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APPLICATION NOTE

Transforming DART Research

Automated, fast, and scalable 3Rs *in vivo* toxicity testing at the *in vitro* scale

Transforming DART Research

Developmental and Reproductive Toxicity (DART) research focuses on identifying and understanding the potential risks chemicals and pharmaceuticals pose to organism development and reproductive health. With increasing growing need for safer products, the demand for efficient, reliable, and scalable in vivo tools for DART testing has never been greater.

Nagi Bioscience offers a groundbreaking *in vivo* solution at the *in vitro* scale specifically designed for DART studies, providing researchers with real-time, actionable insights into the effects of diverse compounds on development and reproduction.

Our ethical and scalable platform simplifies the assessment of toxicity profiles, enabling faster and more reliable identification of potential risks, ultimately advancing the development of safer therapeutics and consumer products.

Achieve the otherwise unattainable

Automated *in vivo* healthspan and lifespan at *in vitro* scale: Nagi's technology uniquely combines the benefits of *in vivo* testing with the efficiency and scale of classical *in vitro* setups. This approach enables rapid, scalable studies, reducing reliance on vertebrate models and the associated ethical concerns.

Precise quantification of reproductive and developmental toxicology: Leverage systemic analysis unprecedentedly detailed. Accelerates decision-making, enabling the distinction between drug mechanisms of action on multiple generations, and the detection of subtle physiological changes often missed by traditional endpoint assays.

Cost-effective preclinical solution: Leverage the *C. elegans* model to obtain translationally relevant in vivo results earlier in the compounds development process, bridging the gap between in vitro systems and costly vertebrate models. Conduct low-cost, ethically sound preclinical studies and aim for publication-ready data.

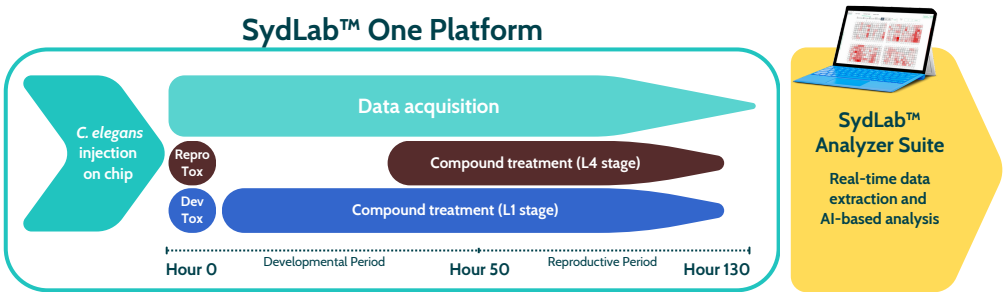
	in vitro	nagi bioscience	Zebrafish	Mice
Throughput	> 384 drugs/month	384 drugs/month	30-40 drugs/month	3-5 drugs/month
Translational value	Low	High	High	High

The numbers of drugs per month/year refer to the number of compounds that can be tested in 30 days, without technical repetitions or controls.

Explore the technology:
SydLab™ One Technical Note

From research to results: Our approach

Age synchronized populations of *C. elegans* are injected into the microfluidic chips and controlled by a fully automated protocol. In each channel, *C. elegans* are exposed to a well-defined liquid environment, including the compounds to be tested. All readouts are monitored all along their life cycle. In addition to DART-related insights, the high-content imaging enables the analysis of diverse phenotypes, supporting broader applications.



READOUTS

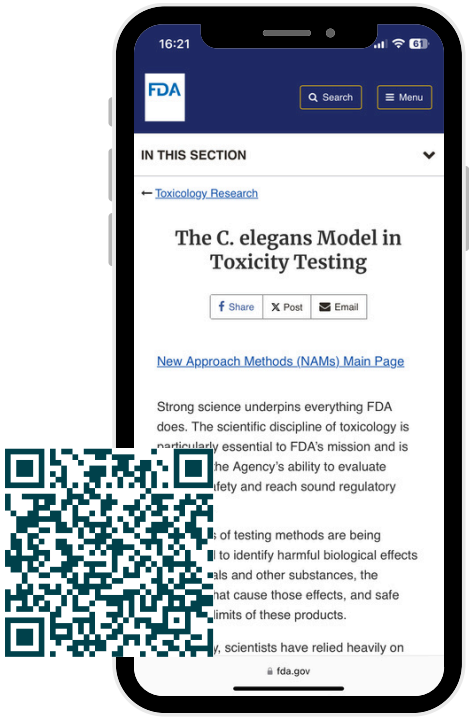
- Worm maximum size
- Growth dynamics
- Sexual maturity
- Egg accumulation
- Embryo survival
- Larvae emergence
- Larvae accumulation
- Progeny size

C. elegans: A Gateway to Early Toxicology studies

Caenorhabditis elegans has become an invaluable, cost-effective, and ethically favorable model for advancing research on developmental and reproductive toxicity (DART), with 60-80% of its genes homologous to humans.

With its short life cycle, genetic similarity to humans and well-characterised development cycle, *C. elegans* allows researchers to study the effects of various compounds on development and reproductive health with greater efficiency. As a whole-organism model, *C. elegans* offers a more integrated and relevant system for DART studies than *in vitro* models, while remaining more cost-effective and ethical than vertebrate assays.

