THE IRISH SCIENCE AND TECHNOLOGY AGENCY.

CONFIDENTIAL REPORT

ENVIRONMENTAL IMPACT STATEMENT -
PROPOSED FACILITY FOR PELLETISING, TABLETING AND CAPSULE PRODUCTION.

FOR

FOREST (IRELAND, LTD.

MARCH, 1993.

GROUP ..... TECHNICAL AND CONSULTANCY

DEPT. ..... ENVIRONMENTAL SERVICES.

Sheet no. 1 of 63 sheets

EOLAS
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Gníomhaireacht Eolaíochta agus Teicneolaíochta Éireann

CONFIDENTIAL REPORT

Client

Forest (Ireland, Ltd.,
Clonshaugh Industrial Estate,
Dublin.

Title

Environmental Impact Statement -
Proposed Facility for Pelletising,
Tableting and Capsule Production.

Report ref. :

Order no. :

File no. :
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Report by. :
John Kilgallon.

Date recd. :

Approved by. :
Richard Foley, Ph.D.

Copies to :

Date :
12th March, 1993.

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Client: Forest (Ireland) Ltd.,
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Proposed Facility for Pelletising,
Tableting and Capsule Production.

Report By: J. Kilgallon.
M. Reilly.

March, 1993.

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1 INTRODUCTION

Forest Laboratories proposes to establish a facility at Clonshaugh Industrial Estate, Dublin for the production of pharmaceutical products in the form of granules, tablets and capsules.

The operation will be located in an existing building which will be modified internally to the requirements of the project.

Operations essentially involve the weighing, mixing, granulation, tableting and packing of bought-in raw materials. The operation is physical/mechanical and involves no chemical synthesis.

Following an initial briefing meeting, the local authority, Dublin Corporation, indicated to the company that an Environmental Impact Statement (E.I.S) would be required in support of the planning application.

Accordingly, Forest retained EOLAS to prepare this E.I.S., the scope and format of which are in accordance with S.I. 349 of 1989 and S.I. 25 of 1990 (which give effect to EC Directive 85/337/EEC).

2 NON-TECHNICAL SUMMARY

Forest Laboratories is a U.S. company which develops, manufactures and sells a range of pharmaceutical products. Forest has a subsidiary, Tosara Group, which currently employs 35 at its existing facility at Baldoyle Industrial Estate in the manufacture of Sudocrem®. Forest will develop the proposed Clonshaugh project in association with Tosara. The facility will produce three products at Clonshaugh - a vasodilator for angina treatment , an anti-viral product and an anti-colinesterase (Alzeimers medication). The first will be produced in granular and tablet form while the other two will be tablet products. Initially 30 will be employed. It is envisaged that, subject to satisfactory progress of the project, employment could increase to an ultimate 110. However, this is very much a long term projection.

The manufacturing process involves receiving the raw materials in drums for storage in the factory warehouse or secure storage area until required for production. When required, the materials are weighed and formulated. Subsequent operations include coating, granulating, blending, tableting, and packing - after Quality Assurance testing.

Process wastewaters will arise from the cleaning of plant equipment and vessels, hand wash basins, sinks and showers and laboratory effluent. These wastewaters will be combined and discharged to a holding tank for discharge to sewer. The effluent pH will be corrected in the laboratory prior to discharge to this tank. Total process effluent volume will be less than 20 m^3/d and its characteristics will be similar to domestic sewage. It will not contain substances likely to be hazardous within the sewer or to the water environment.

Domestic sewage arising from the 30 employees will discharge to sewer separately from the process effluent discharge.

Emissions to atmosphere from the proposed facility will be well controlled by means of bag filters and HEPA (High Efficiency Particulate Air) filters. The dust removal efficiency of these devices is well in excess of 99.9%. As such there will be no impact from dust emissions on the environment.

The most significant emissions will be of isopropyl alcohol and ethyl alcohol, neither of which are toxic at the maximum possible concentrations which could be emitted from the facility. There will be three boilers in the plant fired on natural gas and these will be fitted with flues of adequate height to ensure dispersion of the combustion gases.

Noise will be generated by production equipment, process services plant and heating and ventilation plant. The design of the building is such that noise sources within the building envelope will not be radiated externally to a significant degree.

Noise emission levels from plant venting to atmosphere will be controlled by the use of quiet plant, silencers, attenuators and acoustic screening. The proposed equipment and building layout is such that the plant will be designed and built to meet appropriate criteria at local residences.

The facility has no potential to significantly impact the existing status of roads and traffic or other aspects of the environment.

3 COMPANY DETAILS

3.1. Company Background

Forest Laboratories, Inc. Forest Laboratories, Inc. ("Forest") is incorporated in the USA and is publicly traded on the American Stock Exchange. Forest develops, manufactures and sells both branded and generic forms of ethical drug products, which require a physician's prescription, as well as non-prescription pharmaceutical products sold over the counter, which are used for the treatment of a wide range of illnesses. Forest products are marketed principally in the USA, western and eastern Europe, and in Puerto Rico and other Caribbean Islands. Marketing is conducted by Forest and through independent distributors and under exclusive marketing contracts with major pharmaceutical companies. In the US, Forest's ethical specialty products are marketed directly by the Company's 440 person salesforce. In the US and Puerto Rico the Company employs approximately 950 people. Forest maintains manufacturing facilities in Inwood, New York, St. Louis, Missouri, Cincinnati, Ohio and San Juan, Puerto Rico in the USA.

In the United Kingdom, Ireland and certain export markets, Forest products are marketed directly by the Company's subsidiaries, Pharmax Limited and the Tosara Group. Forest currently employs approximately 190 and 35 people at Pharmax in the UK and Tosara Group in Ireland, respectively. Pharmax has manufacturing facilities in Bexley, UK.

Tosara Group. The Tosara Group of companies ("Tosara") was acquired by Forest in 1987. With this acquisition Forest obtained a state-of-the-art manufacturing facility with an experienced and skilled management team and workforce. Tosara's product Sudocrem® is the brand leader in the nappy rash market in the UK and is also proving to be equally successful in the incontinence rash and bedsore markets. Sudocrem is marketed by Tosara group of companies in Ireland and Northern Ireland and by Pharmax Healthcare Limited in Great Britain. The Clonshaugh, Dublin, project which is the subject of this report is being developed by Forest in association with Tosara.

3.2. General Proposal and Site Selection Factors

The proposed facility will initially employ about 30 in the production of granules, tablets and capsules. Employment is expected to increase to about 60 and may ultimately reach 110.

In selecting a location for the project, Forest was anxious to establish the facility in the Dublin area. This would facilitate Tosara - which is located at Baldoyle Industrial Estate - in participating in the development of the project. Clonshaugh was chosen because a suitable building became available through the assistance of the IDA. It is also convenient to Dublin Airport, through which some materials may be shipped.

Fig. 3.1. shows the location of the Clonshaugh Industrial Estate in relation to the adjacent road system. The position of the proposed Forest facility within the industrial estate is shown on Fig. 3.2. Fig. 3.3 is a plan of the existing building including the modifications which Forest propose.

3.3. Products

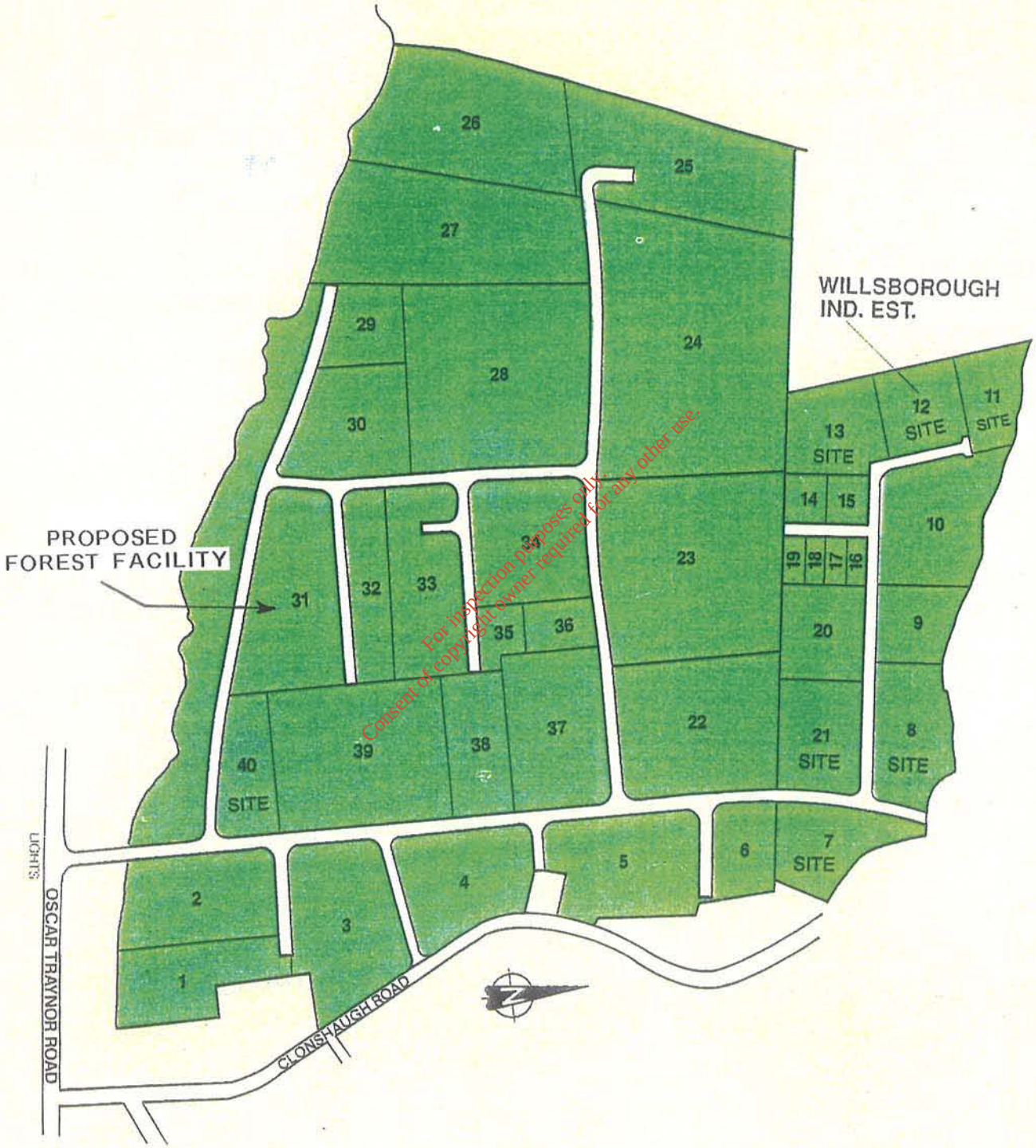
The products to be manufactured at the Clonshaugh facility are:

