European Roadmap of Process Intensification

- Technology Report -

Technology: Supercritical Separations

Technology Code:

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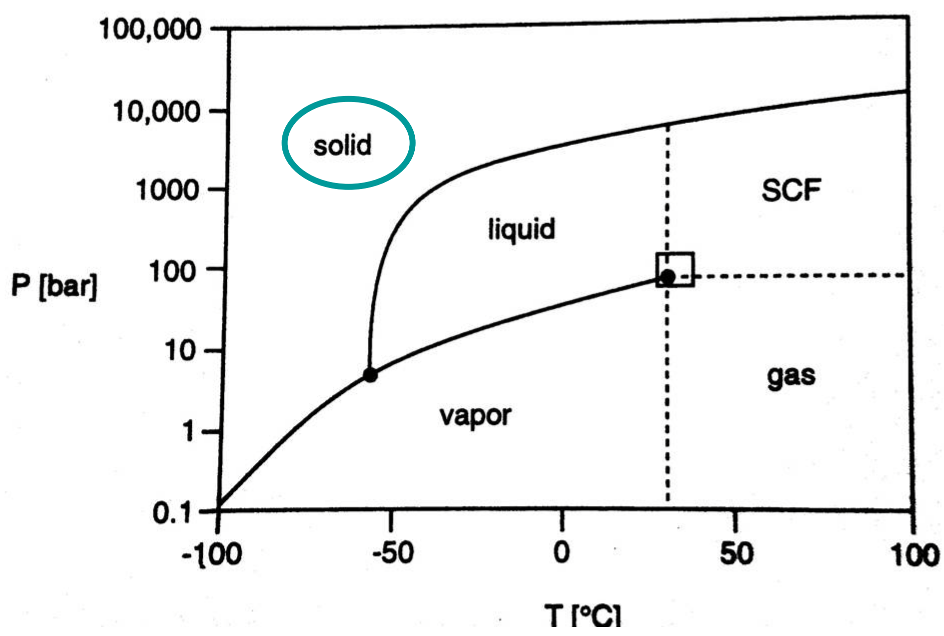
1. Technology

1.1 Description of technology / working principle

(Feel free to modify/extend the short technology description below)

Consider the phase diagram of carbon dioxide, by far the most promising solvent for supercritical processing. The principle, however, applies to many other compounds.

Phases of carbon dioxide (Jessop &Leitner)

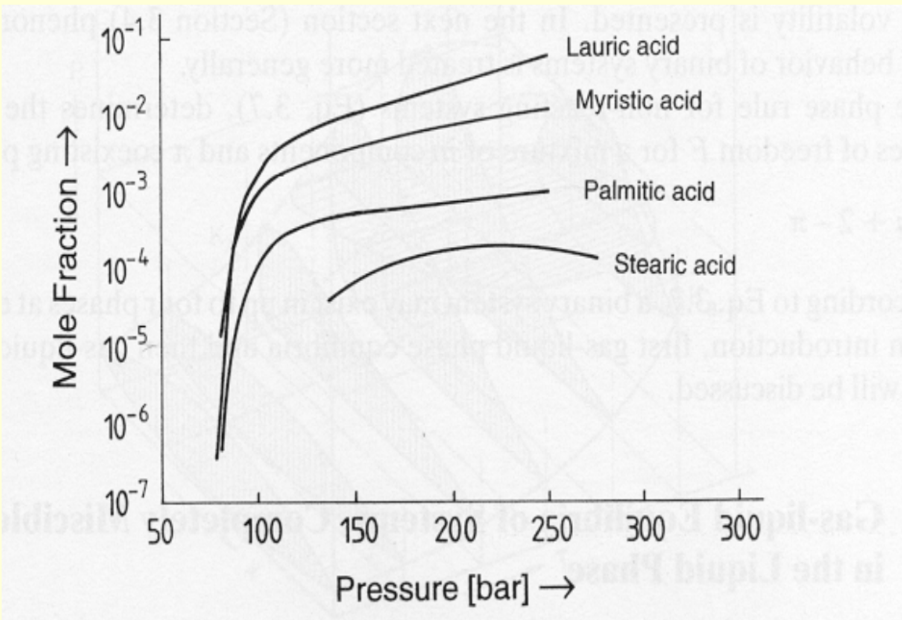


Low pressures generally give a gaseous or vapour phase, while at higher P values CO_2 is a solid. Following the boiling line, which separates the vapour and liquid phase regions, from the triple point at around -56 ^{o}C to higher temperatures, the vapour becomes more dense while the liquid gets slightly less dense. At the critical point (31 ^{o}C, 73 bar, with the square), vapour and liquid have become equal. Above this temperature and pressure, the CO_2 is a *supercritical fluid* (SCF). The occurance of the solid phases is further not taken into account in this report.
The above diagram is roughly similar to that of most compounds. For water the critical point lies at 378 ^{o}C, 220 bar, while for e.g. propane these are 97^{o}C and 43 bar.

