ALMAC

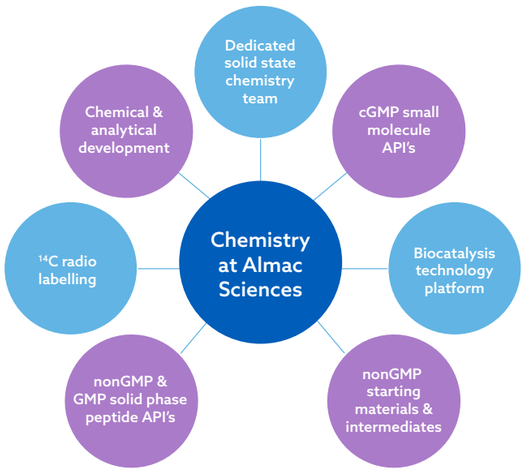
Partnering to Advance Human Health

Almac Sciences

API Services and Chemical Development: your molecule, our expertise

About Almac Sciences

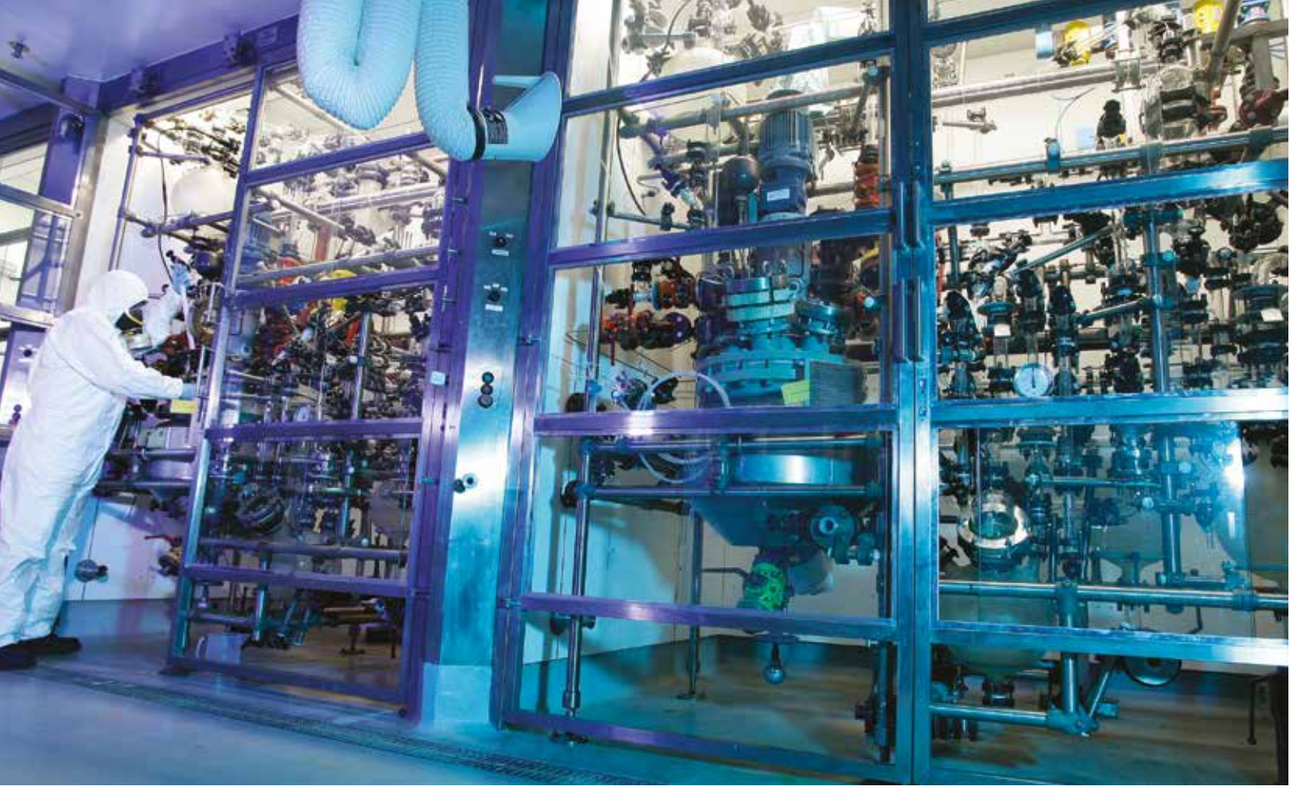
Almac Sciences is a provider of integrated services from development to commercial scale of advanced intermediates and Active Pharmaceutical Ingredients (API). We provide a range of services for small molecules (including highly potent) and peptides. We have a proven track record of saving time and costs through the integration of our services and application of innovative biocatalysis and technology solutions.



