

Heraeus



**Highly Potent  
Active Pharmaceutical Ingredients**



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## Heraeus – from Platinum to hAPIs

Heraeus is an innovative, globally active precious metal and technology group based in Hanau, near Frankfurt am Main/ Germany. The company has been family-owned for 160 years - its business covers precious metals, materials and technologies, sensors, biomaterials, medical and pharmaceutical products, quartz glass, and specialty light sources.

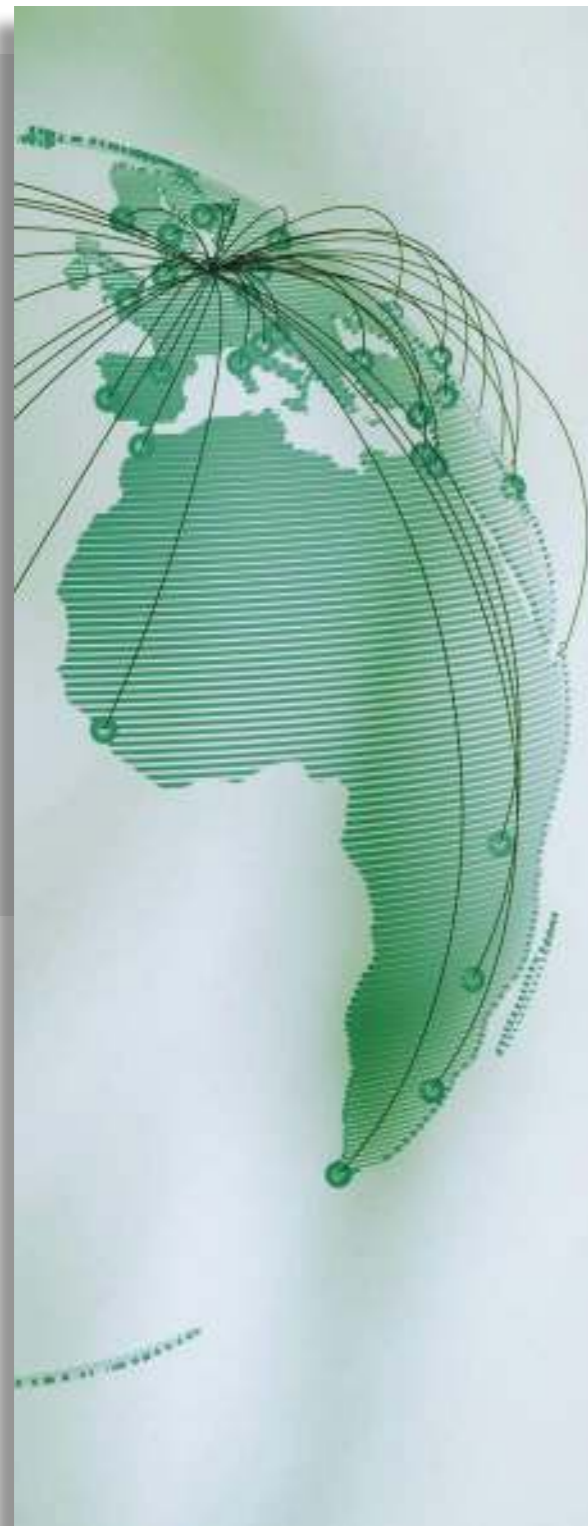
Heraeus Precious Metals GmbH & Co. KG is a world leader in industrial precious and special metals. A global network of companies in Europe, North America, Asia, and Africa includes first class production facilities for all phases of precious metal production and refining. With decades of expertise based on precious metal trading, the business group provides professional precious metal management

throughout the precious metal cycle. Heraeus Precious Metals' core clients operate in the environmental, mobility, communications, and energy sectors, and also in the growing health care industry.

The outstanding experience in the ambitious handling and processing of precious metals has served as a basis for today's activities of Heraeus' Pharmaceutical Ingredients Business Unit: the development and commercial production of highly potent APIs (hAPIs) for cancer treatment.

Additional information on Heraeus' outstanding history, its diversity and its Vision and Mission is available at [www.heraeus.com](http://www.heraeus.com).

