TopChem Pharmaceuticals Limited,
Ballymote Business Park,
Carrownanty,Ballymote,
Co. Sligo.
Tel / Fax: 071 918 9685 / 071 9197864

September 19th 2007

Office of Licensing and Guidance,
Environmental Protection Agency,
Johnstown Castle Estate,
County Wexford.

Dear Elizabeth,

In response to the letter received from Mr. Patrick Byrne, Office of Climate Change Licensing & Resource Use, dated 09 August 2007 Re Article 11(2)(b)(ii) of the EPA (Licensing) Regulations 1994 to 2004, attached please find enclosed the following documents in support of our application under Article 10 of the regulations;

- Updated sections B.3 and B.10.
- Clarification on the source and possible emissions associated with the air emission point referred to as 'muffle furnace exhaust'.
- Information on the scrubber system installed on one of the Production Laboratory fume hoods together with periods of operation and controls employed.
- Clarification on the hourly flow rates for emission point E1 (fume hood 1) and E2 (fume hood 2) plus the predicted concentration and mass emission of TA Luft Class 1, 2 and 3 associated with each emission point.
- Completed table G.1(ii) for each of the materials identified under table G.1(i).
- Names of contractors used to remove and dispose / recover wastes generated on site.
- Letter from Bank of Ireland Re TopChem Pharmaceuticals Financial track record.
- Updated Attachment No. A.1 which includes the above information.

If you have any questions in relation to the enclosed documents please feel free to call us on 071-9189685.

Yours sincerely,

_____
Nigel Cannon
General Manager TopChem Pharmaceuticals Limited. **Date: _____**

_____
Dr Donal Coveney
Managing Director TopChem Pharmaceuticals Limited. **Date: _____**

Item 1 of letter dated 09 August 2007:

EPA Comment:

It is considered that class 5.16 of the EPA Acts 1992 and 2003 and paragraph 4.5 of the IPPC Directive (96/61/EC) are the most appropriate descriptions of the activity; please complete sections B.3 and B.10.

TopChem Pharmaceuticals Response:

Sections B.3 and B.10 (attached) updated to reflect the above.

B.3. Class of Activity

Identify the relevant activities in the First, Third or Fourth Schedule of the PoE Act 2004 to which the activity relates:

Schedule	Class	Description[Note 1]
Chemicals	5.16	The use of a chemical or biological process for the production of basic pharmaceutical products.

Note 1: In order to give a precise identification **select only those words** from the description of the class or classes that best describes the nature of the activity for which the licence is being applied for.

B.4. Employees/ Capital Cost

Give-

(i) In the case of an established activity, the number of employees and other persons working or engaged in connection with the activity on the date after which a licence is required and during normal levels of operation, or

(ii) In any other case, the gross capital cost of the activity to which the application relates.

Number of Employees (existing facilities):	**Current 6 employees, projections to get to 10 by December 2007.**
Gross Capital Cost (new proposals) €	**€800K**

B.5. Relevant Planning Authority

Give the name of the planning authority in whose functional area the activity is or will be carried out.

Name:	**Sligo County Council**
Address:	**County Hall**
	Riverside
	Sligo
Tel:	**(071) 9111111**
Fax:	**(071) 9141119**

Planning Permission relating to this application:

has been obtained	**x**	***is being processed***	
is not yet applied for		***is not required***	

Local Authority Planning File Reference Nº:	**PL 06/314**

Attachment B.5 should contain all planning permissions, including a copy of ***all*** conditions, and the required copies of any EIS should also be enclosed. For existing activities, **Attachment Nº B.5** should also contain all licences and permits past and present in force at the time of submission.

B.10 IPPC Directive

Specify whether the activity is a category of industrial activity referred to in Annex I of the IPPC Directive (96/61/EC) and if yes specify the category.

Supporting information should be included in **Attachment Nº B.10**.

Yes, the activity is a category of industrial activity referred to in Annex 1 of the IPPC Directive (96/61/ec) where paragraph 4.5 of the directive is the most appropriate description of the activity .

