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Introduction to Arran

Overview of technologies and manufacturing capabilities

16 February 2025

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Location

ALMAC

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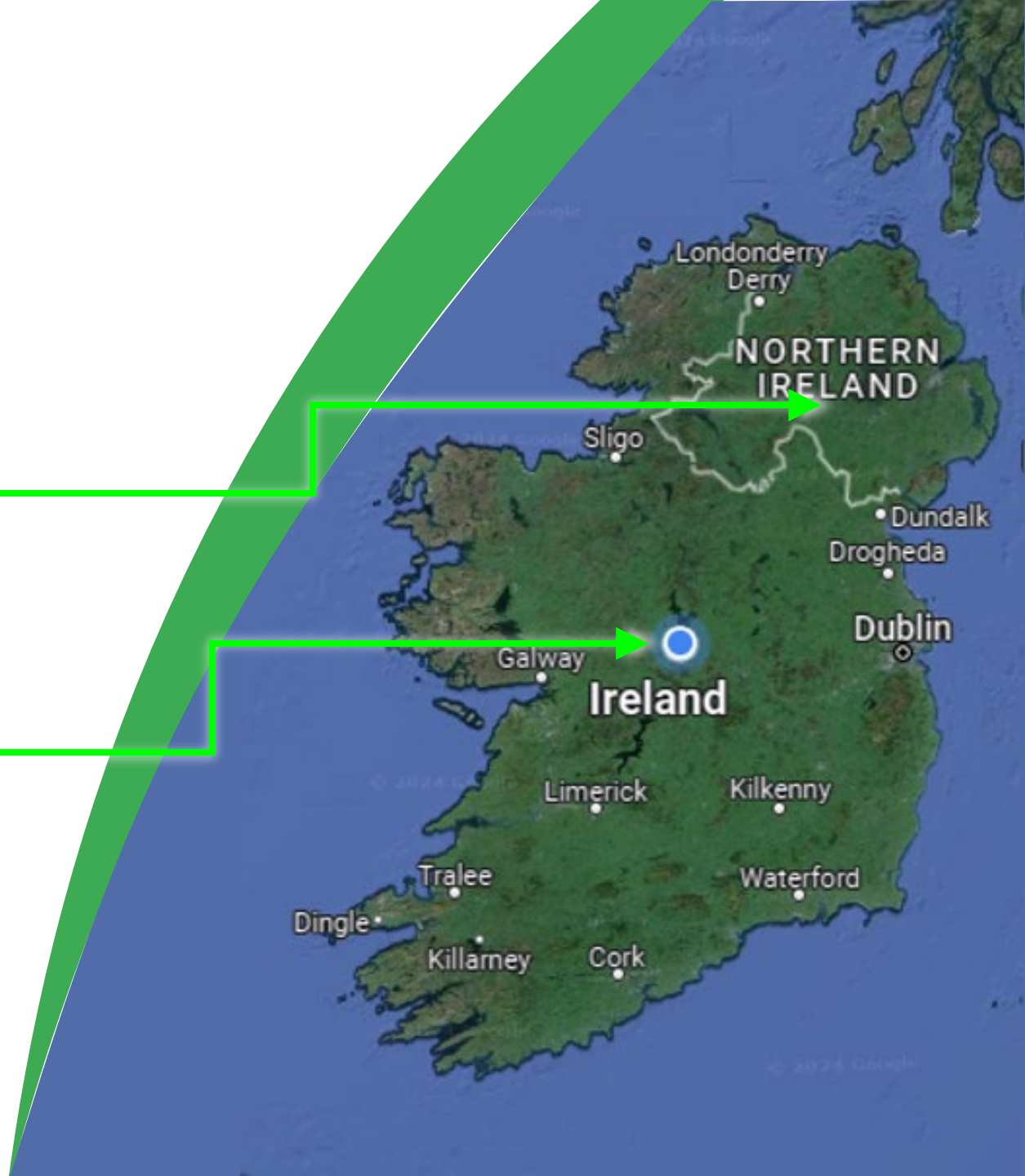

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Arran differentiators

Chemistry experience:

- Over 30 years of experience in handling difficult small molecule chemistry.
- Modular, flexible, adaptable equipment to suit many processes.
- Flexibility to supply kg to 100 tonnes

Quality:

- Routinely audited by top pharma companies.
- EU based manufacturer with REACH compliance experience
- ISO compliant and approved by US FDA Food division.
- Excellent health and safety and environmental standards.
- Registered on over 30 Drug Master Files.

