

Definiens provides effective candidate support

CASE STUDY

ALTANA Pharma AG

ALTANA Pharma AG is a part of Nycomed, a leading European pharmaceutical company with operations all over the world. ALTANA employs around 8,600 people and provides a range of innovative pharmaceutical products with a focus on prescription drugs for gastrointestinal and respiratory diseases.

In a pre-clinical safety study, Definiens' technology automatically measured the height of the fundic and antral mucosa in rat stomachs. The study identified a potentially toxic compound, supporting ALTANA's 'no-go' decision for an expensive clinical trial. ALTANA has now adopted Definiens as its image analysis platform for selected pre-clinical safety assessments.

Background

ALTANA owns a valuable ATPase inhibitor, marketed under the trade name Pantoprazole. Annual sales of the drug are €1.4 billion worldwide. The compound comes off patent in 2010 and ALTANA is keen to find a replacement.

The Challenge

The Institut für Präklinische Arzneimittelsicherheit (IPAS) is the preclinical site of ALTANA and conducts in silico, in vitro and in vivo safety studies for drug candidates.

IPAS was engaged to study cell proliferation in the gastric fundus of rats as part of a safety assessment of potential successor compounds to Pantoprazole.

For the study, IPAS wanted to measure the height of the fundic and antral mucosa of the rat stomach as well as the number and area of particular structures called eosinophilic aggregates in the gastric fundus which are formed under treatment of acid secretion inhibition.

The study used Ki67 to detect mitosis which in turn indicated proliferation of cells in the gastric fundus and the newly formed eosinophilic aggregates. The study was carried out in two different rat strains, in controls and dosed animals. The critical challenge was analyzing the images to identify and measure the fine structures involved.

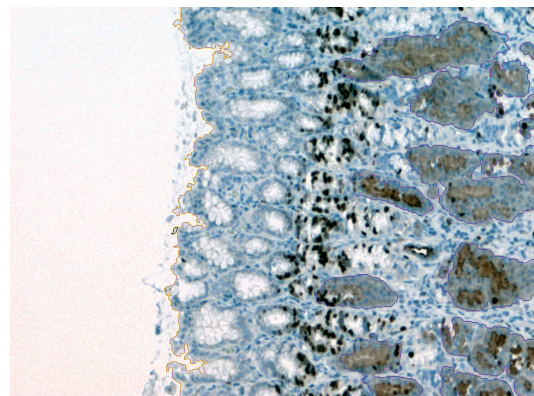
"Image analysis has always been the bottleneck when evaluating drug candidates," says Dr. Tuch, Head of Toxicological Pathology at IPAS.

The Solution

IPAS was using a semi-automated image analysis system. This was very time consuming since a pathologist needed to examine every image of every slide and take measurements. Furthermore, distinguishing between a Ki67 positive nuclei and a Ki67 negative nuclei can be a subjective judgement, even for experienced pathologists.



A Normal gastric fundus mucosa



B Eosinophilic aggregates in the mucosa of high dose treated rats

Together with a Definiens' consulting team, IPAS developed an image analysis application using Definiens Enterprise Image Intelligence™ Suite. Since the number of images was small, IPAS chose to develop a semi-automated solution that could be built quickly. The application identified regions of interest, which were then checked by a pathologist. The required measurements were then performed automatically.

"Definiens is a self-learning system. You can teach it to identify and detect structures in complex images," explains Dr. Tuch. Images can be imported into a database and analyzed automatically in batch mode.

The application was developed and calibrated in just 4 weeks. The images were analyzed in a matter of days as opposed to the estimated 16 weeks for manual processing and the amount of time required by a pathologist to check each image was just 30 seconds.

The Results

Dr. Tuch was struck by the quality of the analysis produced by Definiens' technology.

"Definiens exactly identified all Ki67 labeled cell nuclei. Even when analyzing images of high heterogeneity, Definiens provided data with high precision, which was impossible with pixel-based image analysis systems."

"With Definiens, image analysis results are much less dependent on the quality of staining and image acquisition. For large volumes of images the time to completion is reduced enormously coupled with a significant increase in quality and objectivity."

ALTANA adopts Definiens

As a result of the study, Definiens' technology has become an integral part of the process of evaluating drug candidates at ALTANA.

"Definiens is our platform of choice and is applied in selected routine toxicologic pathology assessment," says Dr. Tuch. "It enables an automatic extraction of regions of interest to discriminate changes in the histological slides of organs investigated. Furthermore, the automated workflow increases throughput dramatically which gives us a much more accurate picture of possible changes due to toxicity in the early stage of the drug development process."

ALTANA is setting up a Pathology Centre of Competence in Hamburg for image content analysis studies.

"In the new Centre, Definiens will make an important contribution to toxicologic assessment," says Dr. Tuch. "Moreover, Definiens software will be used on an enterprise-wide basis to solve problems for other departments."

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Definiens is the number one Enterprise Image Intelligence™ company for analyzing and interpreting images on every scale, from microscopic cell structures to satellite images.

The patented Definiens Cognition Network Technology®, developed by Nobel Laureate Prof. Gerd Binnig and his team, emulates human cognitive processes of perception to extract intelligence from images. If you are interested in learning more about how Definiens could address the challenges you face, please contact us at info@definiens.com or visit our website at

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