

## Use case

# Enabling a modern, efficient approach to pharmacovigilance



# A modern, cost-effective approach to pharmacovigilance

It is not possible for clinical trials to be either sufficiently large or sufficiently long to detect all potential safety issues associated with a drug, such as those with a low incidence rate or those resulting from drug-drug interactions.

Regulatory bodies require all Pharmaceutical companies to establish Pharmacovigilance teams dedicated to the detection, assessment, monitoring and reporting of potential adverse events identified in patients taking their medicine and ultimately for the prevention of such events.

However, maintaining safety and compliance amid evolving, globally diverse and increasingly stringent regulations puts significant demands on resource-constrained Pharmacovigilance teams.

Here we describe examples of how SciBite’s customers are leveraging our technology to deliver resource-effective solutions to address the challenges faced by their Pharmacovigilance teams, enabling efficient and comprehensive monitoring of adverse events reported by patients and clinicians and safety signals derived from a wide range of heterogeneous and cross-disciplinary sources.

## Intelligent Automation of Adverse Event Case Management

Every year a typical Pharmaceutical company can receive hundreds of thousands communications, or cases, related to potential adverse events. Increased patient engagement, such as through patient support programmes, and new product releases coupled with data from new sources, such as growing use of connected smart devices actually results in more cases to process year on year.

Challenges associated with the growing volume of cases are exacerbated by the wide variety and range of quality of the information provided: pharmacovigilance teams receive information in various formats including emails and handwritten notes in different languages and formats, making the data hard to manage. Converting each case from its initial format to one that can easily be reviewed by regulators is a complex, highly manual process. Each case needs to be read, interpreted and prioritised. The vast majority of cases do not mention new adverse events but still require review by highly skilled professionals, whose time and expertise could be better applied elsewhere.

This is clearly not scalable. Inspired by the way large insurance companies use algorithms to automate the routing and processing of claims, one of SciBite’s global pharmaceutical clients has leveraged Artificial Intelligence (AI) to build a system which facilitates the triage and management of cases. As illustrated below, the system ingests structured and unstructured case data from global call centres, emails and patient forums into a data lake from where it is fed into an automated pipeline to triage the data.

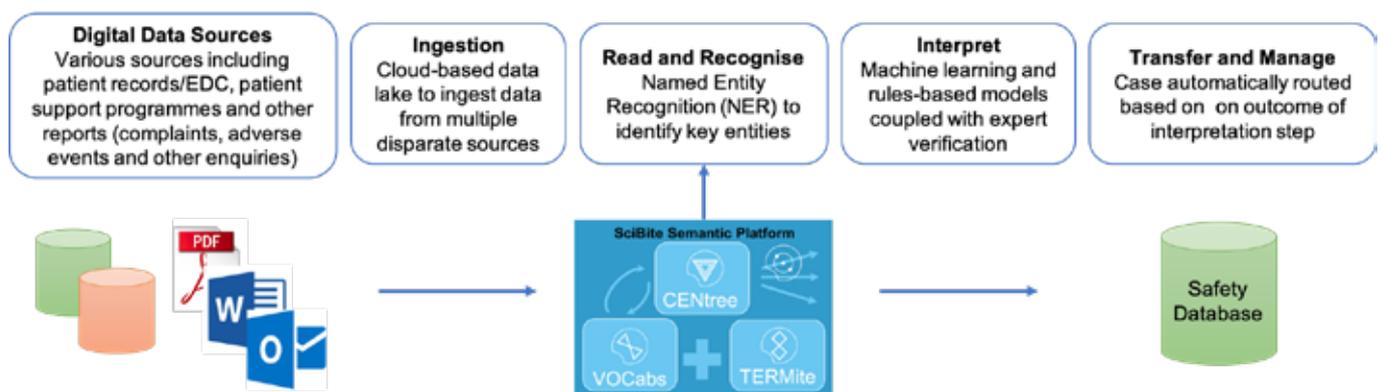
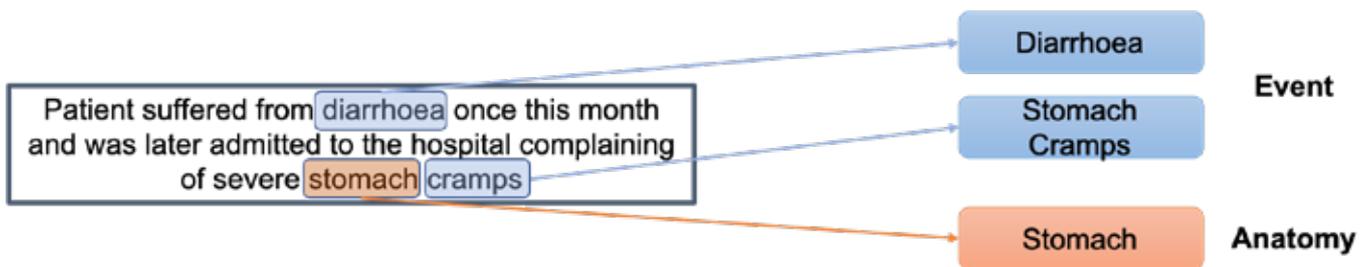