Foundation status

PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

IRDG THE INNOVATION NETWORK

nqa. ISO 50001 ENERGY MANAGEMENT

GOLD 2023 ecovadis Sustainability Rating

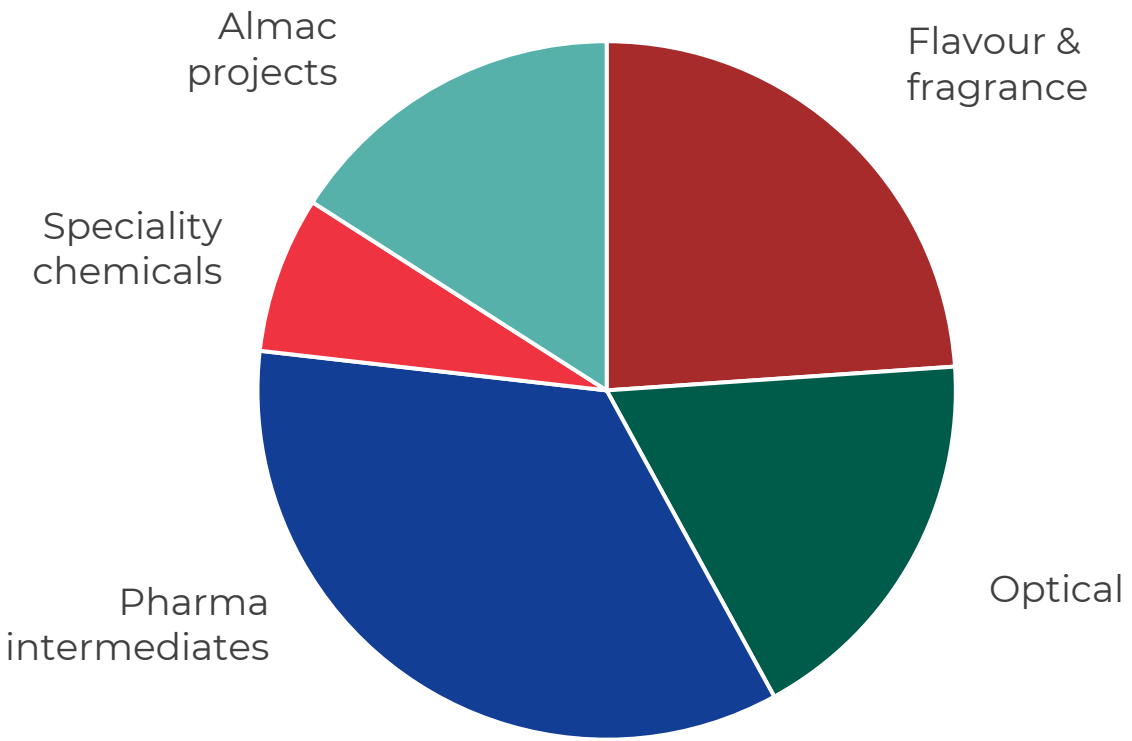
nqa. ISO 14001 ENVIRONMENTAL MANAGEMENT

nqa. ISO 9001 QUALITY MANAGEMENT

EU REACH COMPLIANT

FDA AUDITED BY HUMAN FOODS

Arran client base



Calculated as percent of revenue in 2023-2024 financial year

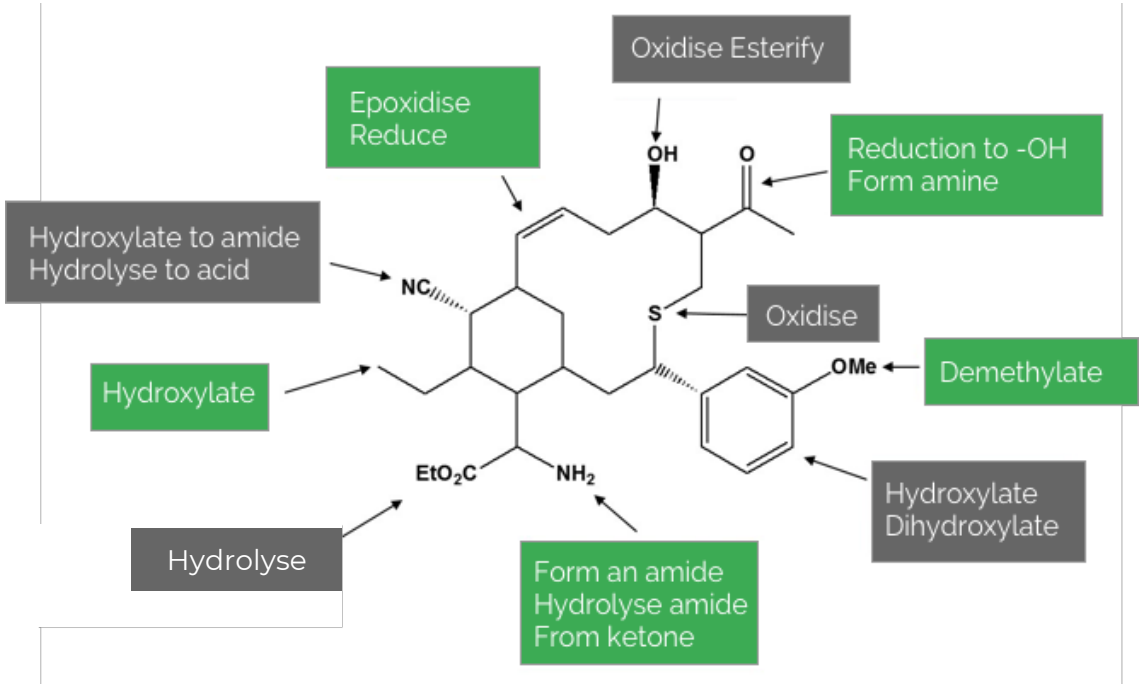
Geography	Revenue
Europe	45%
United States	40%
Asia	10%
Rest of world	5%

Chemistry experience

Classical:

Alkylation	Methylations
Aminoalkylation	Michael reaction
Asymmetric synthesis	Optical resolution
Condensations	Organometallic
Dealkylation	Organosilicon
Dieckmann condensation	Oxidation
Diels Alder reaction	Ritter reaction
Grignard reactions	Stereo-selective reactions
Heck reaction	Suspension polymerisation
Leuckart reaction	Flow hydrogenation
Mannich reaction	Transfer hydrogenation

Enzymatic:



Core technology: Biocatalysis

Fermentation development

Fermentation scale up

Bulk enzyme supply

Proof of concept
Laboratory sample

Process development
Fit for purpose

Scale up
Raw material sourcing
Quality considerations

Isolation

Extraction & purification:

- Distillation
- Crystallisation
- Reslurry
- Bio polish
- Solvent extraction

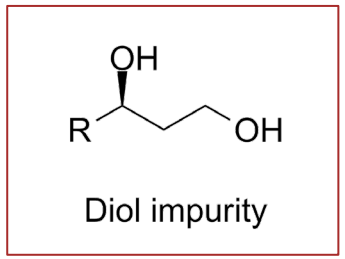
Enzyme screen

Enzyme build and selection

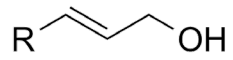
Enzyme engineering

Case study: RSM manufacture (1 of 2)