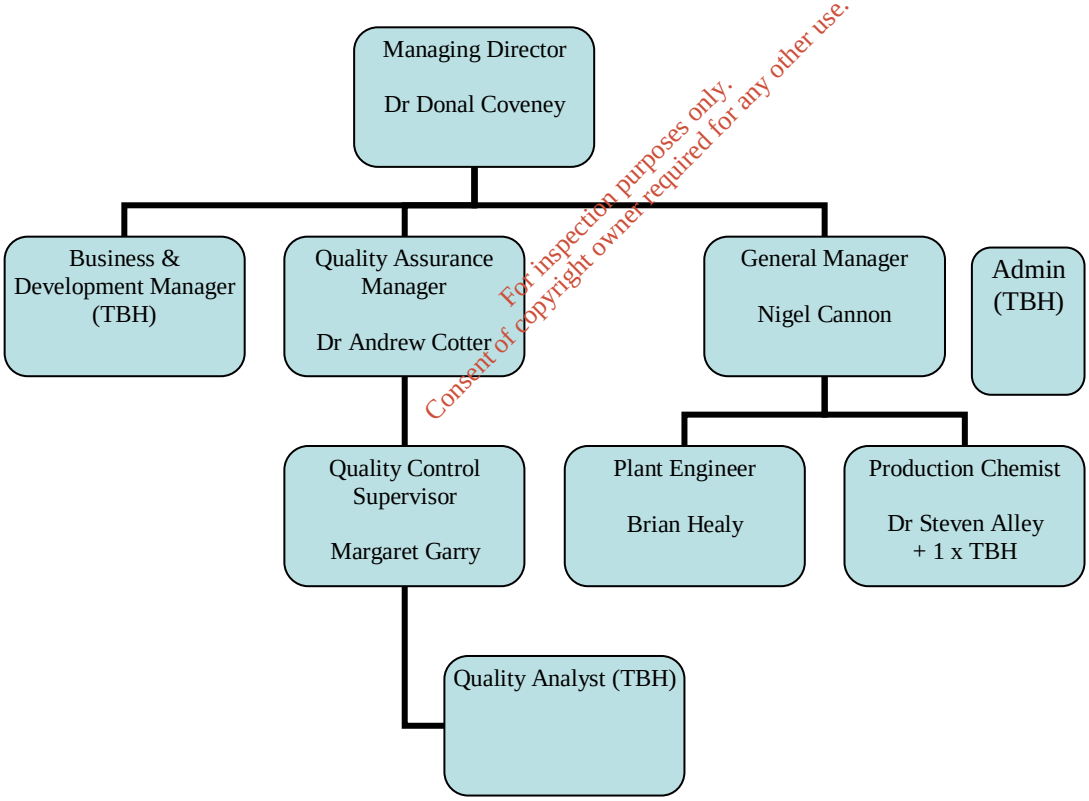
TopChem Pharmaceuticals will be involved in the manufacture of Malathion as a pharmaceutical substance.

SECTION C: MANAGEMENT OF THE INSTALLATION

C.1 Site Management & Control

Details should be provided on the management structures for the activity. Organisational charts and all relevant environmental management policy statements, including provisions for on-going assessment of environmental performance, are required.

On-site management structure:



Responsibility for environmental management is part of the General Managers Job Description until such time as a permanent Environmental Health and Safety Officer is appointed in Q1 2008. Specifically, this will involve ensuring compliance with all aspects of the Integrated Pollution Control Licence and the preparation of any relevant reports. The General Manager is responsible for ensuring that all documentation relating to environmental matters and waste disposal are properly recorded and stored. It is the General Managers responsibility to educate relevant staff in matters relating to environmental issues including IPCL compliance

Item 2 of letter dated 09 August 2007:

EPA Comment:

Please clarify the source and possible emissions associated with the air emission point referred to as “muffle furnace exhaust”.