Figure 1: The SciBite Platform in Enables AI-Driven Intelligent Case Management



## EXAMPLE CASE TEXT

## ENTITIES



**Figure 2:** Using Named Entity Recognition (NER) to extract entities from the unstructured text within a patient history

In the first step of the pipeline, SciBite's Named Entity Recognition (NER) engine, TERMite, extracts key entities from the text, such as the name of the drug name, part of the body and event.

The foundation of the SciBite platform are VOCabs - the vocabularies and ontologies which apply an explicit, unique meaning and description to a term. Comprising tens of millions of synonyms, SciBite's manually curated vocabularies have unrivalled depth and breadth, ensuring comprehensive coverage of relevant terminology and providing the robust foundation necessary for an effective and impactful Pharmacovigilance strategy. SciBite's ontology management platform, CENtree, enables organisations to maintain up to date ontologies representing evolving scientific language. Subject matter experts can easily contribute to keeping things current and augment our manually curated standard reference vocabularies with proprietary information.

Coupled with the contextual disambiguation of scientific terms, SciBite's platform transforms unstructured text into clean, structured data that can be read and interpreted by machine learning and rules-based models which assess the seriousness of the case and route it accordingly.

The company has been able to move from a highly manual labour intensive process to one that is highly intelligent, dynamically learning and automated. The result has been a 75% reduction in case processing cycle times and more than 30% reduction in the overall 'hands on' effort required to examine a case. This 'intelligent automation' has increased productivity and reduced the cost of processing adverse events, while maintaining a high standard of data quality and compliance. Importantly it also enables medically trained experts to spend their time on higher value-add activities, such as focussing on the prevention of adverse events.

## Streamlining Detection of Safety Signals from the Literature

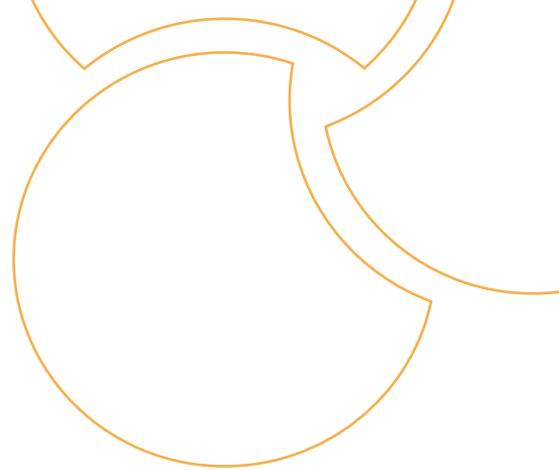
Regulatory bodies expect Pharmaceutical companies to maintain an up-to-date awareness of the safety implications of not only their own drugs but also those from the same drug class and with the same target that are marketed by competitors.

A wealth of safety-related material can be found within the biomedical literature, such as MEDLINE, and other credible resources, such as new drug applications (NDA) to the FDA and EMA and conference abstracts and proceedings.

Historically, many Pharmacovigilance teams have applied a laborious and subjective triage process to review the biomedical literature, involving searches for a predefined set of terms and reading the full text of all hits to check their relevance – a task that is frequently outsourced. Any articles deemed to contain potential safety signals are sent to experts for assessment.

