that people in the chemical industry normally focus on making things, the delivery comes a poor second, and care in storage a very distant third (see Arkema example earlier).

Although we cannot hope to get the CFCs manufactured to GMP, we can use many of its principles to inform our position on their storage. In particular:

a. *Analysis*  
All analysis – CFC acceptance to stock, commissioning of tanks and isotanks, routine 6 monthly checks where carried out – must be done using fully validated sampling and analytical techniques operating to GMP. No shortcuts.

b. *Storage equipment*  
A new storage facility (ie one not previously used for this specific purpose) should be properly validated, with all the key steps of Design Qualification, Installation Qualification, Operational Qualification and Performance Qualification. A Validation Master Plan should exist.

A simpler but still rigorous validation protocol should exist for isotanks. Once in traffic, isotanks should be controlled with valve seals at all times, and any absence of sealing should return the isotank to a non validated status.

c. *Control and inspection*  
Such standards cannot be assumed unless checks and inspection by audit are carried out to determine compliance with the required standards. There are a number of specialist auditors, who could be hired to assist in such a programme. Ministry of Health inspection is a possibility as well, and may be a requirement of some of the MDI manufacturing countries.

However, it would not have medical propellant expertise and as such should be considered in addition to, rather than instead of, expert inspection. Such inspectors would have to be appointed by a UN body and would report to that body.