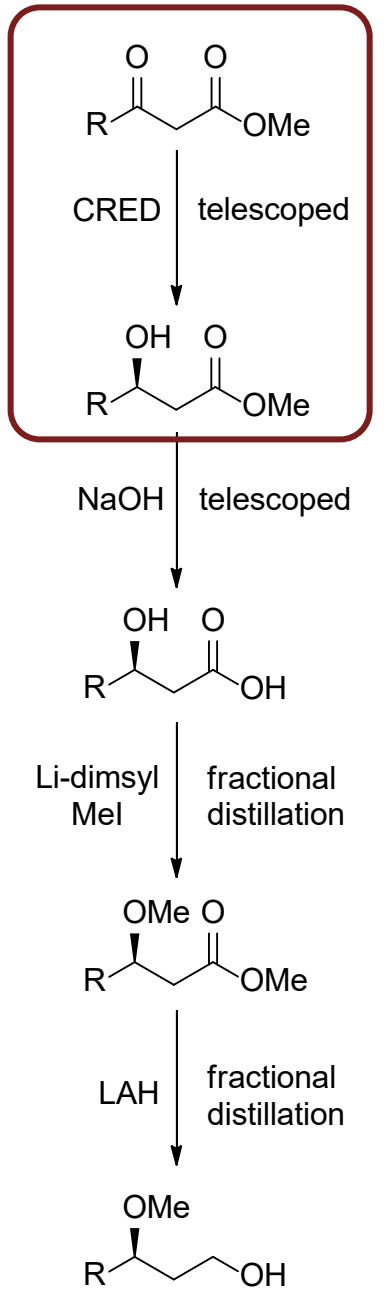
- Japanese client requires regulatory starting material for Phase 3 clinical trials.
- Chemocatalysis failed to deliver target specification (99.2%) for enatiomeric excess.
- New synthetic route, process development and multi tonne supply necessary.
- Strategies developed for control of:
  - Diol impurity
  - Vinyl impurity



Diol impurity



Vinyl impurity



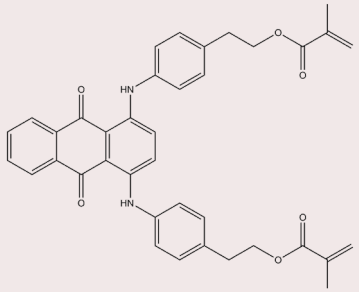
Case study: RSM manufacture (2 of 2)

Properties	Specification target	Specification achieved	
Enantiomeric excess	Greater than 99.2%	99.3%	✔
Named impurity (Diol)	No greater than 0.5%	Less than 0.2%	✔
Named impurity (Vinyl)	No greater than 0.5%	Less than 0.15%	✔
Named impurity (BHT)	No greater than 0.5%	Less than 0.2%	✔
Named impurity (Me-BHT)	No greater than 0.5%	Less than 0.2%	✔
Unnamed impurities	No greater than 0.1%	Less than 0.1%	✔

Core technology: Optical production suite

Case study: Products for optical industry

Monomers
ÙV blockers, Co-polymer
and Reactive Blue dyes



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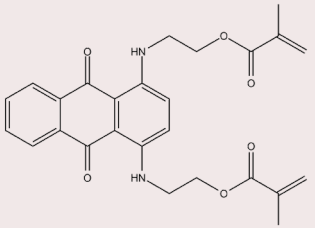

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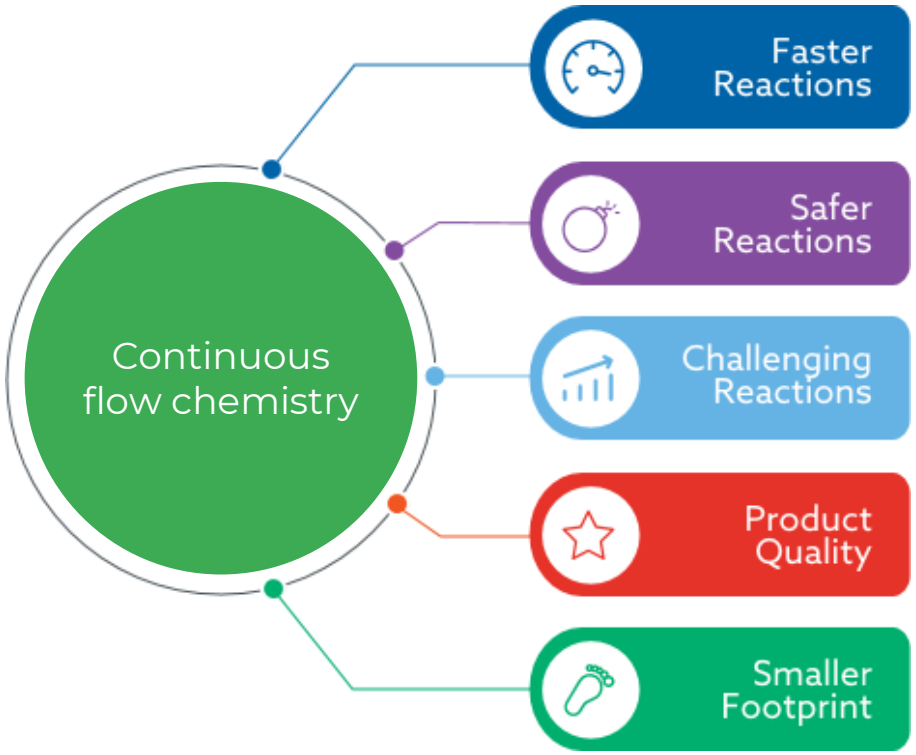
Core technology: Flow chemistry