Supercritical fluids on the one hand possess properties that are quite similar to those of a liquid such as their density, which makes them a solvent, but on the other hand they behave like a gas, or as a fluidum between a gas and a liquid, e.g. they exhibit low viscosities, low surface tensions, high diffusivities for solutes and high compressibilities especially around the critical point.

Inspecting the phase diagram already gives a clue for possible processes. One could, for instance, turn the liquid into a vapour without vapourizing or boiling, or vice versa turn the vapour into a liquid without condensing, by bypassing the boiling line on the right side through the supercritical zone.

The capabilities for separations is best illustrated by an example. The solubility of some fatty acids (and most compounds) changes over decades around the critical point, and they also vary per



SOLUBILITIES IN SUPERCRITICAL CO2 (Brunner)

compound.

This allows purification and an easy recovery of products once they have been dissolved in CO_2, simply by varying the pressure.
This also holds for other supercritical solvents. CO_2, however, is a very favourable solvent, because it is non-flammable, non-toxic, cheap even at very high purities, reasonably inert, odorless, tasteless. Its convenient critical conditions make it well suited for application to thermosensitive compounds such as pharmaceuticals. CO_2 is a good solvent for small, non polar molecules like itself, but larger molecules of up to a few hundred grams/mole can also be dissolved, especially when they contain fluor groups. Inorganic salts generally do not dissolve into CO_2.
Often co-solvents are added to modify the properties of CO_2, e.g. adding alcohol allows more polar compounds (even water) to be moderately soluble in the extractant.

Ideally, reactions, separations purification and product formulations are carried out in as little different process steps as possible. For pharmaceuticals not only the molecular composition, but also the crystal structure (polymorph) and particle size determine the functionality, in terms of e.g. a controlled drug delivery path and rate. SCF processing allows particles to be produced with according to existing requirements or with fully new properties, provided the crystallisation or precipitation behaviour is controlled.

Supercritical water is better suited for processes in which e.g. oxidation or other reactions at elevated temperatures need to be carried out, and for inorganic (salt type) separations. Supercritical steam turbines are not part of this report.

There is a wide variety of supercritical separation processes, discussed in section 1.2. Many of those also have a preparative/formulating functionality.

1.2 Types and "versions"

(Describe the most important forms/versions of technology under consideration, including their characteristic features, differences and similarities)

The (potential) types of processes with supercritical fluids vary widely in nature. Below a classification is made, but when combinations of them have been made, they are listed only once.

Extraction

The most widely applied supercritical process is extraction of valuable natural compounds mostly from solid materials by contacting those with a supercritical fluid (SCF), mostly carbon dioxide. Even though CO_2 is generally not a very powerful solvent, the ease of product recovery by either re-extraction or by partial pressure release, leaving no traces of solvent in the product, more than compensates for this.

For solids the process is typically carried out batchwise, while for extraction from liquids by SCF's a packed or an open column is used.

Caffein extraction from coffee or tea, hops extraction for beer preparation are the best known industrial examples of supercritical extraction.

Vice versa, the process can be used to impregnate solid products. The high mobility, low surface tension of CO_2 make it an excellent carrier for impregnates to enter pores of product.

Fast pressure relief: Rapid expansion

Processes exploiting the great effect of the pressure, or rather of the solvent density on the solubility of the solutes are among the oldest. An example is the separation of a polyethylene melt out of a supercritical ethylene-polyethylene mixture by flashing, relieving the pressure from above 1000 bars to a few hundred bars.

RESS (Rapid Expansion of Supercritical Solution) is a process where a solute is separated from the solvent by spraying the mixture over a nozzle to atmospheric conditions. Typically the solvent/solute mixture reaches the speed of sound, the solute nucleates and grows or demixes from the solvent extremely fast and is obtained as a fine solvent free powder.

The depressurization can also be carried out very slowly (SESS), resulting in a crystallisation or precipitation process in the case of a solid product. Not so many investigations exploit this possibility.