TopChem Pharmaceuticals Response

The muffle furnace referred to in our application is a laboratory oven used for reducing test samples to ash (this is used for further testing in the laboratory).Typical sample quantity used for this test is ca 1-2g of material and we estimate a maximum of 25 samples per year to be subjected to this test. The purpose of the exhaust fan is to vent waste gases (mainly carbon dioxide and traces of halides / nitrogen oxides) from the laboratory area for the comfort and safety of laboratory personnel.

Attachment No. A.1 (attached) updated to include the above information.

Attachment N^{o} A.1

TopChem Pharmaceuticals Limited is located in the Ballymote Business Park, Carrownanty, Ballymote, Co Sligo. The Company is leasing 2 standard industrial units from a block of 4 with other light Industrial activites performed nearby. The buildings occupy a floor space of approx 5,000 square feet and are situated in close proximity to the Sligo – Dublin Train station. The Company will be involved in the manufacture of low volume active pharmaceutical ingredients, starting with Malathion, Monday to Friday 8.00am – 18.30pm with overtime as necessary but not beyond 23.00pm. Our customer will formulate Malathion into their application for the treatment of head lice infestation.

All operations for the manufacture of Malathion will be performed on a laboratory scale within Fume-Hoods which are installed for the comfort and safety of the persons working in the Production & laboratory areas. Their primary purpose is to remove ambient vapours generated during certain processing operations (e.g., the dispensing of chemicals and solvents from stock containers (i.e., containers as received from supplier) to another container (e.g., laboratory flask, 10L reactor) by drawing air away from the work area and venting it through a flue located 1.5 metres above the roof height of the building. Losses to atmosphere from these operations are expected to be minimal due to (a) the relatively small volumes used (max 10L), (b) processing operations are not continuous over 24 hours. Also, one fume hood in the Production Laboratory is fitted with a scrubber system to permit extraction of any noxious gases generated as process by-products. The scrubber solution is water based and can be acidic or basic. It works by allowing the gases to be passed through the scrubber system at which point the gases are extracted. At the end of the processing step, the scrubber is drained and the waste solution disposed of as per standard procedures.

Malathion is generated from starting materials of ammonium salt of Dimethylphosphorodithoic acid and diethyl maleate. The crude material is isolated and purified using a short path distillation unit. Approximate batch size for this product will be 2Kg using max 20l reactors.

The list of raw materials used in the manufacture of Malathion is as follows;
Diethy Maleate,
O,O-Dimethylphosphorodithoic acid,
Sodium Hydrogen Carbonate (NaHCO3),
Ethanol, *
Hydroquinone,

Triethylamine,
Dichloromethane, *
Toluene,
Hydrochloric acid (HCl) gas *

As of August 2007 these raw materials will no longer be used in the process.

No auxillary materials will be used while Electricity is the source of energy on site. In view of the fact that TopChem Pharmaceuticals Limited is a start-up facility, we can only estimate at this stage that our energy usage will be €10,000 per annum, however, once we are up and running more detailed figures will be provided in due course.

The potential sources of emissions from the site are minor emissions from the fume-hoods which have emission points located on the roof of the building plus surface water from the site. The muffle furnace referred to in our application is a laboratory oven used for reducing test samples to ash (this is used for further testing in the laboratory).Typical sample quantity used for this test is ca 1-2g of material and we estimate a maximum of 25 samples per year to be subjected to this test. The purpose of the exhaust fan is to vent waste gases (mainly carbon dioxide and traces of halides / nitrogen oxides) from the laboratory area for the comfort and safety of laboratory personnel. All manufacturing and storage is bunded and / or enclosed and there are no surface water emissions from the site. The fume-hoods are installed in such a way that the exhaust fans are only running when the fume-hoods are required. One Production laboratory Fume Hood contains an inbuilt scrubber which was purchased as an optional extra but is not in use. If it's decided to use the scrubber system in the future it will be drained and disposed of as per normal procedure.