- Design
- Screen
- Implement
- Manufacture



Case study: Price saving from flow hydrogenation

Description	Batch process	Flow process
Mass of substrate to process	117 kg	
Hydrogenation catalyst deployed	Pd on activated carbon	Pd on Al_2O_3 pellets
Loading catalyst	10% weight	1.07% weight
Mass of catalyst	11.7 kg	1.25 kg
Catalyst price contribution (EUR)	€49,217	€5,250

Core technology: Pilot plant

Glass lined

Stainless steel

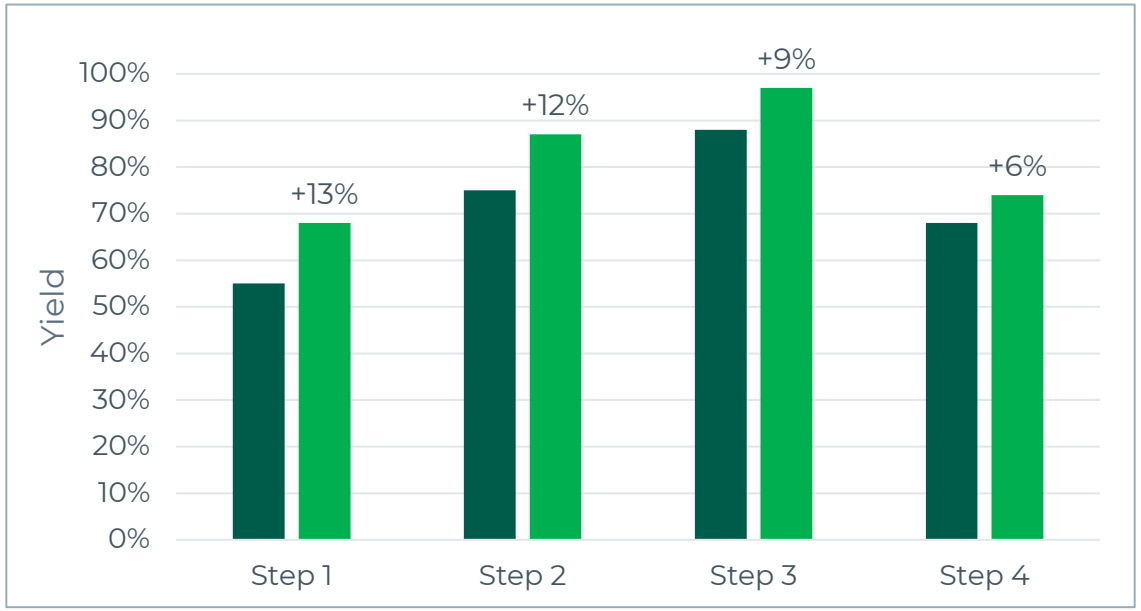
Hastelloy

Case study: Process optimisation (1 of 2)