Antisolvent precipitation

When a supercritical fluid is dissolved in a solution consisting of a conventional organic solvent with a solute (e.g. a pharmaceutical), the solution expands. The resulting decrease in density reduces the solvent power of the solvent, and precipitation occurs. Related are the processes GAS (gas antisolvent) SAS (supercritical antisolvent), PCA (precipitation with a compressed antisolvent.

SEDS(solution enhanced dispersion by supercritical fluids).

SEDS combines dispersion, solvent extraction and particle formation in one process step.

Another type of process is one where a water soluble compound is sprayed together (as an emulsion, since water does not dissolve very well in CO_2, about 1 gram/L) with CO_2 in a concentric nozzle into a vessel containing a huge excess of still supercritical CO_2. As a result an aqueous dispersion is formed, from which gradually the water is extracted into the CO_2 (which might contain a modifier such as alcohol to increase the water solubility), causing the solute from the water to precipitate out in a controlled way. With this technology the shear stress is less, which makes it more suitable than RESS for shear sensitive products, like certain proteins and DNA.

Supercritical chromatography and adsorption

Well known from analytical chemistry, chromatography can be carried out classically (batchwise, in a cocurrent column), or quasi continuously (simulated bed fluid chromatography), and there are developments in centrifugal partition chromatography.

Processes where CO2 dissolves into a compound

When CO2 dissolves into a compound, it can plasticize it (polymers), or lower its melting point (fats, oils), and/or lower the viscosity dramatically so that it can be handled better. Examples are the winning of oils from seeds with higher yield, the melting of fats so they can be sprayed better to produce the right particles, or the removal of monomers from polymers (enhanced extraction). The Unicarbide process is based on using the CO_2 as an atomisation vector as well as as a viscosity reducer, to spray powders to form coatings. The particle producing processes exploiting this principle are called PGSS (Particles from Gas Saturated Solutions), and have wider applications in food, cosmetic, industry.

Double retrograde condensation

Combining with ionic liquids:miscibility windows

The solubility of CO_2 in ionic liquids is surprisingly high (typically about 70 mole% at 200 bar). It was found that in general by means of changing the CO_2 pressure over a short range only, the system could be reversibly switched from a homogeneous system to one with a phase split into an ionic liquid rich and an ionic liquid free phase (with CO_2 and product). A variation in CO_2 mole fraction by only a few percent already effectuates this. This opens up the possibility to carry out a reaction, e.g a hydrogenation or hydroformylation in a homogeneous phase, and to separate the product by a slight change in CO_2 mole fraction. The product can be won from the CO_2 by e.g. RESS. Another technology is to precipitate the product out of the ionic liquid by using the CO_2 as an antisolvent.

CO_2 as a volatile acid

Pressurised carbon dioxide is able to acidify reversibly aqueous solutions. In this way it can replace mineral acids (e.g. sulfuric acids). Since the minimum pH is limited also locally by the CO_2 pressure, there are no issues with locally very low pH values anymore which there are in case of mixing strong acids with aqueous solutions. Using CO_2 also implies that the products (e.g. isoelectrically precipitated proteins) are solvent free.

Separation of CO_2 by mineralization

By contacting carbon dioxide in an aqueous slurry with minerals such as $CaSiO_3$, stable $CaCO_3$ is formed plus SiO_2, a valuable product, withdrawing CO_2 from our atmosphere.

Pressurised CO_2 to from gas hydrates

Although the temperatures for CO_2 hydrates lie below 9 ^oC so this is not a strictly supercritical technology, it is worth mentioning that for CO_2 sequestering and for eutectic freeze crystallization hydrate formation is very strongly related to energy saving and CO_2 emission reduction.

1.3 Potency for Process Intensification: possible benefits

(In Table 1 describe the most important documented and expected benefits offered by the technology under consideration, focusing primarily on energy; CO_2 emission and costs, providing quantitative data, wherever possible. Add other benefits, if needed).