## A Global Player in a Global Market



For some 30 years Heraeus has been a reliable and innovative partner to pharmaceutical companies around the globe.

We provide exclusive contract services in the field of hAPIs and in strict confidentiality throughout all phases of a product's life cycle. Long-term, reliable partnership is an essential element of our company policy. Our technical team works for your proprietary products on all scales from R&D to commercialization.

A selected portfolio of generics complements these activities. Heraeus holds a leading position in the market for platinum hAPIs as well as for various other high potency molecules.

The industry's demand for high-tech, profitable and economic production processes of increasingly complex molecules oblige also hAPI manufacturers to enter new technological paths.

Heraeus perceived this trend early-on and continues to invest into innovative facilities and technologies. Today our Pharmaceutical Ingredients Business Unit can offer a broad range of capabilities: from sophisticated inorganic chemistry to organic synthesis.

## "Made in Germany" in Full Compliance

All our hAPIs are fully developed and manufactured at our parent site in Hanau/Germany. We have been FDA-approved for more than 25 years and have an excellent track record with all major Health Agencies. The statutes of our company include a detailed Code of Conduct strictly regulating our activities in compliance with all applicable laws.

Our company guidelines enable us consequently to meet all rules and regulations required by the environmental legislation in Germany and the EC. We employ sustainable processes and "Green Technology" wherever possible.



## Production

Heraeus has developed the full range of Pt-based hAPIs for cancer therapy. From multiple facilities at our main site in Hanau we serve our customers in all pharmaceutical markets worldwide. Due to our comprehensive expertise and reliable services we have gained the status of the preferred manufacturer of platinum anti-cancer hAPIs.

Our key features are:

- 100% experienced and qualified team
- in-house precious metal sourcing
- precious metal refining
- most products supplied ex stock
- all reference standards available
- back-up facilities
- successful history with innovator companies
- continuous 5S and LEAN program

For the "Platinums" we offer comprehensive contract development and production services for the whole life cycle of a pharmaceutical product, i.e. in all preclinical, clinical, and commercial phases.

Using the skills and knowledge in manufacturing Pt-based hAPIs, Heraeus took the next step some 15 years ago to synthesize organic hAPIs.



Our outstanding capabilities include:

- metal compounds
- highly toxic products, e.g. aziridine and thio derivatives
- natural and complex molecules
- alkylating agents
- photochemical and diazotation reactions
- conjugation technologies

Heraeus' manufacturing facilities have fully closed reactor trains to meet the highest safety standards. Our production capacities are mainly glass-lined equipment and range from 20 L to 2,000 L. We are licensed even to handle chlorinated solvents and highly corrosive reagents.



## Custom Manufacturing

Long-term experience in the field of hAPIs is the foundation of our exclusive contract manufacturing services:

- strict protection of customers' IP
- a unique high containment R&D site
- a specialized R&D team with ever curious, experienced scientists
- fully dedicated project management.
- advanced process development and optimization
- comprehensive GMP documentation
- outstanding global regulatory support
- establishing required analytical methods and reference standards
- batches from gram to 100 kg scale
- proven track record with multinational companies and "Spin-offs"

Decades of experience are waiting to contribute to your success!