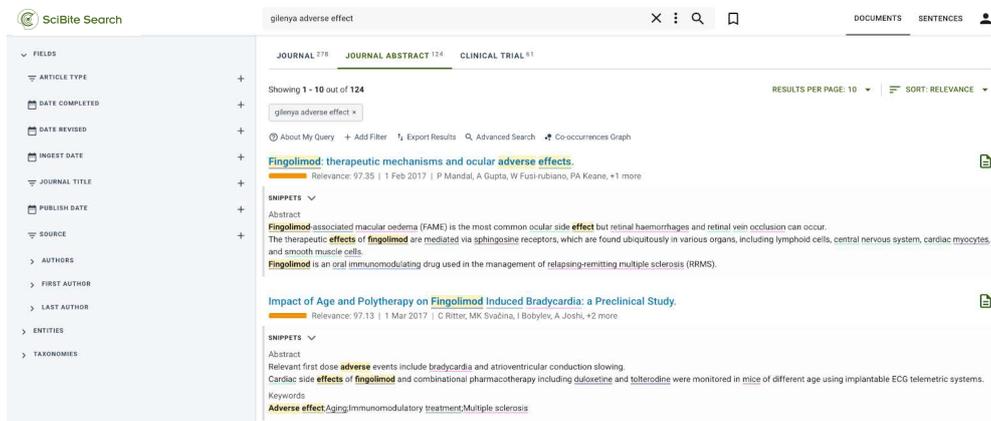
The exponentially growing volumes and diversity of information make it challenging to maintain a comprehensive and up-to-date awareness of relevant safety-related data. The legacy approach of manually scanning the biomedical literature is prohibitively time consuming, has a high risk of missing safety signals and is no longer a viable option.

SciBite's ontologies deliver the standardisation necessary to link data from heterogeneous biomedical sources, including both those that are focussed on safety information (such as DailyMed label information) as well as those that don't (such as ChEMBL drug targets), facilitating the generation of a semantic network of interconnected facts. SciBite enables Pharmacovigilance teams to build up a richer picture, find supportive information to validate potential safety signals and infer additional insights that are only possible through semantically enriched, linked data.



The SciBite platform also includes an algorithm that has been trained with a range of phrase constructs that describe adverse events. This not only identifies possible connections between drug and adverse events but also calculates an associated confidence value and predicts if the identified relationship describes a positive or negative association.

The SciBite platform can rapidly process a huge volume of biomedical content from a diverse range of sources, accurately mark-up all relevant terms and concepts present within each article and rank articles by their relevance to a particular search without being limited by the indexing terms used by the data source. The intuitive interface also enables users to quickly identify the co-occurrence of drug and side effect terms.

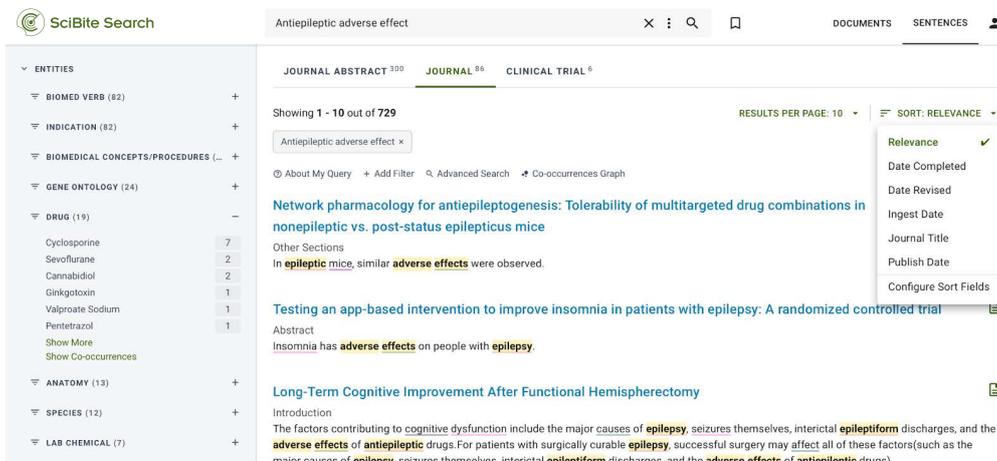


The screenshot shows the SciBite Search interface with a search query of "gilenya adverse effect". The left sidebar lists various fields for filtering, including Article Type, Date Completed, Date Revised, Ingest Date, Journal Title, Publish Date, Source, Authors, First Author, Last Author, Entities, and Taxonomies. The main content area displays search results, including a snippet for "Fingolimod: therapeutic mechanisms and ocular adverse effects" and another for "Impact of Age and Polytherapy on Fingolimod Induced Bradycardia: a Preclinical Study".