We have responded to our clients' needs of leading their molecules through clinical development faster, smarter and cost effectively, ensuring projects are delivered to the highest quality, on time and in full.

As part of the wider Almac Group, we are a stable, privately owned business that is growing globally in line with increased customer demand.

Almac Sciences...an integrated chemistry provider



API Development & Manufacture

Our technical expertise and extensive facilities enable us to offer integrated API contract manufacturing solutions through all stages of the drug development lifecycle. We are fully supported by dedicated analytical and regulatory teams.

We offer numerous support capabilities, including:

- rapid implementation of chromatography for purification
- containment equipment for potent compounds
- micronisation to control particle size

Our dynamic team successfully address many complex project challenges, and implementing our on-site biocatalysis technology expertise is one example of our responsive solutions.

Early clinical phase

We have significant experience in the first time scale-up of APIs. Starting with the medicinal chemistry route, our knowledgeable chemists can quickly identify the most pressing parts of the chemistry to develop.

Our chemists work closely with our development analysts and production teams to ensure that controls are appropriately embedded into the process IPCs, intermediate specifications and processing instructions. The salt form and polymorph landscape are explored within our physical sciences teams and drive the development of the API isolation process. Particle size is controlled through our micronisation suite.

Late clinical phase

We have an established reputation for developing processes for late clinical stage. Our extensive experience lies in taking processes from inception through to process validation, both in small molecule chemistry and peptides.

As an API moves from early clinical phase towards late clinical phase, the emphasis of the project changes. Whereas in early clinical supply, a lean fit-for-purpose approach is appropriate, other factors start to dominate when moving towards late phase, particularly process efficiency and knowledge. We strategically integrate the principles from regulatory guidelines (FDA, ICH, USP), such as risk management and quality by design, as a basis for development and manufacturing strategies.

Highly potent manufacture

We have responded to the growing need for manufacture and handling highly potent compounds, including cytotoxics, in a dedicated and separate contained manufacturing suite.

Our evaluation process begins with a thorough review of current knowledge of both the API and intermediates, including the appropriate health and safety, toxicology and operations experts. Comparison to known compounds is used and additional testing is carried out where necessary. Clear SOPs and operating instructions are generated based on this thorough review.

We are one of the first companies in Europe to receive SafeBridge certification. Our containment and isolation facilities allow the handling of compounds with OELs down to 0.1 µg / m3. We use isolators in a GMP Class 100,000 facility, featuring pressurised anti-rooms, door interlocks and separate equipment and personnel movement.

Facilities

The non-GMP manufacture of APIs up to 1 - 2 kg is performed in our kilo lab, in reactors ranging from 30 L to 100 L.

The GMP manufacture of APIs up to 100 kg is performed in our GMP manufacturing plant. Our reactors range from 100 L and 1000 L, with capabilities for hydrogenations, cryogenic chemistry, photochemistry and ozonolysis, as well as a very wide range of operational capabilities for API manufacture.

Appropriate containment is provided for potent compounds, including contained micronisation capability and a dedicated and separate contained cytotoxic suite.

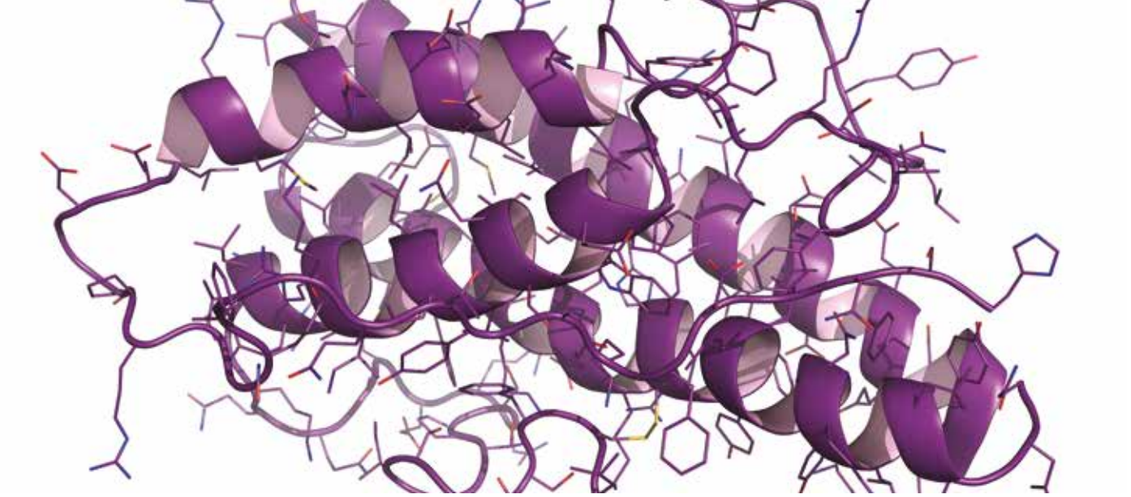
Why choose Almac for API development & manufacture?