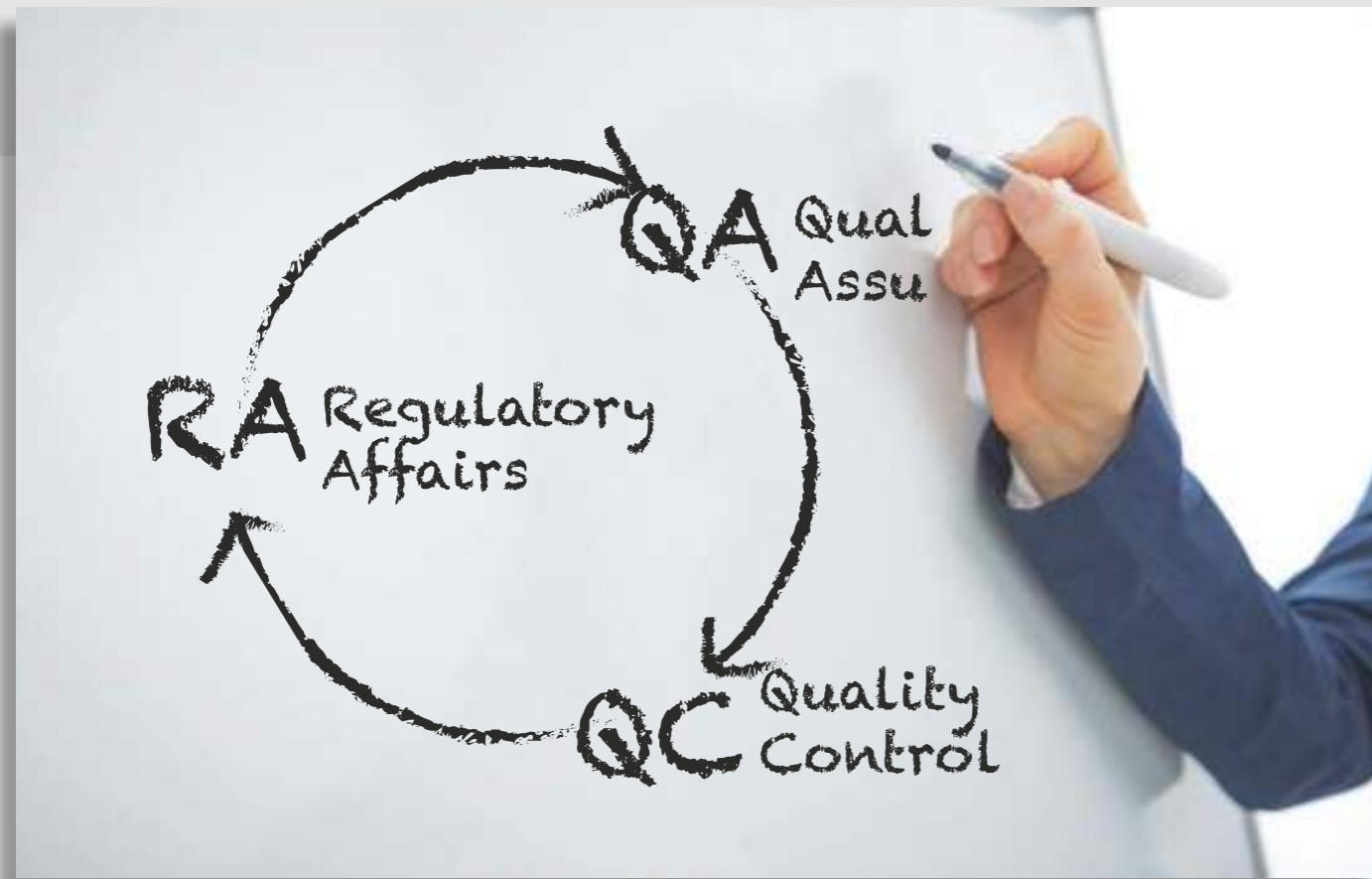
# Quality Assurance

Heraeus' Quality Assurance department (QA) constantly secures the outstanding quality of our active pharmaceutical ingredients and strictly follows international regulations. Our products and processes are developed and continuously adapted to current ICH guidelines in line with the international cGMP requirements.

Heraeus' quality standards and Environmental, Health and Safety Policy (EHS) fully meet the various increasing national and international requirements. Our Quality Assurance department is organized in accordance to DIN EN ISO 9001:2008, and Heraeus Precious Metals GmbH & Co. KG is certified according to ISO 14001:2004.

The focus of our team is to improve the quality, safety and environmental standards constantly. We consider partnership with you to be a matter of full and long-term reliability. The highest quality of our hAPIs and service is the core of our activities.

The translation of instructions and processes always conforms to valid GMP standards. Regular and thorough audits and inspections by our customers, by the national and international authorities (e.g. the Food and Drug Administration, USA) and by relevant certifying bodies validate the extraordinary quality system of our Pharmaceutical Ingredients Business Unit. Quality is our priority!