**Figure 3:** The example shows text from MEDLINE relating to fingolimod, which was automatically recognised as synonymous to Gilenya

SciBite enables reviewers to focus on the articles of highest relevance and broaden their search to include closely related terms. The ability to rapidly identify the

topics covered in each article, assists human review and eliminates the trade-off between the volume of content and the time available to review it.



The screenshot shows the SciBite Search interface with a search query of "Antiepileptic adverse effect". The left sidebar lists various entities for filtering, including Biomed Verb, Indication, Biomedical Concepts/Procedures, Gene Ontology, Drug, Anatomy, Species, and Lab Chemical. The main content area displays search results, including a snippet for "Network pharmacology for antiepileptogenesis: Tolerability of multitargeted drug combinations in nonepileptic vs. post-status epilepticus mice" and another for "Testing an app-based intervention to improve insomnia in patients with epilepsy: A randomized controlled trial". A dropdown menu on the right side of the screen allows users to rank query results by relevance and summarise all terms identified within the results.

**Figure 4:** Ranking query results by relevance and summarising all terms identified within the results (right hand side of the screen) to enable users to easily navigate to the most interesting articles

## Exploration of Genotype Based Personalized Prescription of Valproate Sodium in Anti-epileptic Treatment

Study ID	VPA20100716
Recruitment Status	Unknown status
First Posted	30 July 2010
Last Update Posted	30 July 2010
Study Type	Observational
Enrollment	150
Start Date	1 August 2010
Completion Date	1 July 2013

<https://clinicaltrials.gov/show/NCT01172626>

Sponsor	Collaborator	Information provided by
Sun Yat-sen University	First Affiliated Hospital, Sun Yat-Sen University	Sun Yat-sen University

### Study Description

The purpose of this study is to investigate the relationship between the side effects of valproate sodium in the treatment of epilepsy in Han Chinese and the genetic polymorphisms of drug metabolizing enzymes and pharmacokinetics of valproate sodium.

#### Detailed Description

Valproate sodium is a widely applied agent in the treatment of epilepsy. Although Valproate sodium is effective in clinic, it is able to induce several side effects, including weight gain, thinned hair, loss of appetite, nausea, vomiting, hepatotoxicity, hematotoxicity, thrill, etc. However, the remarkable variability of the reactions to the drug – the incidence of side effect or the outcome of the treatment – has been observed among patients. Valproate sodium is metabolized by some enzymes in the liver to transform it into several unreactive chemicals for excretion. Among them there are two toxic metabolites catalyzed by the specific metabolic enzymes. This study is designed to explore the genetic variation among individuals in the key processes of the deactivation and elimination of Valproate sodium in order to find out whether these genetic factors are associated to the side effects or efficacy. The further understanding into the factors concerning on the drug might imply possible solution to minimize the incidence of side effects in epileptic patients.