Our reputation and strength in API development and manufacture precedes us within pharma and biotech companies who seek integrated drug development solutions from molecule to market. Our technical expertise and extensive facilities enable us to offer integrated API contract manufacturing, on one site through all stages of the drug development lifecycle.

Complementing our API services, we support a world-leading biocatalysis platform to secure the supply of biocatalysts for non-GMP and GMP manufacturing projects alike. Additionally our services are supported by specialist departments, including ^{14}C radiolabelling, preformulation, solid state services and analytical support, ensuring the needs of your drug development programme are fully met whilst maintaining our track record of saving time and cost.

"We retain our business with Almac because their technical approach, expertise and communication through project management cannot be matched."

Client testimonial



Peptide & Protein Technology

Almac's Peptide and Protein Technology (PPT) group has been manufacturing peptides for the research community and clinical trials development since 1994. We place significant emphasis on peptide synthesis methodology and have manufactured well over 10,000 peptides for the research community. Focussing on the delivery of high quality products, we have developed a highly differentiated skill set allowing us to tackle challenging projects such as long peptides (>100mers), macrocyclics and conjugates.

Almac has two UK-based sites. Our site in Edinburgh, Scotland focuses on high throughput manufacture for non-GMP research use, and our global HQ site in Craigavon, Northern Ireland on cGMP manufacture.

Non-GMP custom synthesis

Our high throughput, non-GMP group uses the latest peptide manufacturing methodology and equipment for the rapid custom manufacture of peptides for researchers across the globe. Whether the supply of a single peptide for a one-off experiment, or the manufacture of hundreds of peptides for protein mapping, or a clinical lead generation programme, Almac can deliver. Our service is totally customised and we can manufacture peptides that are linear or cyclised, standard or modified, on the milligram to gram scale.

We can incorporate the full range of modifications to your peptide sequence:

- Probes such as biotin or fluorophores
- Cyclised peptides: macrocyclic, side-chain stapling, single or multiple disulphide bridges
- Post-translational modifications such as methylations, phosphorylation and glycosylation

Even in the simplest of projects, Almac will keep the client aware of progress in the manufacture, as well as delivery, so that the client can effectively plan experiments.

Conjugation expertise

Almac has a long standing interest, and over 15 years' experience, in the art of conjugation. Increasingly, chemistry is called upon to join peptides to proteins or other moieties such as fatty acids or PEGs in order to impart favourable qualities such as stability, receptor targeting or half-life extension. In particular, we enjoy a successful collaboration with Albumedix in conjugation of peptides with albumin through their Veltis® platform.

Almac has experience in a wide variety of conjugation chemistries to ensure control and selectivity:

- Thiol – maleimide
- Thiol – bromoalkyl
- Thiol – thioester (native chemical ligation)
- Amine – NHS
- Alkyne – azide ("click" chemistry)
- Aminooxy – aldehyde
- Hydrazide – aldehyde

"We've been working with this molecule for nearly 15 years, and still Almac taught us things about it we didn't already know."

Client testimonial

Specialist catalogue reagents

Almac also provides a range of specialist catalogue products for use in basic research. These reagents are available from stock and shipped within 24 hours of ordering.

Chemokines (wild type, biotin, AlexaFluor® 647 labelled): Chemokines are a family of cytokines comprising 70-80 amino acids, and containing two or more disulphide bridges. They are involved with immune responses and implicated with a range of therapeutic areas such as inflammation, oncology and anti-virals.

Histones: This family of proteins are 120-150 amino acids in length, with high degrees of post translational modifications including Lys/Arg methylations and Ser phosphorylations. Histones are involved with packaging DNA into structural units (nucleozomes), and the reagents are used to investigate wide ranging enzymatic activity.