TopChem Pharmaceuticals Limited will not have any emissions to the sewer apart from normal domestic and soil water. All solids, aqueous and organic wastes will be drummed for off-site disposal using Soltec (Ireland) Limited, Mullingar Business Park, Mullingar, Co Westmeath, waste license number 115-1 & permit register reference number CW058. Non hazardous wastes will be removed and disposed of by Barna Waste – Disposal & Recycling, Carrowbrowne, Headford Road , Co Galway, waste license number 106-2 & permit register reference number CW074.

As per section E of this Application, TopChem Pharmaceuticals Limited does not foresee any significant emissions from the site, hence we don't foresee any requirements to introduce technology or techniques to prevent, reduce or monitor emissions.

With respect to pollution from the site, all fume-hoods are bunded to contain accidental spillages or leakages. Additionally, all storage within the facility area will be bunded to contain spillages.

In terms of emission rates from point E1 (Fume hood 1) and point E2 (Fume hood 2), a worse case scenario of 5% losses of total solvents used is assumed. This corresponds to a total of 50 litres per annum.

This potential loss is split between the two emission points at 25 litres per annum. Based on a 10 hour working day, five days per week, 52 weeks of the year; this

calculates as 10 grams per hour fugitive emissions from each emission point (E1 & E2) as follows:

Per annum:	25 litres
Per Week	0.48 litres
Per Day	0.096 litres
Per Hour	0.0096 litres, rounded up to 10ml per hour

A density of 1 was approximated, resulting in a calculated emission of 0.01 kg/hr. Based on the flow rate of 1,512 m3/hr the concentration can be expressed as 6.6 mg/Nm^3 .

Based on these calculations, the worst case fugitive emissions for chlorinated and non-chlorinated solvents from E1 and E2 are presented in Appendix 1 attached , based on a 25/75 split as projected by our volume usage of both types of solvents.

All wastes generated in the site, i.e. non chlorinated organic solvents, chlorinated organic solvents, waste material (includes paper, plastics, cardboard & packaging), aqueous acidic waste, aqueous basic waste, solid laboratory waste and solid chemical waste will be collected and disposed of by Soltec (Ireland) Limited and Barna Waste – Disposal & recycling as outlined above.

All personnel operating in each of the production, laboratory and stores areas will be trained on how to deal with spillages and what to do in the event of an emergency evacuation of the facility.

Item 3 of letter dated 09 August 2007:

EPA Comment:

Provide details of the scrubber system installed on one of the production laboratory fume hood extraction systems. Identify the periods of operation and any controls employed.

TopChem Pharmaceuticals response:

All operations for the manufacture of Malathion will be performed on a laboratory scale within Fume-Hoods which are installed for the comfort and safety of the persons working in the Production & laboratory areas. Their primary purpose is to remove ambient vapours generated during certain processing operations (e.g., the dispensing of chemicals and solvents from stock containers (i.e., containers as received from supplier) to another container (e.g., laboratory flask, 10L reactor) by drawing air away from the work area and venting it through a flue located 1.5 metres above the roof height of the building. Losses to atmosphere from these operations are expected to be minimal due to (a) the relatively small volumes used (max 10L), (b) processing operations are not continuous over 24 hours. Also, one fume hood in the Production Laboratory is fitted with a scrubber system to permit extraction of any noxious gases generated as process by-products. The scrubber solution is water based and can be acidic or basic. It works by allowing the gases to be passed through the scrubber system at which point the gases are extracted. At the end of the processing step, the scrubber is drained and the waste solution disposed of as per standard procedures.

Attachment No. A.1 (attached) updated to include the above information.

Item 4 of letter dated 09 August 2007:

EPA Comment:

Clarify the hourly flow rates for emission point E1 (Fume Hood 1) and E2 (Fume Hood 2) and calculate the predicted concentration and mass emission of TA luft Class 1,2 and 3 associated with each emission point.

TopChem Pharmaceuticals response:

Attachment titled 'Fume Hood Emission points E1 & E2' outlines the hourly flow rates for emission point E1 (Fume hood 1) and E2 (Fume hood 2)

Appendix 1 attached outlines the predicted concentration and mass emission of TA Luft Class 1, 2 and 3 associated with each emission point calculated.