Product	Active Ingredient	Use
Sustac Granules (Bulk) Sustac Tablets Sustac Capsules	Nitroglycerin	Vasodilator (e.g. angina treatment)
Flumadine Tablets	Rimantadine hydrochloride	Anti-viral (influenza A)
Synapton Tablets	Eserine salicylate	Anti-colinesterase (e.g. Alzeimers medication)

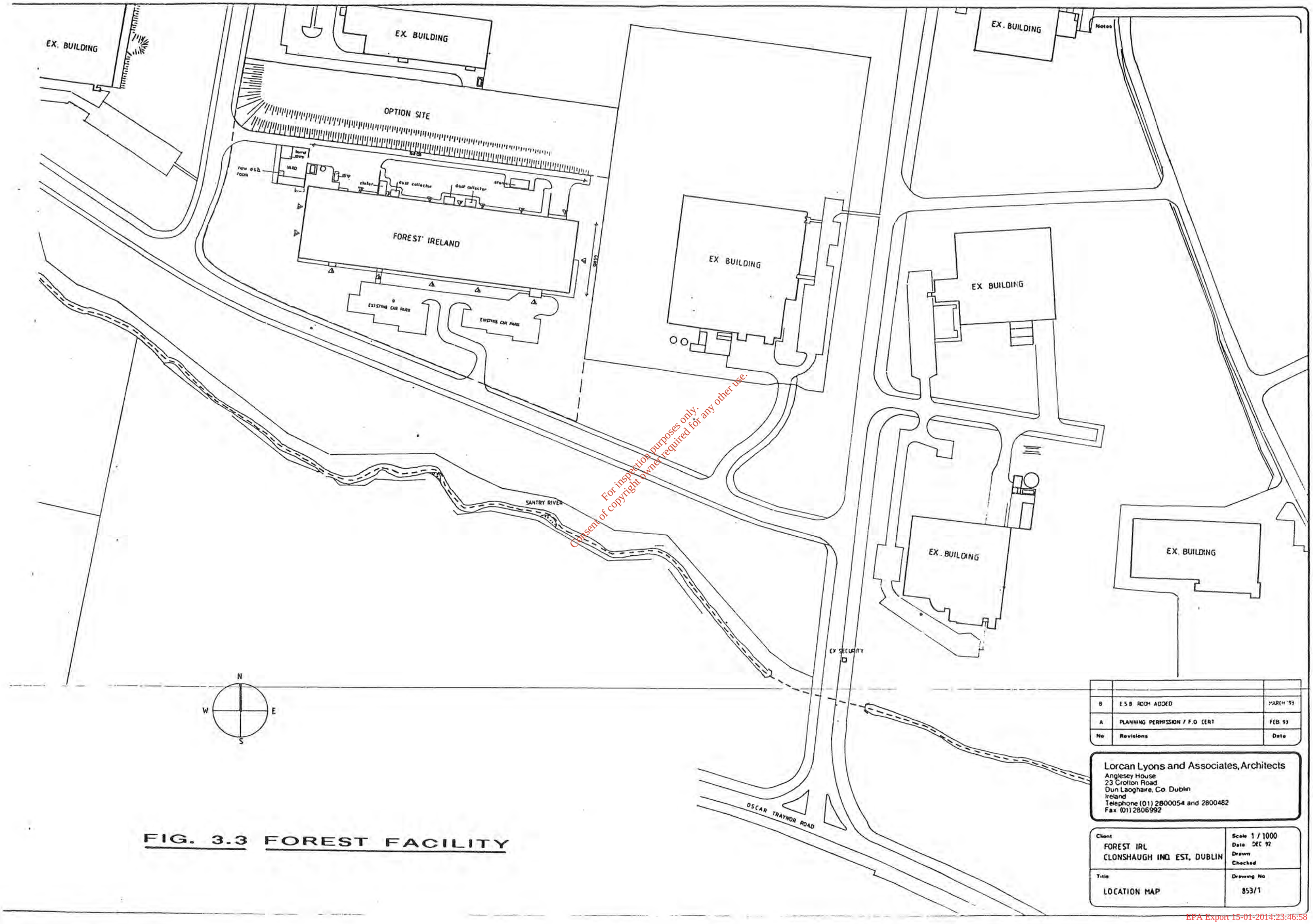
The warehouse will also be used for the storage and distribution of the Tosara Sudocrem® product which is manufactured at the Tosara factory at Baldoyle Industrial Estate.

FIG. 3.1 LOCATION OF CLONSHAUGH INDUSTRIAL ESTATE

FIG. 3.2 LOCATION OF FOREST FACILITY (SITE 31)



LORCAN LYONS, Architects.



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Client: FOREST IRL, CLONSHAUGH IND. EST., DUBLIN	Scale 1 / 1000 Date DEC 92 Drawn Checked
Title: LOCATION MAP	Drawing No. 853/1

FIG. 3.3 FOREST FACILITY

4 THE PROPOSED FACILITY

4.1. Plant Layout

The basic factory layout is shown on Fig. 5.1. (Section 5.1. below). Fig. 5.1. indicates process emissions (to atmosphere and to sewer), and materials storage areas. Drawing No. 853 - 2 (Lorcan Lyons and Associates) shows these and the production areas in more detail and is supplied separately from this report as part of the planning submission.

4.2. Manufacturing Technology

The following is an outline of the manufacturing process for each product. All operations are conducted in strict compliance with Good Manufacturing Practice (GMP).

Fig. 4.1. is a process flow schematic. Sources of wastes/atmospheric emissions are included. These are further discussed in chapters 5 and 6. Section 4.3.3. below discusses materials handling procedures.

4.2.1. Sustac Granules

- The raw materials (active ingredients, excipients and base seeds) are removed from warehouse storage and weighed to a predefined formulation.

- The base seeds (small starch/sugar particles) are placed into a series of eight coating pans. In a coating pan the active ingredients are applied to the base seed. Ethyl and isopropyl alcohols are used as a carrying agent for these ingredients.

- Again on the coating pans, a further coating of a special formulated solution is applied. This controls the timed release of the active ingredient when the product is consumed. Each of the eight coating pans makes a product of different timed release rate.

- The various timed release seeds are then further blended in large coating pans to create a mixture which has the required controlled release pattern.

- The blended timed release active seeds are then packaged in bulk containers for shipment off-site. Alternatively, they are further processed into tablets or capsules.

- Tablets are manufactured by weighing the blended timed active seeds, excipients and lubricants to a predefined formula and blending these together. This blend is then compressed using a tablet compression machine. During tableting, the tablets are searched for foreign materials and dedusted automatically by associated equipment.

- Capsules are produced by introducing blended timed active seeds into an encapsulation machine which produces a set weight of seeds inside a gelatin capsule. This capsule is then checked for proper weight, absence of foreign particles and appearance.

- Packaging is similar for tablets and capsules. The product is placed into bottles, dunnage inserted and the bottle is capped, labelled and packed.

- At all key stages of the above operations there is rigorous quality control and laboratory analysis of materials to the requirements of the Company Quality Assurance Department.

4.2.2. Flumadine

- Raw materials and excipients are weighed to conform to a predefined formulation.

- The raw active ingredient is micronized (finely ground).

- The raw materials are granulated in a high shear mixer/granulator where water is added to assist granulation. The wetted material is passed to a fluid bed drier for drying. It is then milled and blended. Samples are analysed in the laboratory to ensure that they conform to specifications.

- The blended material is then compressed into tablets using essentially the same procedure discussed for nitroglycerin granules above.

- The Flumadine tablets are then coated with a film of pharmaceutical glaze in an automatic coating machine for improved appearance. The machine sprays the glaze onto the tablet and then dries the tablet.

- The coated Flumadine tablets are then passed through an automatic weighing machine and manually (visually) inspected for appearance. Samples are taken and laboratory assayed. Quality Assurance releases the tablets for packaging upon approval.

- The finished tablets are packaged into bottles by the same process discussed in 4.2.1. above.

4.2.3. Synapton

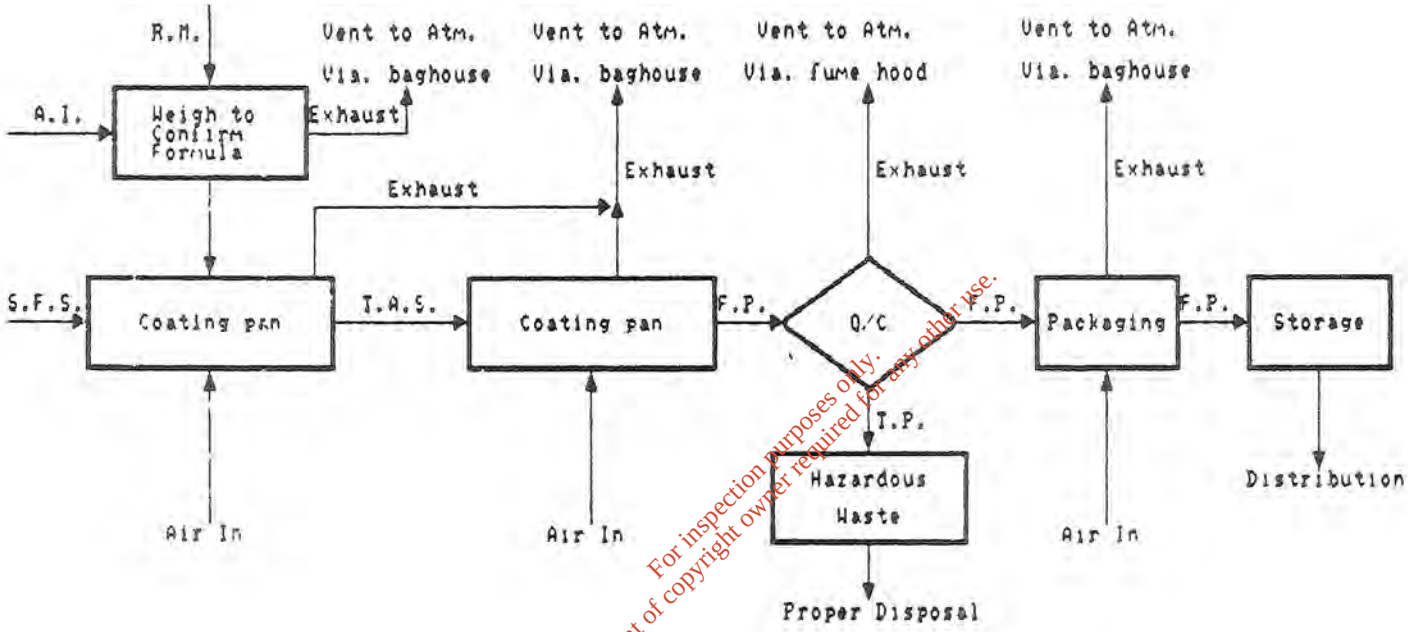
- Raw materials and excipients are weighed to conform to a predefined formulation.