Ubiquitins: Ubiquitin binds to a range of substrate proteins to mark them for degradation or affect their activity through surface Lys or Cys residues. We have a range of ubiquitylated substrates to act as probes investigating enzymatic pathways.

Almac has over 60 wild type and modified chemokines, 20 histone and ubiquitin reagents available from stock, and is also able to provide custom synthesis of bespoke reagents.

GMP peptide manufacture

Almac has been manufacturing GMP peptides since 2007, and has a strong reputation for expertise and service delivery. Our client base is derived across the academic, biotech and pharma sectors through Europe, North America and Asia. All our cGMP projects benefit from support from our experienced project management, analytical and quality assurance functions.

First in human

We have manufactured numerous peptide drug substances for First in Human trials. The package provided can be tailored according to the experiences and needs of the client. Whatever the content, the aim of the package is to ensure that material is provided for the first patients quickly, and under cGMP control. We ensure robust process development techniques are used to define an appropriate manufacturing process for each peptide and we are experienced in defining new processes, or in transferring in existing processes. We have helped multiple SME clients who have since licensed their projects to large pharma, with Almac continuing supply.

Peptide vaccine cocktails

An increasingly popular approach is to use multiple peptides in therapeutic vaccines in fields such as oncology and anti-allergy. Such approaches involve the manufacture of multiple peptide drug substances which are combined in a drug product cocktail for use as a vaccine. Cocktails present multiple technical and logistical challenges which Almac is experienced in overcoming through the delivery of multiple projects.

Late phase and commercial

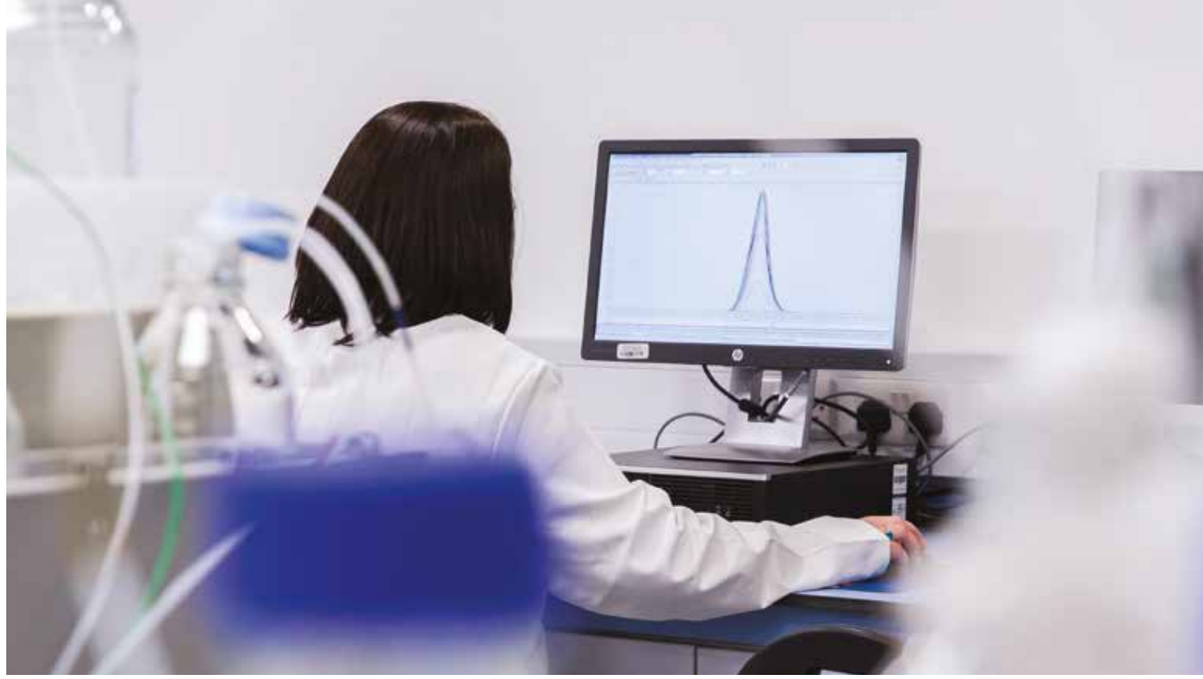
Almac is also experienced at delivering late phase clinical programs towards commercial manufacture. Here the focus is in ensuring a strong understanding of the parameters influencing variation within a manufacturing process and in delivering cost of goods targets. We follow industry guidelines on process validation, utilising modern Quality by Design methods. The key here is to build a full understanding of the manufacturing process, analytical methods, facilities qualification and cleaning procedures. We achieve this through our bespoke Process Validation Roadmap.