# Regulatory Affairs

Heraeus' Regulatory Affairs group (RA) prepares and maintains all documentation for initial and existing registrations worldwide.

Our successful market entry with transparent communication confirms that Heraeus is fully compliant with the strictest requirements for the quality of its hAPIs.

Our preparation of dossiers covers:

- registration documents according to current ICH standards
- all relevant Pharmacopoeias (e.g. Ph. Eur., BP, USP, JP, IP, CP)
- ASMFs based on customer requirements
- CEPs for all hAPIs with a pharmacopoeial monograph
- technical information packages
- eCTD submissions and non-eCTD electronic submissions (NeeS)



We manage the registration for you:

- procedures consistent with current guidelines and predetermined timeframes
- assistance in providing additional technical information
- competent personal contact during all parts of registration

Our life cycle management includes:

- regulatory support for existing products
- continuous improvement of documentation
- established change control system
- professional change management with customers and authorities according to the current Variation Regulations

Regulatory Affairs – a core competence of Heraeus!

## Quality Control

## Heraeus – Top in Anti-Cancer hAPIs



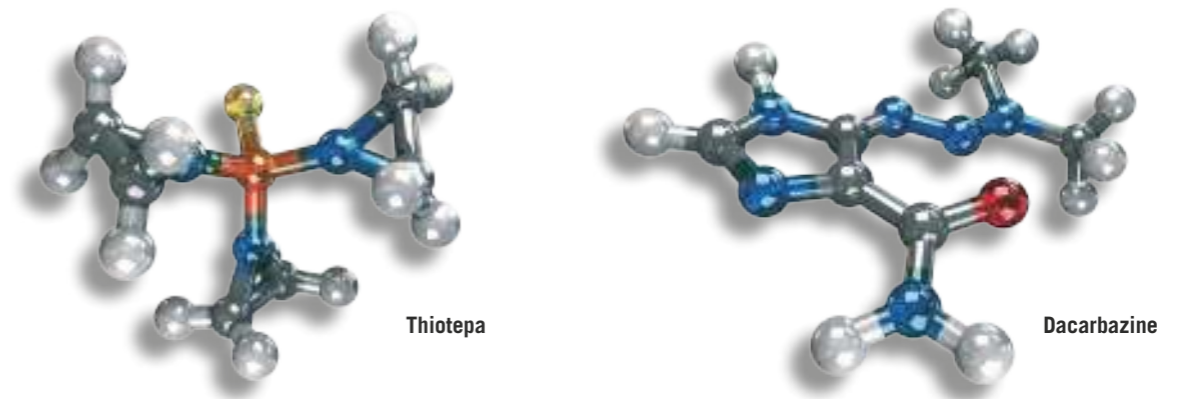
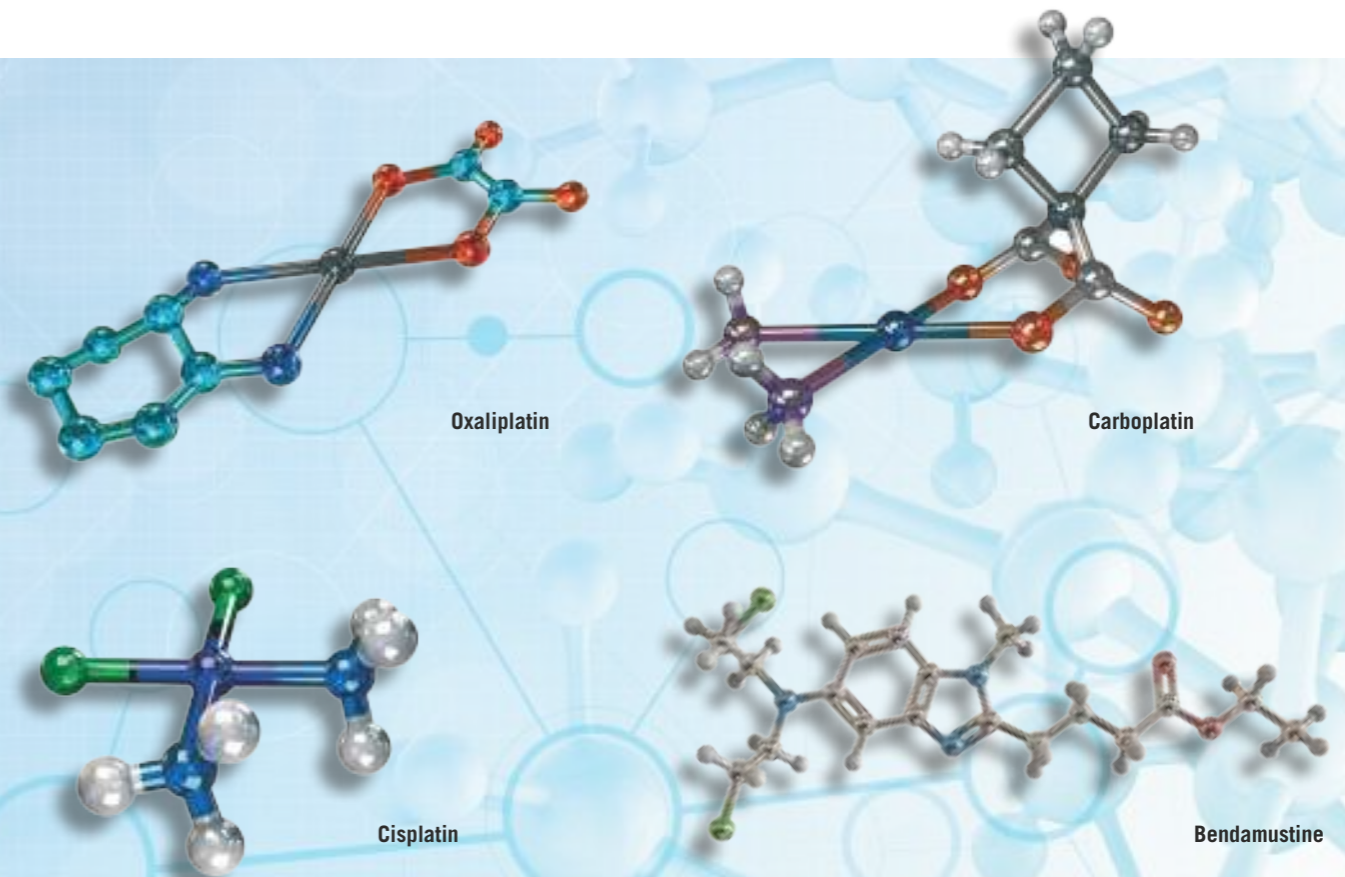