Attachment No. A.1 updated to reflect the above.

Fume Hood Emission Points E1 & E2

This document supports Table E.1 in our IPCC licence application.

Fume Hoods

The Fume Hood fan in the Production Laboratory is rated by the manufacturer at the following flow rate: 0.42 m3/s. This translates to a flow of 1,512 m3/hr.

The Fume Hood fan in the Process Development Laboratory has the same rating and flow rate of 1,512 m3/hr.

Solvent Usage

The total solvents used in the facility is estimated as follows:

Non-chlorinated solvents:	750 litres per annum
Chlorinated solvents:	250 litres per annum
TOTAL solvents:	1,000 litres per annum

Emission Calculations

A worse case scenario of 5% losses of total solvents used is assumed. This corresponds to a total of 50 litres per annum.

This potential loss is split between the two emission points at 25 litres per annum. Based on an 10 hour working day, five days per week, 52 weeks of the year; this calculates as 10 grams per hour fugitive emissions from each emission point (E1 & E2) as follows:

Per annum:	25 litres
Per Week	0.48 litres
Per Day	0.096 litres
Per Hour	0.0096 litres, rounded up to 10ml per hour

A density of 1 was approximated, resulting in a calculated emission of 0.01 kg/hr. Based on the flow rate of 1,512 m3/hr the concentration can be expressed as 6.6 mg/Nm^3 .

Based on these calculations, the worst case fugitive emissions for chlorinated and non-chlorinated solvents from E1 and E2 are presented in the Table in Appendix 1, based on a 25/75 split as projected by our volume usage of both types of solvents.

TopChem Pharmaceuticals Limited, September 17th, 2007.

Appendix 1: Tabulated Emissions at E1 & E2 for each class of Solvent

Solvent	TA Luft Class	E1			E2			Comment
		mg/Nm^3	Kg/h	kg/yr	mg/Nm^3	Kg/h	kg/yr	
Chlorinated	1	2.2	0.003	7.8	2.2	0.003	7.8	Assumed as Methylene chloride, 100%. D 1.32
Non-chlorinated	n/a	4.95	0.0075	18.75	4.95	0.0075	18.76	Average density of 1 assumed

Item 5 of letter dated 09 August 2007:

EPA Comment:

Please complete Table G.1 (ii) for each of the materials identified under Table G.1 (i).

TopChem Pharmaceuticals response:

Table G.1 (ii) (attached) updated to reflect each of the materials identified under table G.1 (i).

Table G.1(i) Details of Process related Raw Materials, Intermediates, Products, etc., used or generated on the site

Ref. Nº or Code	Material/ Substance[1]	CAS Number	Danger[2] Category	Amount Stored (tonnes)	Annual Usage (tonnes)	Nature of Use	R[3] - Phrase	S[3] - Phrase
	Diethyl Maleate	141-05-9	Not Applicable	0.025	0.025	Raw Material	Not applicable	Not applicable
	O,O-Dimethylphosphorodithoic acid ammonium salt	756-80-9 (free acid)	Not applicable	0.05	0.05	Raw Material	Not applicable	S 24/25
	NaHCO3	497-19-8	Not Applicable	0.025	0.025	Base	Not applicable	Not applicable
	Ethanol	64-17-5	Flammable	0.25	0.25	Solvent	R11	S16, 33, 7, 9
	Hydroquinone	123-31-9	Irritant, dangerous to the environment	<0.001	<0.001	Catalyst	R-22,40,41,43,50,68	S-326,36,37,39,61
	Triethylamine	121-44-8	Flammable, corrosive	<0.001	<0.001	Catalyst	R-11,20,21,22,35	S-3,16,26,29,36,37,39,45
	Dichloromethane	75-09-2	Harmful	0.25	0.25	Solvent	R-40	S-2,23,24,25,36,37
	Toluene	108-88-3	Flammable , Harmful	0.25	0.25	Solvent		
	HCL (Gas)	7647-01-0	Toxic, corrosive	0.25	0.25	Acid	R-24,37	S-26,36,37,39,45
	Ammonium Chloride	12125-02-9	Irritant	0.025	0.025	By-product	R-36, 37, 38	S-22
	Acetone	67-64-1	Highly flammable, Irritant	0.025	0.025	Solvent (cleaning)	R11, 36, 66, 67	S2, 9, 16, 23
	Malathion	121-75-5	Harmful, dangerous for the environment	0.025	0.025	Product	R22, 50/53	S2, 24, 60, 61