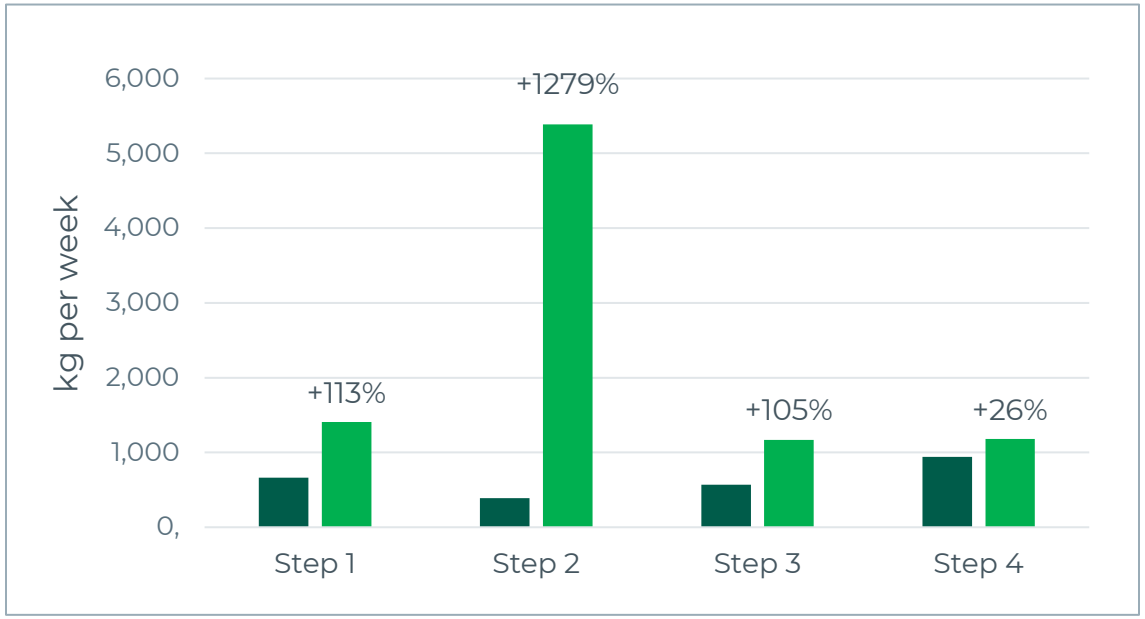
Step 1: Alkylation	• Reduction in reactor days • Reduction in solvent volume • Elimination of one processing solvent	• Elimination of solvent switch • Use of HCl (gas) instead of HCl (solution) • Improved mixing and agitation
Step 2: Boc protection	• Reduction in reactor days • Reduction of solvent volumes • Deployment of less expensive processing solvent	
Step 3: Cryogenic step	• Reduction in solvent volumes • Lowered reaction temperature to -25°C • Incorporated second reactor for quench and work up	• Computer modelling to optimise mixing and reactor fit • Deployment of less expensive quenching agent • Replacement of solvent mix (custom to commercially available)
Step 4: Hydrolysis	• Reduction in solvent volumes • Elimination of one processing solvent	

Case study: Process optimisation (2 of 2)