- Raw materials are milled prior to manufacturing.

- A pre-blend is placed in an oscillator for additional blending.

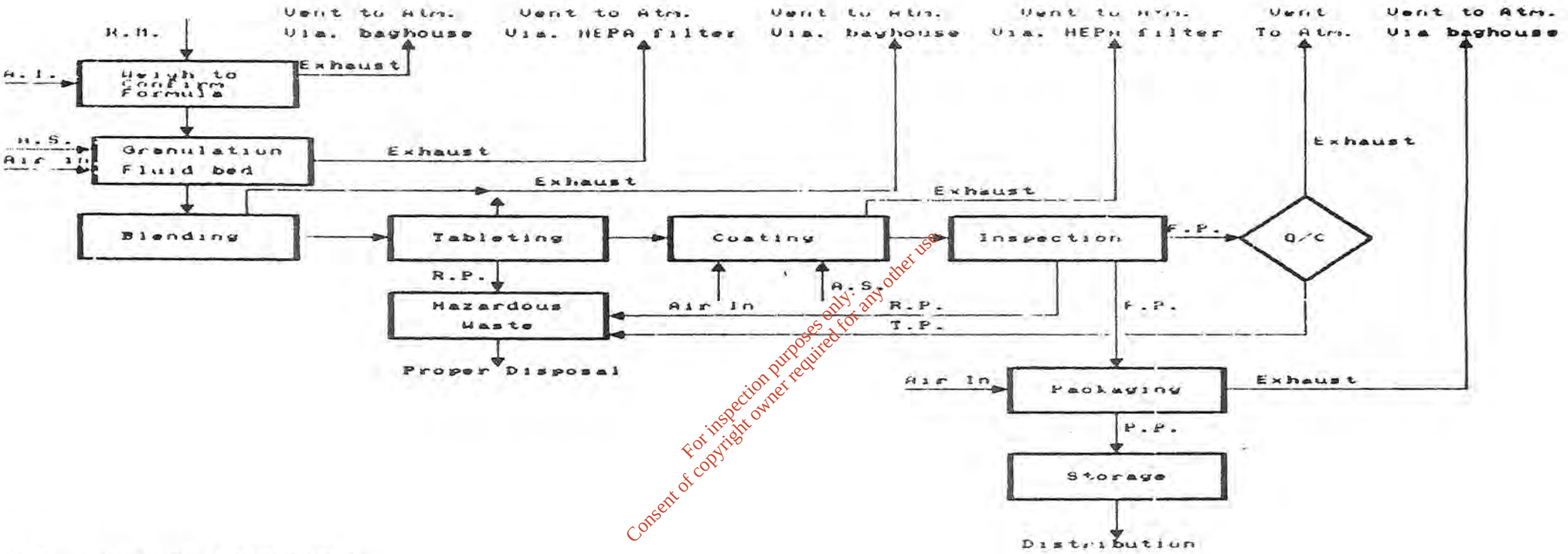
- The pre-blend and excipients are blended using a large "V" shaped dry blender. Samples are taken for laboratory analysis and Quality Assurance.

- Tablets are produced using the same procedures outlined in 4.2.1. above.



A.I. : Active Ingredient
F.P. : Finished Products
R.M. : Raw Material
S.F.S. : Special Formulated Solution
T.A.S. : Timed Active Seeds
T.P. : Tested Products

FIG. 4.1 (a) COATING



A.I. : Active Ingredient
A.S. : Aqueous Solution
F.P. : Finished
P.P. : Packaged Products
R.P. : Rejected Products
T.P. : Tested Products

FIG. 4.1 (b) TABLETING

4.3. Raw Materials - Usage, Transport and Storage

4.3.1. Raw Materials Usage

Table 4.1. lists the raw materials to be used, together with expected usage rates and inventories and the type, number and size of shipping containers. The proposed disposal mechanism for containers is also indicated. Where relevant details of the physical state, toxicity (LD_{50}) and TLV are also given.

These raw materials will make the following product quantities:

Sustac granules	...	45,000 kg/yr
Flumadine tablets	...	30 million/yr (5700 kg/yr)
Synapton tablets	...	100 million/yr (18,800 kg/yr)

As mentioned in 4.2.1. above, some or all of the Sustac product may be produced as tablets or capsules.

4.3.2. Transport and Storage

All raw materials (and products) will be moved to and from the site by road and stored in their shipping containers.

The production building will have an integral warehouse (refer Fig. 5.1.) which will receive all raw materials except the alcohols (cetyl, ethyl and isopropyl). Storage of raw materials in the warehouse will be in drums (fibreboard or polythene with double polythene liners, or steel with inner protection layer).

Storage of ethyl alcohol, cetyl alcohol, and IPA will be in a separate safety storage building, in steel or polythene drums. The storage area will be contained to prevent escape of accidental spillages.

Fuel oil, if used, will be stored in the existing above-ground, steel 5000 gallon storage tank, which is within a containment area.

The following specific arrangements will be made for the storage and security of certain materials.

A. Hazardous Material Store.

This store will hold about 2 m3 of hazardous or toxic and dangerous materials at one time based upon laboratory and production potential for waste creation. This building will have the following specifications:

- Grid work flooring to allow for material to flow to containment sump below.
- Containment of 110% of capacity of the largest container stored.
- Fire proof construction.
- Locking doors (fire proof).
- Blow - out panels (appropriately sized).
- Vented for air flow.
- Appropriate warning signs.
- Fire suppression system (abc extinguisher or Halon.)

B. Fire Proof Store for Alcohol, Pharmaceutical Glaze etc. (Flammables)

This store will hold about 15 m3 of various flammables with appropriate sectioning off to allow for quarantined (untested) versus released (tested and approved) raw materials storage. This store will be built to the same standards as the hazardous material store (A above). Both stores will conform to all applicable Dept. of Justice and/or Fire Officer regulations.

TABLE 4.1 RAW MATERIALS DETAILS

RAW MATERIAL	USAGE (kg/yr)	INVENTORY (kg)	FORM	DETAILS OF CONTAINERS			LD50 (mg/kg)*	TLV - TWA (mg/m3)
				**Type (Size)	Number in Inventory	Disposal ***see footnote		
Active Ingredients:								
Eserine salicylate	1500	1000	Powder	Drum (100 litre)	10	A	2.5 (orl mus)	
Rimantadine hydrochloride	2000	1000	Powder	Drum (100 litre)	10	A	640	
SDM 17**** (nitroglycerin 10% ; lactose 90%)	6000	1500	Powder	Drum (100 litre)	15	A	105 (nitroglycerin)	0.5 (skn; nitroglycerin)
							>10000 (lactose)	10 (assumed; lactose)
Excipients, Solvents etc.:								
Avicel cellulose	1200	600	Powder	Drum (100 litre)	6	B	>5000	10
Cetyl alcohol	400	400	Liquid	Drum (200 litre)	2	C	5000	
Dibutyl sebacate	400	300	Powder	Drum (100 litre)	3	B	>16000	
Ethyl alcohol	10000	2000	Liquid	Drum (200 litre)	10	C	7060	1880
Ethyl cellulose	900	500	Powder	Drum (100 litre)	5	B	>5000	10 (cellulose)
Hydroxypropyl methylcellulose	9050	2000	Powder	Drum (100 litre)	10	B	>10000	10 (cellulose)
Isopropyl alcohol	6000	1000	Liquid	Drum (200 litre)	5	C	5045	980
Lactose	400	300	Powder	Drum (100 litre)	3	B	>10000	10 (assumed)
Magnesium stearate	50	100	Powder	Drum (100 litre)	1	B	4640 (LDL0)	10
Polyethylene glycol	2000	500	Powder	Drum (100 litre)	5	B	>50000 (LDL0)	10
Polysorbate 80	2000	500	Powder	Drum (100 litre)	5	B	25000 (orl mus)	
Silicon dioxide	400	300	Powder	Drum (100 litre)	3	B	>5000	6 (PEL)
Sodium lauryl sulphate	400	300	Powder	Drum (100 litre)	3	B	1288	
Talc	1000	300	Powder	Drum (100 litre)	3	B	>5000	2
Titanium dioxide	1500	500	Powder	Drum (100 litre)	5	B	650 (ipr rat)	10
Permitted Food Additives:								
Food colour	25	25	Powder	Tin (5 kg)	5	B		
Non-pareil seeds	9150	1250	Coarse Powder	Drum (50kg)	25	B		
Pharmaceutical glaze	14000	2000	Powder	Drum (200 litre)	20	B		
Vegetable oil	400	400	Liquid	Drum (200 litre)	2	C		

*orl rat unless otherwise stated

**Drums are steel for liquids and fibreboard for solids.

***Disposal Arrangements for Containers:

A: Drum liner is removed and exported for incineration as a 'Toxic and Dangerous' waste. Drum is crushed and disposed of to landfill.

B: Drum and liner are crushed and disposed of to landfill.

C: Drum is recycled or returned to supplier. If this is not possible it is crushed and disposed of to landfill.

****Also referred to as NG-10

4.3.3. Materials Handling

Materials delivered to the warehouse will be off-loaded from the delivery vehicle by fork lift truck and transferred directly into the warehouse receiving bay or to the safety storage building. Materials will initially receive a 'quarantine' label until such time as satisfactory completion of quality assurance testing and documentation allows their release for use.