Extensive analytical capabilities and full reliability of a partner are extremely important to pharmaceutical clients worldwide. With more than 160 years of experience in quantitative precious metal analysis with highest accuracy and some 30 years in the quality control (QC) of hAPIs, Heraeus is thoroughly established in performing a wide range of the latest analytical techniques.

Heraeus' dedicated QC department acts independently from our Pharmaceutical Ingredients Business Unit, which ensures 100% objective data and services. All work on in-process control, raw materials, intermediates and release testing of hAPIs is conducted according to cGMP and ICH guidelines.

Heraeus' QC services are outstanding:

- comprehensive stability testing programs for both hAPIs and Finished Dosage Forms
- fully characterized reference standards for all our hAPIs
- analytical and technical support during development and commercial production at customers' sites
- development and validation of cleaning procedures – our team is specialized in the analysis of species in rinsing solutions and swabs from the production of platinum-based hAPIs
- identification of impurities and degradation products
- modern analytical methods, e.g. HPLC, GC, IC, FTIR, UV, ICP, DSC, TGA, KF, AAS, XRF, XRD
- advanced analytical technologies, such as UPLC and Raman spectrometry
- close and long-term partnerships with external providers of special analytical technologies
- development and validation of analytical methods
- NMR and MS (in cooperation with an external laboratory)

Heraeus' QC – it's a comprehensive service!



Call us for our products above or our services to your NCEs:

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