Why choose Almac for peptides?

Almac has developed a reputation for sound technical capability and excellent customer relations skills. We achieve these capabilities through structured knowledge management and a culturally embedded project management philosophy bringing together multidisciplinary teams for drug substance manufacturing programmes. Our highly motivated teams work tirelessly to deliver projects to customer requirements.

Client testimonial: "We found the methodology Almac used to transfer the process to their facility was really well structured. We've started to use the same approach for our internal projects."

Client testimonial



Analytical Services

From our state-of-the-art FDA and MHRA audited laboratories in the UK and US, we employ over 250 highly trained analytical scientists with expertise in all areas of drug development, including small molecules, peptides, conjugates and potent materials. Drawing upon our vast pool of scientific knowledge, we can greatly reduce the analytical challenges that typically arise during drug development.

Utilising a wide range of instrumentation, Almac will deliver fit-for-purpose solutions to match your analytical requirements.

Clients who use Almac to release drug substance and drug product in the EU and US benefit from shortened transfer time, cost savings and minimized disruption thanks to scientific and procedural continuity. Almac is unmatched in its ability to manufacture clinical trial supplies and provide analytical support.

"Almac's Analytical Team continually demonstrate that we can rely on their services and timelines as promised."

Client testimonial

Drug substance & drug product testing	Analytical support for clinical supplies
Physical & chemical characterisation	Method development & validation
ICH stability testing	Release testing of commercial product

Why choose Almac for analytical services?

Communication and scientific continuity are key, whether your analytical requirements are stand-alone or form part of a drug development or commercial manufacture project. Our analytical scientists work with our drug substance and drug product formulation scientists, forming an integral part of the project team. This means they can share data, easily coordinate planning and scheduling and deliver maximum efficiency.

Solid State Services

Our Physical Sciences group unites chemists, analysts and formulators in one team, adding value through synergy. They have a considerable breadth of expertise in form screening and selection, so they can skilfully guide you to make the right decisions at the right time.

We develop and validate processes and methods to control and deliver the desired form during scale-up, troubleshoot existing problems and provide support for your intellectual property.

	Solid State Characterisation	Solid state screening & API manufacturing support	Preformulation / enabling formulation	Stability
Small Molecules	Crystallinity Hygroscopicity Particle size, shape surface area Moisture / solvent content	Polymorph screening Salt / cocrystal screening Amorphous dispersion screening Stable form determination Crystallisation development	pH-solubility profile, pKa & logP Permeability BSC classification Solubility in pharmaceutical solvents & bio-relevant buffers formufast™ screening	Development of stability indicating LC-MS method Solid state stability (heat, humidity, light) Solution stability (pH, oxidation heat, light)
Peptides	LC-MS Absorption & fluorescence spectroscopy Circular dichroism NMR	Enabling salt screen	Solubility in pharmaceutical solvents & bio-relevant buffers Precipitation assessment	

Our highly skilled scientists have undertaken thousands of studies that range from routine analysis to challenging characterisation under GMP studies.

Why choose Almac for solid state services?

We are experts in solid state chemistry. We understand that identifying and consistently producing a drug in its optimal physical form is vital to the success of drug development programmes, and we ensure our services are specifically tailored to our clients' needs. We have a proven track record with >150 virtual, biotech and large pharma clients in screening, troubleshooting and providing analytical solutions spanning the entire drug lifecycle.

"Given their expertise in drug substance and drug product development, Almac's Physical Sciences Team were especially well positioned to identify physical forms that may give rise to valuable sources of intellectual property."

Client testimonial

^{14}C Radiolabelling

We provide industry-leading ^{14}C labelled drug substance and drug product services to meet your quality, cost and delivery expectations. With our extensive experience in the synthesis and analysis of stable and ^{14}C isotope labelled compounds, we can label any compound from simple molecules to complex structures including small molecules, peptides and bio conjugates, in our MHRA approved facilities.

^{14}C is the radioisotope of choice in preclinical and clinical ADME studies, avoiding the challenges encountered with tritium labelling such as label exchange and the loss of label due to radioactive decay.

Isotopic labelling imposes many synthetic challenges beyond those found in normal chemical synthesis, and when the isotope is radioactive this adds further safety and regulatory requirements. By choosing Almac as your isotope labelling provider you will have access to our wealth of experience in both stable- and radio-labelled synthesis.