Table 1: Documented and expected benefits resulting from technology application when using carbon dioxide (unless stated otherwise)

Benefit	Magnitude	Remarks
No emission of organic solvents	VOC emission would be reduced by 2 MTon/y (order of magnitude). Represents 10^{18} J/y in saved processing energy.	My estimate is a current 20 Mton VOC/y emission. Assume we can replace 10% of the organics by CO_2
Textile dyeing:no water necessary, efficient dyestuff use, energy saving	Saves 10 billion m3/year clean water prevents same amount of polluted water emitted, prevents 100.000 tons/y of dyestuff related chemicals emission, cheaper dyeing	Applies to 40Mton textile/y
RESS,PCA etc.		
Miscibility windows with ionic liquids: more efficient, selective reacrtions and seprations.	Included in the above mentioned VOC emission reduction	Reactions and separations in one vessel
Polymer foaming: no VOC emission	30.000 ton pentane emission/year	
CO_2 as acidifier: No sulfuric acid use in dairy, in soy industry. No waste stream No sulfuric acid in protein product, higher added value product. No neutralization necessary afterwards.	Netherlands: 6 billion kg dairy waste/year by one company alone.	
Reacting CO_2 with minerals	Capture of 85% of large sources of CO2 emission, power plants	Extra energy use for CO2 capturing ; about 15%.
CO_2 capture by gas hydrates	Capture of a significant fraction of large sources of CO2 emission	
No exposure of workers to VOC's.		
Energy saving when used to produce gas hydrates for salt crystallization/desalination	30% compared to eutectic freezing, 70-90% compared to evaporative crystallisation	Compare with concentional eutectic freeze crystallisation
Combine separation and formulation in one step	Reduce the current amount of waste (100 kg/kg product), and the related processing costs.	

1.4 Stage of development

Extraction/impregnation is well developed
Extraction of valuable compounds from natural solid materials is being applied on industrial scale (hundreds of installations).
Industrial dry cleaning with pressurized CO_2 has been commercialized.
Supercritical textile dyeing is entering full scale demonstration, commercialisation will soon follow.

RESS/GAS/SEDS etc are on the verge of entering the market but are not well understood
Preparations of pharmaceutical products is in begin of commercialisation phase first products are commercial). However, these are complex systems which are poorly understood, even though RESS is very old already. Scientific investigations continue with great intensity.

Processes where CO_2 is dissolved into a compound
A hard statement cannot be made, but scientifically this seems further on the road than RESS etc. The number and scales of industrial realizations is clearly greater.

Double retrograde condensation
This is mainly a scientific topic at this stage. This is due to the fact that the thermodynamic operating range is very narrow, yet the number of potential applications is probably great because of the generality of the technique.

Combining with ionic liquids:miscibility windows
Ionic liquids as process solvents are quite new, yet there are industrial implementations. The combination with CO_2 is even newer, and the status is that the prove of concept is there. For an L-dopa precursor the possibility of separating has been demonstrated at 1L scale.

CO_2 as a volatile acid
The advantages of very good pH control have been proven, separation of proteins is well possible. Pilot scale, patents.

Separation of CO_2 by mineralization
Principle proven at 1 L scale, and technical and costs evaluations have been made. The very large scale CO2 capture in aquifers also involves carbonation.

Pressurised CO_2 to form gas hydrates.
Shown to be possible. Eutectic freezing at 1 L scale demonstrated. Whether large scale demo's have been performed on pure CO2 hydrates was not investigated.

2. Applications

2.1 Existing technology (currently used)

(Describe technology (-ies) that are conventionally used to perform the same or similar operations as the PI-technology under consideration)

Extraction of natural materials is mainly done with hexane
Purifying or separating pharmaceuticals currently takes place using organic solvents as a result of which often 100 kg waste/kg product is generated. For formulations spray drying and milling is being used.

Foaming of polymers is mainly done with pentane, though certain applications (isolations plates for construction) already use CO2.
Textile dyeing is currently performed with water, which not only leads to dyestuff losses, but also requires large amounts of energy due to the necessary treatments and drying steps.
For acidifying protein solutions mineral acids such as sulfuric acid are being used.
The resulting high separation efficiency is not available commercially, only as an analytical technique.
Dissolving CO_2 in a compound : CO_2 is already being used for paint spraying, but for micronising normally melt crystallisation, granulation and prilling are the common techniques.
Drying of food is done e.g. by freeze drying, air drying.

2.2 Known commercial applications

(Is the technology broadly applied on commercial scale? In which process industry sectors is the technology most often applied: large volume chemicals – specialty chemicals & pharma – consumer products – ingredients based on agro feedstocks? What is the estimated number of existing applications? In Table 2 provide the most prominent examples of realized applications and provide their short characteristics)

Table 2. Industrial-scale applications of the Technology (existing and under realization). All processes use carbon dioxide, unless stated otherwise.