Active ingredients (S.D.M. 17, Rimantadine and Eserine salicylate) will be taken as required from storage to an enclosed weighing area where the amount required for each production run will be removed from its container. Containers will be moved between the warehouse and weigh room by pallet trolly.

Small amounts (approx. 30 - 40 kg/d) of active ingredients are needed. These will be taken manually to the liquid preparation area where they are added, with the specially formulated solution and base seeds to the coating pans. Subsequent handling of granules, tablets and capsules will be by manual movement in IBC's (intermediate bulk containers) or equivalent, on pallet trolleys.

Final products (granules, tablets and capsules) will be packed in suitable containers for shipment off-site.

4.3.4. Cleaning

The manufacturing and preparation environment is essentially dry. Normal cleaning, including any accidental solids spillages, will be by mobile vacuum cleaner.

Periodically, machines and vessels will be cleaned using small amounts of IPA, water or detergent solution, as appropriate.

4.3.5. Spillages

Should any spillage of SDM 17 occur, it will first be contacted with nitroglycerin destroyer solution in the manner described in the Material Safety Data Sheet (refer Appendix) for this material. The clean-up procedures also described in the Safety Data Sheet will be followed.

In the case of spillages of other materials, clean-up will be by dry vacuum cleaning whenever possible in accordance with the appropriate material safety data sheet. If a liquid is involved it will be mopped up if the spillage occurs within the production area. If it occurs in the storage building it will be contained.

All waste materials, whether solid or liquid, arising from spillages will be regarded as 'Toxic and Dangerous' wastes and handled accordingly (refer also Section 5.3. below).

4.3.6. Safety in Handling and Storage

The SDM 17 raw material contains 10% nitroglycerin. The company has contacted the Dept. of Justice concerning the need to obtain a licence for the handling and storage of this material. Should the Department decide that a licence is required, any conditions contained therein which govern the handling/storage of the material will be implemented.

4.4. Roads and Traffic

The following vehicle movements are anticipated:

Raw Materials Delivery	...	2/week (HCV)
Laboratory Materials	...	2/week (light vans)
Finished Goods	...	1/week (HCV)
Packaging Materials	...	2/week (HCV)
Wastes	...	1/week (skip:HCV)
Other Storage	...	1/day (HCV)
Motor Cars (incl. sales reps/etc).	...	40/day

Thus, on average, there will be about 2 HCV (Heavy Commercial Vehicles) arrivals and 2 HCV departures per day. About 40 arrivals and departures of motor cars will take place.

The proposed facility is designed to comfortably handle this amount of traffic and future traffic arising from any envisaged future increased production and employment. The Forest facility will not make a significant impact on the overall Clonshaugh Industrial Estate or on the public road system.

5 PLANT EMISSIONS

Fig. 5.1. is a schematic of process emissions (to sewer and to atmosphere). It also indicates materials handling/storage facilities.

5.1. Wastewaters

5.1.1. Process Effluent

Process wastewaters will arise from the following sources:

Plant Equipment/Vessel Cleaning

This is essentially a dry operation. However, there will occasionally be a need to hand wash some items of plant. Small amounts of water and isopropanol would be used for this purpose on an intermittent basis.

Hand Wash Basins, Sinks and Showers

Plant operators will use water in these areas for personal cleaning. Again, the quantity used will be small.

Laboratory Effluent

Dilute acid (H Cl) solution arising from Quality Assurance testing of product and raw materials will arise in small amounts (approx. 10 litres/d). Some water miscible solvent will also be present in this effluent. There would also be some effluent (about 4 m^3/d) arising from the laboratory water purification plant. This comprises reject reverse osmosis water and backwash from an ion-exchange unit.

Combined Process Effluent

The above wastewaters will be combined and discharged to a holding tank of capacity approx. 20 m^3. The effluent pH will be adjusted prior to this tank and the neutralised wastewater will then discharge to sewer. The anticipated characteristics of the process effluent as discharged to sewer are summarised in Table 5.1. below.

Table 5.1.

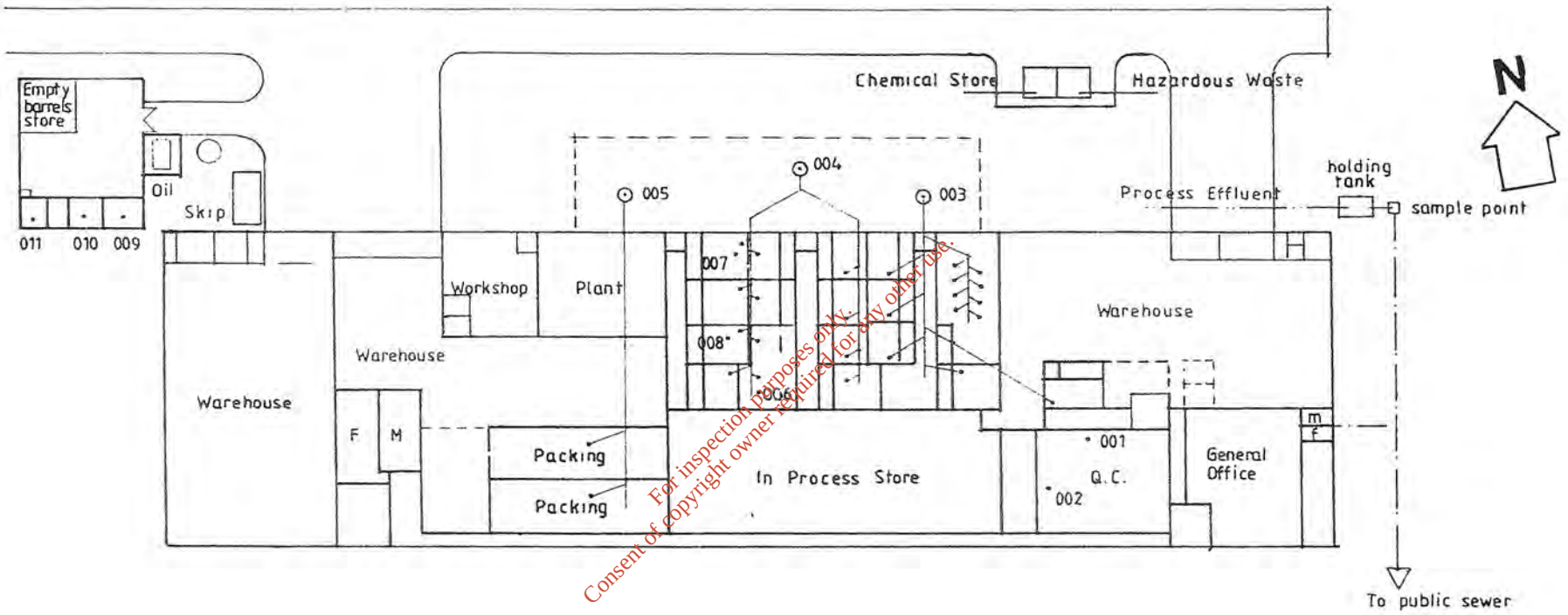
Process Wastewater Characteristics
(as discharged to sewer)

Parameter	Units	Discharge to Sewer
Volume	m3/d	20
	m3/h	4
pH		5.5 - 9
BOD	mg/l	400
COD	mg/l	1500
S.S.	mg/l	200
Oils/Fats/Grease	mg/l	100
Solvents		negligible
Temperature	°C	<30

Domestic Effluent

Domestic effluent arising from the 30 employees will amount to about 3.5 m3/d containing about 0.8 kg BOD per day. The domestic effluent line will join the sewer downstream of the discharge from the process effluent holding tank. At full capacity (110 employees) this would increase to about 13 m3 containing about 3 kg BOD per day.

FIG. 5.1 PROCESS EMISSIONS



NOTE : HAZARD MATERIAL AND CHEMICAL STORES-CONTAINMENT AT 110% OF CAPACITY OF LARGEST CONTAINER-VENTED- WITH FIRE SUPPRESSION-BLOW OUT PANELS

FOREST IRELAND

5.2. Atmospheric Emissions

There will be a total of 11 emission points to atmosphere from the proposed facility. These are summarised in Table 5.2. below. The various emission points are indicated on Fig. 5.1. They are all a minimum of 3 m above the apex of the factory building.

Table 5.2.

Emissions to Atmosphere

Emission Point No.	Process Description	No. of Pick Up Points	Stack Diam mm	Discharge Volume m^3/hr	Stack Height m	Emission Control Equipment
001	Q.C. Lab Fume Hood	3	305	2,550	8.5	None
002	Extra Fume Hood	2	305	2,550	8.5	None
003	Seed Coating	13	305	10,880	8.5	Cylindrical Baghouse
004	Tablet Mfg	12	305	16,320	8.5	Cylindrical Baghouse
005	Packaging	2	203	1,360	8.5	Cylindrical Baghouse
006	Granulation	1	305	3,570	8.5	HEPA Filter
007	Tablet coating	1	305	4,250	8.5	HEPA Filter
008	Tablet coating	1	305	4,250	8.5	HEPA Filter
009	Boiler	1	450	-	9.75	None
010	Boiler	1	450	-	9.75	None
011	Boiler	1	450	-	9.75	None

These emission points are discussed in turn below.

Emission Points 001 and 002

The Quality Control laboratory will be provided with 5 fume cupboards. The exhaust air from each of these will be combined into two ducts before discharge to atmosphere. As is normal practice with fume cupboards, there will be no emission control on this source. Emissions will be negligible. The two most common solvents to be used in the laboratory will be isopropyl alcohol and ethyl alcohol. The emissions of each of these is unlikely to exceed 0.006 kg/hr.

Emission Point 003

This emission point is designed to collect the exhaust from 13 units, 11 seed coating pans, 1 solution tank and 1 weighing station and will discharge to atmosphere through a cylindrical baghouse. The baghouse has an efficiency of 99.9% for particulate sizes less than 1 μm and 100% for particulates greater than 2 μm. The total quantity of particulate accumulated in the baghouse is estimated to be 4.5 kg/week. The emissions to atmosphere are therefore 0.113 g/hr (assuming all material is less than 1 μm). The constituents of these particulates are pharmaceutical glaze, talc, sugar and SDM-17. In addition, cetyl alcohol, isopropyl alcohol and ethyl alcohol will be emitted from this point. The quantity of cetyl alcohol emitted will be 0.06 kg/hr. The amount of isopropyl alcohol emitted will be 1.6 kg/hr and of ethyl alcohol 1.4 kg/hr at full capacity. The corresponding concentrations are 150 mg/m^3 and 130 mg/m^3 of isopropyl alcohol and ethyl alcohol respectively.