**Figure 5:** Marking-up relevant terms within an article facilitates interpretation

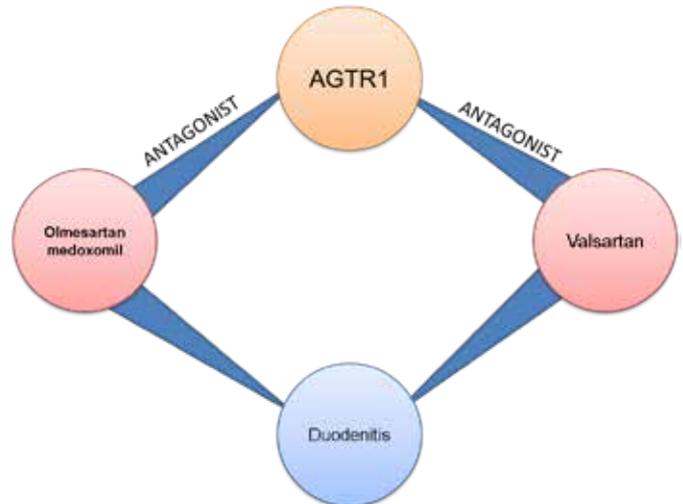
SciBite enables the automation of the process of pre-screening and prioritizing documents through the application of a series of rules to capture statements pertaining to drug-induced adverse events. By including a broad range of synonyms for a term of interest, the chance of missing a critical safety signal are minimised. SciBite also applies rules to reduce the number of false positives, for example where a term like 'pain' could describe an adverse event or a symptom being treated.

SciBite is developing the ability to automate this process by issuing alerts in near real-time only when something noteworthy is found. This will remove the need for manual triage of documents, changing the role of expert resources to one of oversight, only getting involved in the detailed review and assessment of more ambiguous cases. Outsourcing costs can be reduced and the costs that would arise from delays in identifying important safety signals can be eliminated, enabling efficient and comprehensive monitoring of direct and indirect safety signals derived from a wide range of heterogeneous and cross-disciplinary sources.

### Predictive Analytics

With the vast and growing amount of data in the public domain, even knowing which drugs belong in a particular class can be a challenge. SciBite ensures all existing information is considered when looking for likely side effects.

For example, there is a direct relationship between the drugs Valsartan and Olmesartan medoxomil and inflammation of the lining of the digestive system (duodenitis). SciBite reveals extended connections, enabling the identification of a potential relationship between Angiotensin II Receptor Type 1 (AGTR1) antagonists and duodenitis, something that would be missed by traditional keyword-based search strategies.



**Figure 6:** Identifying potential relationships from connected data sources

SciBite can generate new hypotheses and help predict which adverse events may occur, however infrequently, including potential drug-drug interactions, preparing clinicians and study teams with the knowledge of what to look out for when treating a specific condition.

Once a drug is in clinical use, SciBite enables Pharmacovigilance teams to rapidly confirm or reject unexpected safety issues based on their biological plausibility using evidence from a comprehensive, interconnected knowledge base.



## Summary

SciBite enables an integrated approach to Pharmacovigilance, enabling Pharmaceutical companies to:

- Expedite the process of identifying, validating, reporting and acting upon adverse events
- Achieve a comprehensive, up-to-date awareness
- Explore, analyse, query and manage underutilized sources of safety information

... and ultimately to protect patient safety, mitigate risk and ensure compliance in a resource-effective manner.

## About SciBite

SciBite is an award-winning semantic software company offering an ontology-led approach to transforming unstructured content into machine-readable clean data. Supporting the top 20 pharma with use cases across life sciences, SciBite empowers customers with a suite of fast, flexible, deployable API technologies, making it a critical component in scientific data-led strategies. Contact us to find out how we can help you get more from your data.

To learn how SciBite can unlock the value of your data, speak to one of our experts today or email us at [contact@scibite.com](mailto:contact@scibite.com)



SciBite's data-first, semantic analytics software is for those who want to innovate and get more from their data. At SciBite we believe data fuels discovery and we are leading the way with our pioneering infrastructure that combines the latest in machine learning with an ontology-led approach to unlock the value of scientific content. Supporting the world's leading scientific organisations with use-cases from discovery through to development, SciBite's suite of fast, flexible, deployable API technologies empower our customers, making it a critical component in scientific, data-led strategies. Contact us to find out how we can help you get more from your data.

To learn how SciBite can unlock the value of your data, speak to one of our experts today or email us at [contact@scibite.com](mailto:contact@scibite.com)

**Head Office:**

SciBite Limited  
BioData Innovation Centre  
Wellcome Genome Campus  
Hinxton, Cambridge CB10 1DR  
United Kingdom

 [www.scibite.com](http://www.scibite.com)  
 [contact@scibite.com](mailto:contact@scibite.com)  
 LinkedIn: SciBite  
 Twitter: @SciBite  
 +44 (0)1223 786 129