Sector	**Company - Process/Product name/type**	**Short characteristic of application**	**Production capacity/ Plant size**	**Year of application**	**Reported effects**
Large Volume Chemicals	Various Plastics producers Polyethylene	Polymerisation in scEthylene, followed by separation	multi Mtons/y	’50 s	
Food/	Caffein extraction	From coffee beans alkso tea	Germany, us Canada france italy	’80 s	
Agro Feedstocks	In India. Spices, aromas separated on site.				
Large volume chemicals	Rose	Deasphalting of lubrication oil with near critical propane			
Food	Solexol	Sep purify vegetal and fish oil . kellog 1946. propane.			
Tobacco denicotisation	p.259				
Specialties	Fluoropolymers, DuPont		40 M€	2000	
Chin, south korea	Phytopharmaceuticals				
Food	Hops resins extraction	For beer	germany		
Food	Choleresterol	For butter etc			
	Colorants, diet lipids				

Food/pharma	Active compounds	Also toll rorcessing			
Parts cleaning	Cf techn (hyde park MA), enviro pro		p.115		
Painting	Union carbide	Spray			
Soil recovery	Gaiker pilot				
Misc.	100 plants [perrut]				
Extraction	Solid natural materials for food and phytopharmaceuticals/nutraceuticals	P 171			
Fractionation	Aromas from fermented and distilled beverages, polyunsaturated fatty acids, active compound from fermentation broth, specialty pharmaceuticals				
	Yara	Developed by universities en Raps (Kulmbach), Natex Prozesstechnologie Ternitz	CO2 psoiene (CPF, SEDS)		
Food		Enantiomer and fatty ester (DHA, EPA) separations from fish oil			
Misc.	Swan	1000 ton/y Multipurpose reactor/separator for supercritical applications			
Consumer	Hangers, Fred Butler	Textile dry cleaning		Since 200 mainly	
Pharma	Echo Pharmaceuticals	Granulate of THC-9 (cannabonoid) medical tablets		2007	
Food	Feyecon	Extraction of trichloroanisol from cork (for wines)		2007	In addition, fungi are killed
Medical	Feyecon	Biopt treatment, separation of water and fat from tissue samples		2007	Higher quality samples for pathology, faster results during surgery available
Specialty	Separex	Purification of oils for harddisks			

2.3 Known demonstration projects

(Are there any demonstration projects known related to the technology under consideration? In which process industry sectors are those projects carried out: large volume chemicals – specialty chemicals & pharma – consumer products – ingredients based on agro feedstocks? In Table 3 provide the short characteristics of those projects.)

Table 3. Demonstration projects related to the technology (existing and under realization). Note: since for certain applications the production scale is small (pharma), bench scale, pilot and industrial scale are not more than one or two order of magnitude different. Some of the demonstrations are therefore also found under commercial applications

Sector	**Who is carrying out the project**	**Short characteristic of application investigated, including product name/type**	**Aimed year of applicati on**	**Reported effects**
Specialty/p harma	Peter York Bradford Particle design (now part of Nektar)			•
Specialties	Feyecon	Supercritical Textile Dyeing	2008	
Specialty/p harma	Feyecon/Leiden/ Delft university	Centrifugal partition chromatography, cannabinoid seprations	2010	
Specialty	Kemira	Melamin synthesis in $scNH_3$		

2.4 Potential applications discussed in literature

(Provide a short review, including, wherever possible, the types/examples of products that can be manufactured with this technology)

Most potential applications have also inevitably been discussed above. Therefore the application fields are listed only.

Natural products (perfumes, spices, oils, aromas).
Pharmaceuticals, formulations of drugs with better delivery properties.
Neutraceuticals (remove cholesterol).
Polymers: synthesis, separation, impregnation, monomer removal.
Synthesis and separations of intermediate products for the pharmaceutical industry.
Textile dry cleaning, textile dyeing.
Protein separation (food, pharma) and formulation.
Protein drying. Drying of food.
Parts cleaning.
Silicon wafers.
Medical implants.