Emission Point 004

This emission point is designed to collect the exhaust from 12 points in tablet manufacturing. The proposed controls and their efficiency will be the same as for point 003. Total particulates to the dust extraction system will be 0.1 kg/hr. After a minimum of 99.9% removal the emission to atmosphere will be negligibly small. There will be about 0.3 kg/hr of isopropyl alcohol resulting from cleaning. This amounts to a concentration of 18 mg/m^3.

Emission Point 005

This emission point is designed to collect the exhaust from 2 points in packaging. The baghouse will have the same efficiency as for point 003. Particulates involved at this stage in the process and the quantity emitted will be negligible, at most 0.0001 kg/hr. Additionally, a maximum of 0.15 kg/hr of IPA will be emitted as a result of cleaning.

Emission Point 006

An aqueous base process will take place at this emission point, which will be equipped with a fluidised bed system. At the fluidised bed system, fresh air enters through a 250 mm duct into a chamber for filtration and condition adjustment. The processed air will then enter the granulation chamber and exhaust into the pre-filtration system. The HEPA (High Efficiency Particulate Air) final filtration system is rated at 99.9% efficiency for particulate collection.

The mixture processed at this point includes Rimantadine, cellulose, F D + C food colour, starch, hydroxypropyl methylcellulose and magnesium stearate and purified water which enter the fluidised bed.

The total mixture processed at this point is estimated to be 4,000 kg/year. Based on a 1% loss rate the emission will therefore be 0.02 g/hr of total particulate comprising 60% Rimantadine, 32% hydroxypropyl methylcellulose and cellulose and 8% remaining material.

Emissions Points 007 and 008

Two (2) identical processes of tablet coating will take place at the plant and exhaust to atmosphere through emission points 007 and 008. It is estimated that a batch mixture consisting of Rimantadine, cellulose, hydroxypropyl methylcellulose, ethyl cellulose, food colour, starch, lactose, physostigmine salicylate, polyethylene glycol, polysorbate 80, silicon dioxide, titanium dioxide

and magnesium stearate (all particulates), vegetable oil and purified water will be processed. The airborne particulates that may be created as a result of this processing will be collected by a HEPA filtration system rated at 99.9% efficiency for particulate collection.

The total mixture to be processed at point 007 and 008 is estimated to be 15,500 kg/yr. Based on a loss rate of 1% the emission will therefore be 0.06 g/hr of total particulate from each point and will comprise 50% hydroxypropyl methycellulose, 10% polyethylene glycol, 10% polysorbate 80, 7.5% Physostigmine salicylate, 10% Rimantadine, 7.5% titanium dioxide and 5% remainder of mixture.

Emission Points 009, 010 and 011

These three emission points are all from natural gas fired boilers, two existing and one new. Gas oil will be used as a backup fuel on one of the existing boilers. The emissions from these will consist of the normal products of combustion of natural gas, carbon dioxide, water vapour, carbon monoxide and nitrogen oxides. The stack height of 9.75 m will ensure adequate dispersion of these emissions.

5.3. Wastes

The nature and quantities of wastes likely to arise, together with their proposed handling and disposal procedures, are as follows:

5.3.1. Plastic Liners

The liners from drums containing active ingredient raw materials (refer Table 4.1. above) will be removed and stored on-site in secure containers pending their shipment abroad for destruction by incineration. There would be about 125 such liners per year; total weight about 20 kg/yr.

5.3.2. Protective Clothing

A total of about 2,000 used disposable protective clothing suits/hats/shoes (typically of paper/polypropylene material) will arise for disposal. These will also be stored pending shipment off-site for incineration. The total weight involved is about 400 kg/yr.

5.3.3. Mixed Process Wastes

The following materials will be collected for secure storage pending off-site disposal for incineration:

- Vacuumed dust arising from cleaning of plant and any spilled material.
- Wet cloths used for mopping up material and cleaning vessels, floors etc.
- Spent air filter cartridges.
- Reject product.

These are not expected to exceed about 300 kg/yr total weight.

These wastes would normally be shipped off-site for incineration. Should a waste containing SDM 17 arise, the nitroglycerin will first be neutralised (as specified in the Material Safety Data Sheet - see Appendix) before being disposed of in consultation with the supplier and with the local authority.

5.3.4. Laboratory/Maintenance Dept. Wastes

The following materials and quantities are expected to arise:

- Used oils/solvents from maintenance shop ... approx. 1m³/yr
- Spent solvents from QC lab. (after in-house solvent recovery) ... 2500 kg/yr.

These will be stored for regular shipment for recovery (if possible) or incineration off-site. The solvents comprise mainly methanol and acetone.

The wastes discussed in 5.3.1. to 5.3.4. above will be handled and disposed of as 'Toxic and Dangerous' wastes (refer EC Directive 78/319/EEC). The safety storage building (refer 4.3.2. above) will house these materials pending their regular shipment off-site.

5.3.5. Fibre Drums and Drum Liners

The total number of fibre drums likely to require disposal will be about 650 per annum. These will be crushed/compacted on-site prior to disposal to a suitable landfill. Plastic liners - other than those referred to in 5.3.1. above - will be included with this waste.

5.3.6. Steel Drums

About 170 steel drums will arise per year for disposal. These will be returned to the supplier if possible. If not, they will be recycled in this country if a suitable recycler can be found. Otherwise they will be crushed on-site for disposal to a suitable landfill.

5.3.7. Other Waste

This will principally comprise paper and cardboard packing waste. About 1 skip (40 cubic yard) per week is expected to arise. The material will be compacted on-site prior to regular off-site disposal at a suitable landfill.

5.4. Noise

5.4.1. Noise Sources

Noise from the production plant radiated from the building envelope - walls, windows, doors. Process and heating and ventilation plant (inside building in plant room). Dust collection systems in yard on north side of main building. This item of plant to be acoustically enclosed.

Vents from process and ventilating plant on the roof of the building.

5.4.2. Building Specifications

Existing External Walls 215 solid block walls, with insulation and metal cladding externally.

Existing Floor 150 Power floated slab to take various finishes.

Existing Frame Structural Steel columns with steel roof trusses.

Existing Roof Galvanised metal deck with insulation and single membrane high performance roofing.

New Walls Generally 215 hollow block plastered both sides with demountable partitions in office area.

Ceilings Plastered ceiling in manufacturing areas and suspended tiles in offices and packaging areas.

5.4.3. Source Emissions Levels

The major items of equipment, together with their noise emission levels as measured for similar plant installed at a Forest facility in the U.S., are listed in Table 5.3.

Table 5.3.

Facility Noise Levels

Source	Source Description	Reading Point	Noise Level (db)
Light Traffic	Residential Road behind the Facility	50' from Property on the Sidewalk	49
Heavy Traffic	Residential, Commercial, Industrial Main Road	50' from Property on the Sidewalk	68 - 79*
Manufacturing Building/Boilers	General Manufacturing Activity	5' from Unit Exhaust on the Ground	61
Q.C. Lab Hood Emission Point	12" Diameter Stack 1,500 cfm Exhaust Fan	5' from Unit Exhaust on the Roof	66
Cylindrical Baghouse Emission Point	12" Diameter Stack 9,600 cfm Exhaust Fan	5' from Unit Exhaust, on the Ground	74 - 76
Fluid Bed Emission Point	12" Diameter Stack 2,100 cfm Exhaust Fan	5' from Unit Exhaust on the Roof	87**
Packaging & Warehouse Emission Point	Employee Traffic, Hand Truck	Ground Level	51 - 56
Tableting	12" Diameter Stack 2,500 cfm Exhaust Fan	5' from Unit Exhaust on the Roof	70
Tablet Coating		Facility Roof	60 - 63

Readings were taken during normal working hours and all units in operation.

* Background noise level outside the facility = 62 db.

** Reading in the machine room while the unit was shut down = 68 db

5.4.4.

Plant noise emission levels will be controlled by equipment selection, the use of silencers and attenuators and by acoustic screening.

5.4.5.

Maximum internal noise levels at ground floor are expected to be 87 dB (A). This refers to levels within the plant room.

5.4.6. Operating Hours

The production process will normally operate from 07.00 to 23.00 hours. Building services plant will operate 24 hours a day.

6 IMPACT OF THE EMISSIONS

6.1. Impact on Water Quality

The quantity of process effluent at 20 m^3/d is approximately equivalent to a population of 80. Taken together with the domestic sewage from the 30 employees, the daytime 'population equivalent' of the facility will be about 110. This may increase somewhat if production increases in the future. However the total effluent volume is likely to remain small even in the context of the existing factory units at Clonshaugh.

The pH corrected process effluent (refer Table 5.1.) is suitable for discharge to sewer. It will not contain substances likely to be hazardous within the sewer or to the marine environment. The process effluent characteristics will be similar to those of domestic sewage.

6.2. Impact of Air Emissions

The only emissions of any significance for the proposed plant are isopropyl alcohol and ethyl alcohol from emission point 003. The concentration of these in the emission are 150 mg/m^3 and 130 mg/m^3 respectively.

The threshold limit values (TLV) for these substances are 983 mg/m^3 and 1880 mg/m^3 for isopropyl alcohol and ethyl alcohol, respectively. These are the maximum concentrations to which workers may be exposed during a working day to prevent adverse health effects. As the concentrations of these substances in the emission itself are below their TLV, they would not have any adverse effects on the environment.

Dust emissions are so insignificant that they would be undetectable.

This facility will have no adverse effect on the atmospheric environment.

6.3. Waste Handling and Disposal

Process wastes classifiable as 'toxic and dangerous' (78/319/EEC) will be exported for incineration or recovery at suitable specialist facilities. These facilities are regulated by the responsible authorities in their respective countries. The procedures and documentation to facilitate the shipment and export of these materials are specified by S.I. 33 of 1982 and S.I. 248 of 1988. No practical problems are anticipated in respect of the handling of these materials in this way. These arrangements pose no significant environmental impact either in relation to the environment of this country or the receiving country.