We provide a complete suite of solutions for your needs, including: non-GMP and GMP radiolabelling / stable labelling, bio conjugate labelling, quality control and analytical support (including method development, validation / transfer and stability studies), storage and repurification.

Why choose Almac for ^{14}C radiolabelling?

Our proven track record in synthesis and purification, coupled with our seamless analytical and QC integration, ensures your labelled product will be manufactured with the desired chemical and radiochemical purity and rigorously analysed using validated equipment. Our strong quality culture will ensure the material manufactured will satisfy the requirements of the the relevant regulatory authority.

"I was very impressed by the planning and execution by the Almac ^{14}C team in the GMP synthesis of our target. Timelines and goals were met. The team also showed flexibility to respond to our ever changing needs"

Client testimonial

Biocatalysis

Almac is recognised globally as a key player in the area of biocatalyst research, development and commercial supply of biocatalytically derived achiral and chiral products at multi-tonne scale. Our expertise ranges from enzyme discovery, engineering and screening to the enzyme applied synthesis of complex chiral products, all based on Almac's selectAZyme™ technology.

Almac has an established platform technology for the secure supply of selectAZyme™ biocatalysts for clients' non-GMP and GMP manufacturing projects. Biocatalysts are now essential tools in chemical synthesis and offer a direct and simple way to synthesise complex achiral and chiral compounds.

Our exclusive selectAZyme™ technology platform consists of multiple recombinant enzyme panels that can be used in chemical processing across multiple functional group interchanges. Enzymes can offer attractive new synthetic routes to compounds and can deliver best-in-class synthesis that offer many advantages over traditional chemistry, such as lower waste, fewer processing steps, high purity and lower cost.

Expertise includes

- Enzyme discovery and engineering
- Active site modelling and enzyme design
- Enzyme kits and bulk supply
- Fermentation development and scale-up
- Enzyme immobilisation development and supply
- Bioprocess and process development
- Bulk manufacture of chemical and biochemical derived products
- Metabolite synthesis

Why choose Almac for biocatalysis?

We can help take your project from conception to scale-up.

Our biocatalysis group consists of computational, molecular and microbiologists, enzymologists, organic chemists and analysts, and have demonstrated expertise in in gene identification, expression, enzyme evolution, fermentation, enzyme production and biotransformation scale-up.

Our team is closely linked to the process chemistry and manufacturing chemistry groups, where enzyme discovery and development is integrated with screening and route definition. Each member of the team brings expertise to complex processes and procedures and can rapidly implement an enzymatic process to significantly improve the yield and timelines of a multistep synthesis.

"I can fully recommend Almac as a partner of choice in the area of bio-processing, enzyme immobilisation and chemistry scale-up."

Client testimonial

Arran Chemical Company

Arran Chemical Company is a member of the Almac Group and part of Almac Sciences. Arran specialises in the manufacture of chemical products for pharmaceutical and health care, flavour & fragrance, personal care and other specialised chemical and industrial applications at kg to tonne scale. We have been established for over 30 years and were acquired by the Almac Group in 2015.

We are specialists in chiral chemistry using both chemocatalysis and biocatalysis selectAZyme™ technologies. We have an excellent track record on process development and bulk supply of chemical intermediates with expertise over a wide range of modern synthetic reactions. The combination of our exclusive biocatalysis technology platform with our large scale manufacturing assets allow fast supply of advanced intermediates from kg to multi-tonne scale.

arran
CHEMICAL COMPANY LTD
A Member of the Almac Group

arranchemical.ie

Expert Supporting Services

Partnering with Almac Sciences, you will have access to our support teams who are critical for the execution and delivery of our clients' complex projects.

Project Management
We understand our clients' needs to progress their projects smarter, faster and cost effectively and our Project Management team include experienced scientists with significant industry experience who work closely with clients to anticipate and respond to project priorities.

A dedicated Project Manager is assigned at contract acceptance and acts as a single point of contact to ensure that all key deliverables and timelines are met and that regular communication is provided through the project lifetime.

Our service is tailored around clients' specific needs and we act as a trusted advisor to many of the Pharma and Biotech companies we partner with.

Quality Assurance
We pride ourselves on meeting the highest standards of quality and safety. Our FDA and MHRA inspected facilities are routinely audited and our quality accreditations demonstrate that we meet these standards, providing complete confidence to our clients.

almacgroup.com

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