Notes: 1. In cases where a material comprises a number of distinct and available dangerous substances, please give details for each component substance.
2. c.f. Article 2(2) of SI Nº 77/94
3. c.f. Schedules 9 and 10 of SI No 62/2004

Table G.1(ii) Details of Process related Raw Materials, Intermediates, Products, etc., used or generated on the site

Ref. Nº or Code	Material/ Substance[1]	TA Luft Class 1, 2 or 3	Odour			EU Lists I and II (Tick and specify Group/Family Number)			
			Odourous Yes/No	Description	Threshold $\mu g/m^3$	Dangerous Substances Directive 76/464/EEC		Groundwater Directive 80/68/EEC	
						List I	List II +129[4]	List I	List II
	Diethyl Maleate	n/a	No	n/a	n/a	no	no	no	no
	O,O-Dimethylphosphorodithoic acid ammonium salt	n/a	No	n/a	n/a	no	no	n/a	Inorganic compounds of phosphorus and elemental phosphorus
	NaHCO3	n/a		n/a	n/a	no	no	no	no
	Ethanol	n/a	No	n/a	Very high	no	no	no	no
	Hydroquinone	n/a	No	n/a	n/a	no	no	no	no
	Triethylamine	n/a	yes	Typical amine	80,000	no	no	no	no
	Dichloromethane	1	yes	Characteristic	743,000	no	no	no	no
	Toluene	n/a	Yes	Aromatic hydrocarbon	24,000	no	no	no	no
	HCL (Gas)	3	Yes	Pungent	15,000	no	no	no	no
	Ammonium Chloride	n/a	No	n/a	n/a	no	no	no	no
	Acetone	n/a	Yes	Characteristic	Very high	no	no	no	no
	Malathion	n/a	Yes	Characteristic, fruity	n/a	no	no	Organophosphorous compounds	n/a

Notes (cont.): 4. The European Commission priority candidate list

Item 6 of letter dated 09 August 2007:

EPA Comment:

Identify, if possible, the contractor who will be used to remove and dispose / recover wastes generated on-site.

TopChem Pharmaceuticals response:

The Contractors used to remove and dispose / recover wastes generated on site are;

- Soltec (Ireland) Ltd -> for Solids / Aqueous / Organic wastes .
- Barna Waste – Disposal & Recycling -> for Non Hazardous wastes.

Attachment No. A.1 updated to reflect the above contractors.

Item 7 of letter dated 09 August 2007:

EPA Comment:

Provide information to show that the person is likely to be in a position to meet any financial commitments or liabilities that may have been or will be entered into or incurred in carrying on the activity to which the application relates or in consequence of ceasing to carry out the activity.

TopChem Pharmaceuticals response:

See attached letter from Hugh Brown, Manager Bank of Ireland, Ballymote, Co Sligo Re above matter.

Bank of Ireland

Ballymote
Co. Sligo

Telephone:
(071) 83325/83159
Fax: (071) 83768
www.bankofireland.ie

24TH August 2007

TO WHOM IT MAY CONCERN

RE: TOPCHEM PHARMACEUTICALS LTD, BALLYMOTE, CO SLIGO

Dear Sir/Madam,

I wish to confirm that the above mentioned company has operated an account at this branch since setting up the new company in Ballymote.

Topchem Pharmaceuticals have operated their account in an excellent manner and have always fulfilled any obligations their undertook with Bank of Ireland.

In my opinion they would not undertake any obligation in which they would not see their will to fulfil.

Yours faithfully

HUGH BROWN
MANAGER