Where practicable, e.g. in the case of used oils, steel drums and possibly some spent solvents, a suitable recovery/recycling option will be used.

Non-hazardous materials will be disposed of by landfill. In general, these materials will be compacted/crushed on-site prior to disposal. The material for landfill will comprise mainly paper and cardboard packing materials, crushed fibreboard drums and plastic liners (from non-toxic raw material containers). The amount of such material will be relatively small - about 1 skip (40 cubic yard) per week. This will be readily assimilated at a domestic refuse landfill site operated by the local authority or at a suitable private landfill. No adverse environmental impact is anticipated.

6.4. Noise

6.4.1. Noise Immission Criteria

We propose the following criteria as appropriate for the assessment of impact in the existing noise environment.

Night	35 dB $L_{(Aeq)}$
Day	45 dB $L_{(Aeq)}$
Early Morning/Late Evening	40 dB $L_{(Aeq)}$

These are limit values for the noise from the plant measured outside any permanent dwelling. There should not be any significant pure tones or impulsive elements in the noise spectrum.

Note: $L_{(Aeq)}$ is the A-weighted continuous equivalent level. The time period for measurement is nominally the whole day or night but in practice sampled measurement periods of 15 minutes will normally give sufficient accuracy.

6.4.2. Control of Noise Emissions

No specific measures are required in the case of plant and equipment located within the building. Silencing and screening of all vents to atmosphere will be an integral part of the detailed design.

6.4.3. Impact

Examination of the proposed plant and building indicates that plant and equipment can be selected and acoustic screening can be arranged to meet the criteria of 6.4.1.

7 OTHER ASPECTS

7.1. Flora and Fauna

The proposed project will not involve any significant ground disturbance or interference with existing vegetation. No felling of trees is involved. Plant emissions will be such as to cause no adverse impact on the existing environment.

The site location is a well established urban, industrial complex. There are no natural or unusual habitats in the immediate vicinity.

Consequently, there is no potential for any significant impact on the status of flora and fauna in the area.

7.2. Soil

The building is on a fully paved site. The fuel oil storage tank is within a containment area. As far as can be ascertained, previous operations on the site had no potential for soil contamination. Materials handling and storage arrangements in the case of the proposed new operation will be such as to ensure that the soil environment remains protected.

7.3. Landscape

The project does not involve any substantial changes to the external appearance of the existing building. In its context as a unit within an industrial estate the project involves no significant impact on the existing landscape.

7.4. Climate

The project has no potential to significantly affect the climate.

7.5. Material Assets and Cultural Heritage

Apart from the positive impact arising from job creation the project does not significantly impact these aspects.

7.6. Human Beings

All aspects discussed above are of relevance to human beings but there are no significant impacts not already described.

APPENDIX

MATERIAL SAFETY DATA SHEETS FOR ACTIVE INGREDIENTS

SDM 17 (LIKELY TO BE SUPPLIED FROM THE U.K. BY ICI AS "NG - 10")

ICI Specialties

1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION AND COMPANY/UNDERTAKING

PRODUCT NAME: NG-10

Address/Phone No. : ICI Specialties
PO Box 42
Hexagon House
Blackley
Manchester, M9 3DA
(061) 740 1460
Emergency Phone No.: (0484) 538444

2. COMPOSITION/INFORMATION ON INGREDIENTS

1 part of nitroglycerin in 9 parts lactose.

HAZARDOUS INGREDIENT(S)	CAS No.	%(w/w)	Symbol	R Phrases
Nitroglycerin	000055-63-0	10	E, T+	R3,R33
				R26/27/28

3. HAZARDS IDENTIFICATION

Highly flammable.
This product contains nitroglycerin which is covered by the EEC Dangerous Substances Directive (CPL Regulations). It has therefore been labelled in accordance with these regulations.
Heating may cause an explosion.
Very toxic by inhalation, in contact with skin and if swallowed.
Danger of cumulative effects.
Nitroglycerin is a vasodilator and can result in hypotension. Exposure is known to cause throbbing headache that may persist for hours or days. Headache is usually an early sign of overexposure in workers.
Nitroglycerin can induce cyanosis (blue tinge to skin, fingers and lips), euphoria, headache, flushing, dizziness, ataxia, weakness, rapid heartbeat, laboured breathing, nausea, vomiting and confusion.
These effects may occur as a result of skin contact, inhalation and ingestion.
Toxic to fish.

4. FIRST-AID MEASURES

SPEED IS ESSENTIAL.

Inhalation : Remove patient from exposure, keep warm and at rest. OBTAIN IMMEDIATE MEDICAL ATTENTION.

Skin Contact : Take off immediately all contaminated clothing. Wash immediately with water followed by soap and water. OBTAIN IMMEDIATE MEDICAL ATTENTION. Contaminated clothing should be laundered before re-issue.

Eye Contact : Immediately irrigate with eyewash solution or clean water, holding the eyelids apart, for at least 10 minutes. Obtain medical attention.

Ingestion : Provided the patient is conscious, wash out mouth with water and give 200-300 ml (half a pint) of water to drink. Do not induce vomiting. OBTAIN IMMEDIATE MEDICAL ATTENTION.

Further Medical Treatment
Symptomatic. Administer oxygen if there are signs of cyanosis. If clinical condition deteriorates, administer 10cc Methylene Blue intravenously. It is unlikely for this to be required with a methaemoglobin level of less than 40%.

5. FIRE-FIGHTING MEASURES

The explosive ingredient in this substance could concentrate and explode during a fire, or after the fire if it is subjected to impact, friction or heat.

DO NOT ATTEMPT TO DIRECTLY FIGHT ESTABLISHED OR SLOW SMOULDERING FIRES as explosion is possible. Move as far away as possible (more than 500 metres) and only use remote monitors to fight the fire.

FOR SMALL LOCALISED FIRES IN THEIR INITIAL STAGES, fire fighting may be appropriate if it is believed that total extinguishment can be quickly effected. In these cases, use chemical powders, CO2, halogenated hydrocarbons or foam. Excessive water can dissolve the lactose causing dangerous accumulations of nitroglycerin.

AFTER THE FIRE, be extremely cautious when approaching to clear debris, as accumulations of nitroglycerin may have formed.

If product is not directly involved in a fire, remove product packages from the fire area if this can be done without risk.

Fire Fighting Protective Equipment : Full protective equipment including suitable respiratory protection.

6. ACCIDENTAL RELEASE MEASURES

Ensure full personal protection (including respiratory protection) during removal of spillages.
Protect against dust.
Keep product dry.
If the product is wet add an inert, non-flammable absorbent material and allow time for the absorption of any liquid.
Clear up dry spillages and absorbed damp spillages by gentle sweeping, so as to avoid dust cloud formation, and by shovelling into non-metallic containers using non-sparking and non-static generating tools.
If the spillage area shows signs of separated nitroglycerin (a yellow oily liquid) then it must be treated with fresh nitroglycerin destroyer (see appendix 1).
Do NOT incinerate or include in any waste to be sent for incineration. (see 'Disposal considerations')
Spillages or uncontrolled discharges into watercourses must be IMMEDIATELY alerted to the National Rivers Authority or other appropriate regulatory body.

7. HANDLING AND STORAGE

7.1 HANDLING

Heating may cause an explosion.
Avoid contact with skin and eyes.
Do not breathe dust.
Full handling precautions should be taken at all times.
Keep away from moisture, acids, alkalis, oxidising agents.
Keep stocks of nitroglycerin destroyer readily available (See Appendix 1).
Never add water to this product.

7.2 STORAGE

On storage this product should be segregated from other flammable materials.
Storage rooms should be temperature controlled.
This product may cake and lose its normal flowability properties if the temperature of storage is allowed to fall below 10 Deg C. If this happens raise the ambient temperature of storage to between 20 Deg C and 30 Deg C for a minimum of 3 days to restore the original properties before use.
Keep container tightly closed.
Keep away from moisture, acids, alkalis, oxidising agents.
Keep away from heat and sources of ignition.
Keep away from direct sunlight.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Where suitable engineering controls are not fitted or are inadequate, wear suitable protective equipment.

- Respirators : Yes
- Eye Protection : Yes
- Gloves : Yes. Gloves should be changed regularly to avoid permeation problems.
- Other : Wear suitable protective clothing.

Occupational Exposure Limits

HAZARDOUS INGREDIENT(S)	LTEL 8hr TWA ppm	LTEL 8hr TWA mg/m3	STEL ppm	STEL mg/m3	Time mins	
Nitroglycerin	0.2	2	0.2	2	10	OES SK

9. PHYSICAL AND CHEMICAL PROPERTIES

Form	: powder
Colour	: white
Odour	: odourless
pH (Value)	: Not applicable.
Boiling Point (Deg C)	: Not applicable.
Flash Point (Deg C)	: Not applicable.
Flammable Limits	: Not applicable.
Auto Ignition Temperature (Deg C)	: Not applicable.
Oxidising Properties	: Not oxidising
Vapour Pressure (mm Hg)	: Nitrogylcerin: 0.00025 At 20 Deg C 0.00055 At 25 Deg C 0.00083 At 30 Deg C
Density (g/ml)	: Not applicable.
Solubility (Water)	: Nitroglycerin: 0.17% At 20 Deg C 0.19% At 30 Deg C Lactose: soluble
Solubility (Other)	: No data.
Partition Coefficient	: No data.
Specific Gravity	: Not applicable.
Viscosity (mPa.s)	: Not applicable.

10. STABILITY AND REACTIVITY

Hazardous Reactions	: Stable under normal conditions, but under fire conditions the nitroglycerin may detonate. Can react with acids, alkalis, oxidising agents. No hazardous reactions with water, but contact with water will release the active material, which is a powerful explosive.

11. TOXICOLOGICAL INFORMATION

This product contains Nitroglycerin which is covered by the EEC Dangerous Substances Directive (CPL Regulations). It has therefore been labelled in accordance with these regulations.
Nitroglycerin is a vasodilator and can result in hypotension. Exposure is known to cause throbbing headache that may persist for hours or days. Headache is usually an early sign of overexposure in workers.
Nitroglycerin can induce cyanosis (blue tinge to skin, fingers and lips), euphoria, headache, flushing, dizziness, ataxia, weakness, rapid heartbeat, laboured breathing, nausea, vomiting and confusion.
These effects may occur as a result of inhalation, ingestion or skin contact.