Yield



Throughput

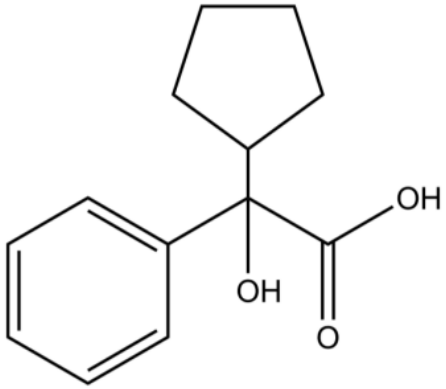


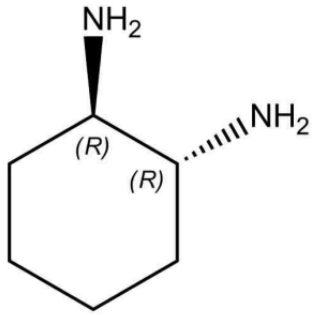
Before optimisation	EUR €1,154 per kg

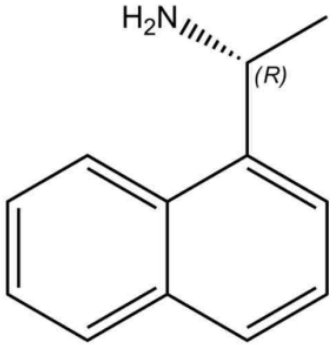
After optimisation	EUR €815 per kg

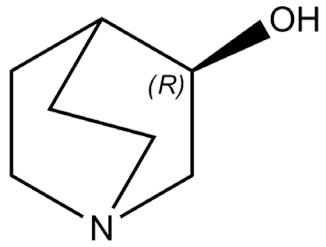
Core technology: Production plant

Case study: Regulatory starting materials









Cyclopentyl mandelic acid (and derivatives)	(R,R)-(-)-1,2-Diaminocyclohexane (and diastereomers)	(R)-(+)-1-(1-Naphthyl)ethylamine (and enantiomer)	(R)-(-)-3-Quinuclidinol
Glycopyrrolate (peptic ulcers)	Oxaliplatin (oncology)	Cinacalcet (hyperparathyroidism)	Ibiglustat (liposomal disease)
Hazardous Grignard chemistry	Classical chiral resolution	Leuckart chemistry	Biocatalysis technology
Maximum output: 12,000 kg per annum	Maximum output: 30,000 kg per annum	Maximum output: 20,000 kg per annum	Maximum output: 25,000 kg per annum

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Core technology: Distillation

- Distillation of thermally sensitive materials
- Falling film, thin film and short path
- Up to 200 L per distillation
- Arran has three falling film distillation units

Vacuum	Down to 1 mbar
Output	Up to 15 kg per hour
Materials	Stainless steel and glass lined

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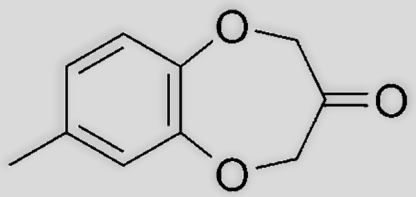
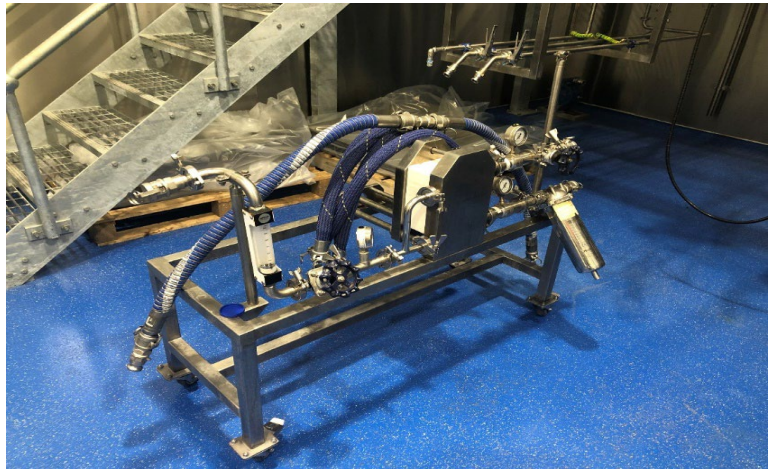
Case study: Manufacture of Calone (WMK)

- Europe’s number one supplier.
- Up to 35,000 kg manufactured by Arran in Ireland per year.
- Industry leading purity with intense marine aromatic note.
- Industry leading quality and environmental standards.
- “Just-In-Time” supply from 25 kg to multi-tonne with short lead times.



Calone (Watermelon ketone)
CAS 28940-11-6

Core technology: Protein purification



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Case study: iLipase beads

- Lipase enzyme immobilised on methacrylate polymer beads.
- Process development on bead formation (polymerisation) and enzyme immobilisation.
- Three clinical trials batches successfully scaled up.
- Approximately 15,500 kg commercial batches manufactured.

ALCRESTA
THERAPEUTICS

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Sustainability

1. Accountable waste stream processing
2. Strict control of gaseous emissions
3. Responsible Care® programme
4. Sustainable manufacture

Summary

- Arran builds long term relationships with companies seeking to develop and manufacture challenging fine and speciality chemicals.
- Manufacturing capacity is available at short notice.
  - This presents an excellent time to partner.
- Arran welcomes visits/audits of our headquarters in Athlone, Ireland and meetings at booth 715.

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