3. What are the development and application issues?

3.1 Technology development issues

(In Table 4 list and characterize the essential development issues, both technical and non-technical, of the technology under consideration. Pay also attention to "boundary" issues, such as instrumentation and control equipment, models, etc.) Also, provide your opinion on how and by whom these issues should be addressed)

Table 4. Technology development issues

Issue	Description	How and by whom should be addressed?
High pressure use	Bearings, sealings, input/output, solids handling	
Low dielectric constant (polarity)	CO_2 is a hydrofobic solvent, reagents and auxiliary chemicals need to be redesigned	

3.2 Challenges in developing processes based on the technology

(In Table 5 list and characterize the essential challenges, both technical and non-technical, in developing commercial processes based on the technology under consideration. Also, provide your opinion on how and by whom these challenges should be addressed)

Table 5. Challenges in developing processes based on the technology

Challenge	Description	How and by whom should the challenge be addressed?
Low cost pressure equipment	Efficient pressure equipment design, including design and production technology, e.g. carbon fibre reinforced thin walled steel, or plastics instead of thick steel.	High tech companies such as Feyecon, Separex
(near) isobaric solvent recycling	Efficient process design	User, engineering bureaus
Overcome prejudices against pressurized processes	Education, demonstrations	Universities, high tech companies, users
Logistic adaptations	When changing one part of a process, e.g. recovering drill liquor by CO2 instead of throwing the material (metal shavings plus liquor)	

4. Where can information be found?

4.1 Key publications

(Provide the list of key publications in Table 6)

Table 6. Key publications on the technology

Publication	Publication type (research paper/review/book/ report)	Remarks
“State of the ART Book on Supercritical Fluids”,		

AINIA, ISBN 84-87345-68-9		
"Supercritical Fluids", Y. Arai et al.	Book	
http://en.wikipedia.org/wiki/Supercritical_carbon_dioxide		
"Gas Extraction", G. Brunner	Book	
"Chemical Synthesis Using Supercritical Fluids", P.G. Jessop & . Leitner,	Book	
"Natural Extracts Using Supercritical Carbon Dioxide", M. Mukhopadhyay	Book	
"The Use of Supercritical Fluid Extraction Technology in Food Processing", R.S. Mohamed, G.Ali Mansoori	Food Tech. Mag. June 2002	Contains illustrations of here discussed technologies
"Particle generation with supercritical CO2", E. Lack et al.		
Clifford		
Eindhoven boek		
Proefschift wubbolts		
Proefschift berends		
Proefschift yohana		
Proefschift vdKraan		
Fernandez Cid		
Roosmalen		
Bouchard		
Jovanovitch		

4.2 Relevant patents and patent holders

(Provide the list of relevant patents in Table 7. Under "remarks" provide, where applicable, the names/types of products targeted by the given patent.)

Table 7. Relevant patents

Patent	Patent holder	Remarks, including names/types of products targeted by the patent
York		
Woerlee textielverven website		
Perrut		
DuPont		Alcohol free wine
Ionic liquid patent		

4.3 Institutes/companies working on the technology

(Provide the list of most important research centers and companies in Table 8)

Table 8. Institutes and companies working on the technology

Institute/Company	Country	Remarks
Aachen RWTD	Germany	Prof. Leitner, prof. Liao
Nektar	UK	P. York
Univ. Nottingham	UK	Prof. Poliakoff
Univ. North Carolina		DeSimeone
Separex	France	
Feyecon	Netherlands	
Textilforschung Inst.	Germany	Dr. Bach
Univ. Harburg Hamburg	Germany	Prof. Brunner, prof. Eggers
	USA	Beckman
Eindhoven University	Netherlands	polymers
Salerno, reverchon		
Delft University	Netherlands	Prof. Peters, prof. Witkamp

5. Stakeholders

5.1 Suppliers and developers

(Provide the list of key suppliers/developers in Table 9)

Table 9. Supplier and developers.. to be completed

Institute/Company	Country	Remarks
UHDE	Germany	
Separex	France	Over 60 pilot /fullscale plants sold
Feyecon	Netherlands	www.feyecon.com
Supercriticalfluids.com	USA	
AIDA	Spain	
Echo Pharmaceuticals	Netherlands	

5.2 End users

(Describe the existing and potential end-users, other than those already listed in Table 2)

A very wide range of producers of pharmaceuticals, fine chemicals, bulk chemicals, polymers, perfumes/fragrances, essential oils, of waste treatment companies.

6. Expert's brief final judgment on the technology

(maximum 5 sentences)

Given large scale proven applications at added value of less than 100€/ton (for polyethylene), there is no question that CO_2 based supercritical separations can be carried out finally at prices below 1 euro/kg. This is a matter of technology development but also of softer (social) factors (innovation cycle). Already, particularly in extraction from natural materials, SCF processes are widely accepted, and next will probably be textile dyeing and pharmaceuticals preparation.