Inhalation	: Very toxic by inhalation.
Skin Contact	: Very toxic in contact with skin. Can be rapidly absorbed through skin.
Eye Contact	: May cause eye irritation.
Ingestion	: Very toxic if swallowed.
Long Term Exposure	: Danger of cumulative effects.

12. ECOLOGICAL INFORMATION

This environmental hazard assessment is based on information available on the components of the formulation.

Environmental Fate and Distribution
For the purpose of this environment assessment: The product is soluble in water.
Solid with low volatility.
By considering the production and use of the substance, it is unlikely

that significant environmental exposure in the air, soil or water will arise.

Toxicity
By assessment of the components of the formulation a value in the following range is anticipated.
LC50 (bluegill sunfish) (96 hour) : 1-10mg/l
Toxic to fish.
WGK 2 (self classification)

Effect on Effluent Treatment
No information available.

13. DISPOSAL CONSIDERATIONS

CONSULT THE SUPPLIER
Disposal should be in accordance with local, state or national legislation.
Waste, even small quantities, should never be poured down drains, sewers or water courses.

14. TRANSPORT INFORMATION

UN No.	: 1325
UN Pack. Group	: III

AIR

ICAO/IATA Class	
-primary	: Not specifically listed but treat as forbidden

SEA

IMDG Class	
-primary	: Product not specifically listed. Treat as 4.1 + ethical 'Explosive in a fire' label
UN Packing Group Sea	: III

ROAD/RAIL

ADR/RID Class	: Product not specifically listed. Treat as 4.1 + ethical 'Explosive in a fire' label
ADR/RID Item No	: 6(c)

15. REGULATORY INFORMATION

This product contains 10% nitroglycerin which is classified as very toxic under the EEC Dangerous Substances Directive (CPL Regulations). It has therefore, been classified as very toxic according to the guidelines laid down under the EEC Dangerous Preparations Directive.

Contains: Nitroglycerin

EEC Classification : HIGHLY FLAMMABLE AND VERY TOXIC

Hazard Symbol : F + T

Risk Phrases : R11: Highly flammable.
R5:Heating may cause an explosion.
R26/27/28: Very toxic by inhalation, in contact with skin and if swallowed.
R33: Danger of cumulative effects.

Safety Phrases : S14: Keep away from water .
S16: Keep away from sources of ignition - No Smoking.
S22: Do not breathe dust.
S28: After contact with skin, wash immediately with plenty of soap and water.
S35: This material and its container must be disposed of in a safe way.
S36/37/39: Wear suitable protective clothing, gloves and eye/face protection.
S38: In case of insufficient ventilation, wear suitable respiratory equipment.
S45: In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible).
S43: In case of fire, use extreme caution. See Firefighting measures.

16. OTHER INFORMATION

This data sheet was prepared in accordance with Directive 91/155/EEC.

Originated by
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ICI Specialties

Appendix 1

PROCEDURES FOR DESTROYING NITROGLYCERIN

I. After cleanup from a spill of material containing nitroglycerin.

(a) The spill area must be treated with fresh nitroglycerin destroyer made up as follows:

- Prepare Solution "A" by mixing 3 parts of ethanol with 1 part of acetone by volume.
- Prepare Solution "B" by mixing 480 grams of 60% Technical Grade Sodium Sulphide into 1500 ml of water.
- Prepare sufficient volumes of the above solutions to generously cover the spill area several times. (See sections e and g).

(b) Clear the spill area of combustibles and disconnect or remove ignition source such as electric fans, motors, and non-vapour proof lights and switches since Solution A is highly flammable.

(c) Ventilate the spill area and remove or neutralise any acids. Solution B will react with acids and liberate hydrogen sulphide gas which is very toxic by inhalation.

(d) Follow your suppliers SDS recommendations for handling the ingredients of Solutions A and B.

(e) When ready to apply Nitroglycerin destroyer, mix 3 parts by volume of Solution A with 1 part of Solution B.

(f) Apply to the spill area. Some bubbling will occur as the reaction releases small quantities of hydrogen sulphide (please refer to local occupational exposure limits). The mixture will turn yellow.

(g) When the reaction appears complete, mop up the residues with a cloth or sponge and repeat step f until no colour change occurs. The used cloths and/or sponges should be discarded along with the sweepings from the spill in the appropriate, approved manner.

Note: All operations should be performed by trained personnel familiar with the hazards of the chemicals used.

II. To dispose of small quantities of samples and laboratory wastes containing nitroglycerin.

(a) Never discard such untreated material down the drain.

(b) Destroy any nitroglycerin present by adding to a fresh solution of sodium sulphide made up as follows:

- For each gram of nitroglycerin to be destroyed, use 2 grams of 60% Technical Grade sodium sulphide in 83 ml of water.
- Heat for 4 hours at 70°C under a well ventilated hood as small quantities of hydrogen sulphide are evolved. Stir occasionally.
- To prove sufficient sulphide, add 5 to 10 ml of reacted solution to a test tube, add 2 ml of concentrated hydrochloric acid and place a moist lead acetate paper over the mouth of the test tube. Excess sulphide will colour the paper brown.
- When decomposition is complete, discard the solution and wash it away with water.

ICI Specialties

SPECIAL DRUG PRODUCTS

NITROGLYCERIN IN LACTOSE

STORAGE AND HANDLING PRECAUTIONS

INTRODUCTION

The purpose of this information note is to further advise those handling our NG-10 product - 10% glycerol trinitrate (nitroglycerin) in lactose - of proper storage and handling procedures for the product and the possible hazards if the product is involved in a fire or the active ingredient (nitroglycerin) is separated from the lactose diluent.

STORAGE

NG-10 should be stored in a cool, dry place away from sources of heat and flammable materials. The preferred temperature range for storage is 15°C - 30°C. Nitroglycerin in lactose may cake and lose its normal flowability properties if the temperature of storage is allowed to fall below 10°C. If this happens the ambient temperature of storage should be raised to 20°C - 30°C for a minimum of 3 days to restore the original properties before using the product. Do not raise the temperature of the product above 40°C.

HANDLING

Direct contact with the product should be avoided, since nitroglycerin can readily be absorbed through the skin (see ICI Specialties Safety Data Sheet for the effects of overexposure to nitroglycerin). Cotton gloves, caps and overalls are recommended. Overalls and caps should be changed daily; gloves should be changed each time they are removed. Cotton clothing and gloves may be washed and reused. While no specific air purifying respirator is approved for use with nitroglycerin, the use of an approved respirator is recommended to minimise inhalation of dust and fumes.

HAZARDS

Concentrated Nitroglycerin

Nitroglycerin in the undiluted state is a high explosive. It is sensitive to detonation by heat, friction , or shock. As long as it remains dispersed in the lactose diluent, it is desensitized and can be safely handled with the normal precautions to avoid exposure.

TOTAL QUALITY

Separation of nitroglycerin from the lactose, whether by extraction with a solvent, dissolving away of the lactose diluent, or application of heat sufficient to cause the nitroglycerin to migrate should be considered as extremely hazardous. Any condition that leads to the presence of concentrated nitroglycerin, an oily liquid, even in small amounts, is dangerous.

FIRE

NG-10 needs an external source of heat to cause it to burn. Fires involving small quantities and no other materials tend to self-extinquish. Fires which involve other materials may be self-sustaining; intense fires consume the product entirely with no other effects. It has been found, however, that some fires can create conditions which can cause the nitroglycerin to explode violently during the fire or even when it has apparently died away. Although no such occurrence has been reported involving 10% nitroglycerin on lactose sold by ICI worldwide in sixty years of commercial operation, burn tests indicate that such a hazard does exist. Under certain fire conditions, therefore, an explosion could occur which might cause serious injury or damage.

PRECAUTIONS

It is recommended that anyone handling, transporting, storing or processing NG-10 take the following precautions:

1. Handle and store the product in a location that reduces to a minimum the risk of exposing the product to fire. Store the product in fire resistant storage facilities and away from any materials that would provide a fuel source for fire; ie do not store on wooden pallets or floors made of combustible material.

2. Take steps to exclude ignition sources, such as flames, sparks or very hot surfaces, from the vicinity of the product.

3. Equip storage facilities with fire prevention and protection devices, such as no-smoking posters, smoke detectors and sprinkler systems.

4. Inform all handling, transport, safety and fire fighting personnel of the contents of this note.

FIRE FIGHTING

1. Explosion Risk

   The explosive ingredient in this substance could concentrate and explode during a fire. It could also explode after a fire if the residues are subjected to impact, friction or further heating.

2. Developed Fires, Major Fires and Slow Smouldering Fires

   Do not attempt to fight established or slow smouldering fires directly from close range, as an explosion is possible. Move as far away as possible (more than 500 metres) and use only remote monitors to fight the fire with foam or water.

3. Small Localised Fires in their Initial Stages

For small localised fires in their initial stages, fire fighting may be appropriate if it is believed that total extinguishment can be quickly effected. In these cases use chemical powders, CO_2, halogenated hydrocarbons or foam. Excessive water can dissolve the lactose and cause dangerous accumulations of nitroglycerine to occur.

4. Evacuation

In the event of a fire evacuate personnel not involved in fire fighting to more than 500 metres away. If the fire becomes established evacuate all personnel including fire fighters.

It is particularly important that this precaution continues to be observed through the smouldering final phase of the fire, since in burn tests those explosions which occurred typically took place at this stage of the test fire.

If the product is not directly involved in a fire, move product packages from the fire area but only if this can be achieved without risk.

5. Protective Equipment

This product will burn with flames and may produce toxic gases. Self contained breathing apparatus or other suitable respiratory protection should be used when fighting fires in confined areas.

6. After all Types of Fires

Use extreme caution when approaching to clear debris after a fire as accumulations of nitroglycerine may have formed.

If water has been used the lactose may have dissolved in it, resulting in dangerous concentrations of free nitroglycerine, which will appear as an oily liquid. This should be treated by the addition of an absorbent such as kieselguhr (see the SDS for further advice).

FLUMADINE

HOFFMANN-LA ROCHE INC.
CORP. ENVIRONMENTAL & SAFETY AFFAIRS
NUTLEY, NEW JERSEY 07110
(201) 235-2323

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MATERIAL SAFETY DATA

ORIGINATED	01/17/86
APPROVED	
REVISED	

CHEMICAL NAME

alpha-Methyl-1-adamantyl methylamine

CODE NO.

CAS NO.	RO NO.
	22-1859

Formula: $C_{12}H_{21}N$
Trade Name:
Synonyms: rimantidine; alpha-methyltricyclo[3.3.1.1/3,7]decane-1-methanamine; alpha-methyl-1-adamantanemethylamine
Chemical Family:
Molecular Weight: 179

HAZARD WARNING:

Clinical Indication: Investigational: treatment and prevention of Influenza A [as the HCl]
Biological Activity or Toxicological Class: Antiviral
Environmental Hazard/Caution: None known
Emergency Hazard Symbol:

I. PHYSICAL PROPERTIES Sources: Ve

Appearance and Odor: Clear colorless liquid; odor of organic amines
Specific Gravity (H_2O = 1): 1.0
Solubility in Water, % by wt. at 20°C: Slight

II. CHEMICAL PROPERTIES Sources: Ve; RRO

Stability: Stable
Conditions to Avoid: None specified
Hazardous Polymerization: Will not Occur

III. HAZARDOUS INGREDIENTS Sources: CESA

Not Applicable

IV. FIRE AND EXPLOSION HAZARD Sources: CESA

None known

Extinguishing Media: Substance is not known to be flammable. If fire occurs in surrounds, use water spray, carbon dioxide, dry chemical or foam as appropriate for the burning materials.

FORM ESSENTIALLY CONFORMING TO LSB 005-4

re Fighting Procedures: Evacuate personnel to an area of upwind direction nd remove unneeded materials; keep fire-exposed containers cool with water spray, and provide fire fighters with self-contained breathing equipment.

V. HEALTH HAZARDS Sources: CESA; To

Threshold Limit Value:
TWA: None established
STEL: None established
Toxicity:
Industrial Exposure: Adverse effects of industrial handling are not known.

The following clinical findings obtained with the HCl formulation may be relevant: good tolerance accompanied twice-daily administration of 100 mg orally. A low incidence of CNS effects and some GI signs are recorded. [Verbal information from Med. Res. 1/86]

Primary Route/s of Exposure or Entry: Inhalation, ingestion, skin contact

Experimental: LD_{50} (mouse, orl) 330 (240-440) mg/kg at 5D: Data obtained with 100 mg tablets [DH 9/6/85]
LD_{50} (mouse, orl) 220 (150-300) mg/kg at 5D: Data obtained with 100 mg/ml syrup [DH 9/9/85]

Emergency and First Aid:
Eye contact: Irrigate surfaces with water thoroughly.
Skin contact: Rinse areas with water thoroughly.
Inhalation of mist: Move to fresh air. Notify physician.

VI. SAFETY MEASURES AND EQUIPMENT Sources: Ve; CESA

Ventilation: Local exhaust
Respiratory: NIOSH-approved respirator for dusts and mists
Eyes: Safety glasses
Gloves: Neoprene
Other Directives:
Precautionary Label: Rimantidine
Ro 22-1859/0
Antiviral
For Investigational Use only
Avoid skin contact and inhalation
Precautionary Measures: Avoid skin contact [Ve]
Storage and Handling Conditions: Store under ambient conditions.

VII. SPILL CONTROL, WASTE TREATMENT AND DISPOSAL Sources: CESA

Spill Control: Wipe small spills with suitable adsorbents; dike larger spills and transfer to labeled containers.

Waste Treatment and Disposal: Transport contained waste to an incinerator approved for industrial waste.

.II. REGULATIONS Sources: CESA

DOT: Not regulated

EPA: Not regulated

OSHA:
Hazard Class: None established

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The information contained herein is, to the best of Hoffmann-La Roche's knowledge, complete and accurate. Roche, however, uses many sources and references for gathering this information. Thus, Roche cannot guarantee completeness or accuracy and disclaims all liability for its handling or use.

SYNAPTON

MATERIAL SAFETY DATA SHEET

LONZA
17-17 Rt. 208
Fair Lawn, New Jersey 07410
800-777-1875 (9-5 P.M.)
309-697-5400 (After 5 P.M.)

EMERGENCY TELEPHONE
800-424-9300 (CHEMTREC)

HEALTH 3
FLAMMABILITY 1
REACTIVITY 0

3009 Eserine Salicylate

****

MATERIAL
Eserine salicylate

DATE ISSUED
04/06/90 -New

HAZARD CLASSIFICATION
Poison B
SHIPPING NAME
Poisonous solid, N.O.S.
LABEL Poison

CAS NO. 57-64-7

FORMULA $C_{15}H_{21}N_3O_2 \cdot C_7H_6O_3$

CHEMICAL NAME Benzoic acid,2-hydroxy-,compound with pyrrolo (2,3-b)indol-5-ol,1,2,3, 3a,8,8a-hexahydro-1,3a,8-trimethyl,methylcarbamate (ester),(3aS-cis)-Physostigmine monosalycylate

********** I - INGREDIENTS **********

	WEIGHT %	TWA/TLV
Eserine salicylate	97-100	None established

********** II - PHYSICAL AND CHEMICAL PROPERTIES **********

APPEARANCE White powder
pH Not applicable
VISCOSITY Not applicable
ODOR Odorless
BOILING POINT Not determined
MELTING POINT 184-187°C
VAPOR DENSITY (Air=1) Not applicable
VAPOR PRESSURE (mm Hg) Not applicable
PERCENT VOLATILE (by weight) 0.1
SOLUBILITY IN WATER less than 5%
EVAPORATION RATE (Butyl Acetate=1) Not applicable
SPECIFIC GRAVITY (WATER =1)Not determined

********** III - FIRE AND EXPLOSION INFORMATION **********

FLASH POINT Not applicable
AUTO IGNITION TEMPERATURE Not determined
LOWER EXPLOSION LIMIT (%) Not determined
UPPER EXPLOSION LIMIT (%) Not determined

EXTINGUISHING MEDIA
FOAM X
ALCOHOL FOAM
CO_2 X
DRY CHEMICAL X
WATER X
OTHER

SPECIAL FIRE FIGHTING PROCEDURES:
Must wear MSHA/NIOSH approved self-contained breathing apparatus and protective clothing.

UNUSUAL FIRE AND EXPLOSION HAZARDS:
Products of combustion are toxic.
As with most powdered organic compounds, dust explosions are possible.

MATERIAL SAFETY DATA SHEET

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800-777-1875 (9-5 P.M.)
309-697-5400 (After 5 P.M.)

EMERGENCY TELEPHONE
800-424-9300 (CHEMTREC)

HEALTH 3
FLAMMABILITY 1
REACTIVITY 0

********** IV - HEALTH EFFECTS INFORMATION **********

PRIMARY ROUTES OF ENTRY - SKIN CONTACT X EYE CONTACT
INHALATION X INGESTION X

EFFECTS OF OVEREXPOSURE
In humans, the first effects following local exposure to vapors or inhalation include ocular (eye) and respiratory effects. Ocular effects can include marked miosis, conjunctival congestion, and browache. Respiratory effects can include a watery nasa discharge, tightness in chest and wheezing respiration.

Effects following ingestion (swallowing) can include, but not be limited to, nausea, vomiting, abdominal cramps, diarrhea, localized sweating, confusion, slurred speech and generalized convulsions. May ve fatal if swallowed or inhaled.

OVEREXPOSURE MAY AGGRAVATE EXISTING CONDITIONS:
Patients with asthma or bronchial disorders.

EMERGENCY AND FIRST AID PROCEDURES:
Ingestion: If swallowed, immediately give 3-4 glasses of water, and induce vomiting by placing a finger or blunt object on the back of victim's tongue. Give fluids unti vomitus is clear. DO NOT induce vomiting or give anything by mouth to an unconscious or convulsing person. Get immediate medical attention.

Inhalation: Remove from area to fresh air. If not breathing, clear airway and start mouth-to-mouth artificial respiration or use a bag-mask respirator. Get immediate medical attention. If victim is having trouble breathing, transport to medical care and, if available, give supplemental oxygen.

Skin: Immediately wipe away excess material with a dry cloth while removing contaminated clothing and shoes. Under safety shower, wash affected areas thoroughly with large amounts of water, and soap if available, for at least 15 minutes. Get immediate medical attention. Discard or decontaminate clothing and shoes.

Eyes: Immediately flush eyes with running water for at least 15 minutes. Hold eyelids apart to ensure rinsing of the entire surface of the eyes and lids with wate Get immediate medical attention.

CHEMICALS LISTED AS CARCINOGEN BY:

NATIONAL TOXICOLOGY PROGRAM - No
I.A.R.C. MONOGRAPHS - No
OSHA - No

********** V - REACTIVITY INFORMATION **********

STABILITY: STABLE X / UNSTABLE

CONDITIONS TO AVOID
None known

HAZARDOUS DECOMPOSITION PRODUCTS
Thermal decomposition may produce oxides of carbon and nitrogen.

HAZARDOUS POLYMERIZATION: MAY OCCUR / WILL NOT OCCUR X

CONDITIONS TO AVOID
Light, heat

INCOMPATIBILITY (MATERIALS TO AVOID)
WATER OTHER None known

********** VI - SPILL AND DISPOSAL INFORMATION **********

STEPS TO BE TAKEN IN CASE MATERIAL IS RELEASED OR SPILLED
Danger! Poisonous solid. Wear appropriate protective equipment and MSHA/NIOSH approved respirator (self-contained breathing apparatus preferred). Shovel spills into appropriate containers for disposal. Keep out of sewers or open bodies of water.

WASTE DISPOSAL METHODS
Dispose of in compliance with all Federal, state and local laws and regulations. Incineration is the preferred method.

********** VII - PERSONAL PROTECTION INFORMATION **********

VENTILATION TYPE
In processes where dusts may be generated, proper ventilation must be provided in accordance with good ventilation practices.

RESPIRATORY PROTECTION
Where dust or particulates are generated by the process, a NIOSH/MSHA jointly approved respirator is advised in the absence of proper environmental controls.

PROTECTIVE GLOVES
Rubber or neoprene, when needed, to prevent skin contact.

EYE PROTECTION
Wear chemical splash goggles where there is a potential for eye contact. Use safety glasses with side shields under normal use conditions.

OTHER PROTECTIVE EQUIPMENT
Eye wash; safety shower; protective clothing (long sleeves, coveralls or other, as appropriate), when needed, to prevent skin contact.