C. elegans therefore provides earlier insights on potential risks and drug mechanisms during compound development.



CASE STUDY

Transforming DART studies with SydLab™ One, an automated 3Rs high-throughput *in vivo* platform

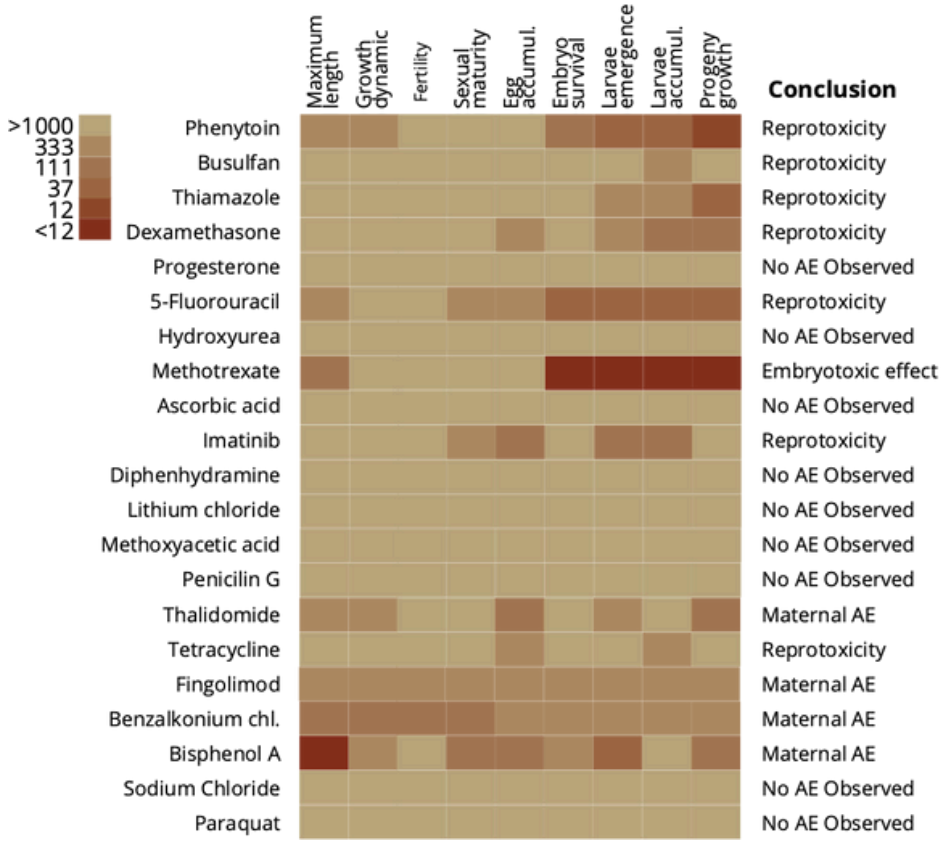
Introduction

In the following case studies, we used Nagi Bioscience's fully automated solution to showcase how the SydLab™ One platform enables efficient prediction of Developmental and Reproductive Toxicity of 21 chemicals. Additionally, we assess the dose-dependent effects of the herbicide Paraquat and the cytotoxic chemotherapy drug 5-fluorouracil (5-FU).

Case study 1

21 benchmark chemicals with known Reprotox effects, either positive or negative, were tested in blind on the microfluidic platform SydLab™ One.

5 concentrations for each chemical (1mM, 333µM, 111µM, 37µM and 12µM) were tested and compared to the negative control (DMSO 1%). Three technical repeats were executed, each chemical being tested twice. No-Observed-Adverse-Effect Level (NOAEL) was determined and their toxicity profile described.

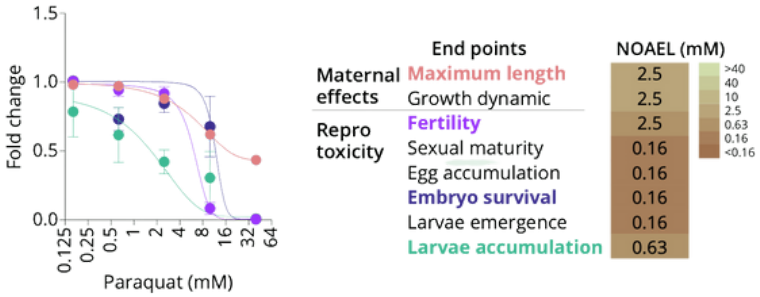


After unblinding, 17 out of 21 were predicted correctly (according to the ECHA database), providing a balanced accuracy of 87.5%.

Case study 2

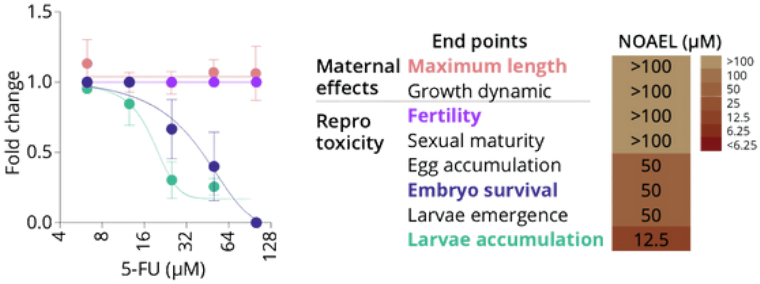
We then assessed the dose-dependent effects on reproductive toxicity of the herbicide Paraquat and the cytotoxic chemotherapy drug 5-fluorouracil (5-FU).
SydLab™ One quantified the dose-dependent effects on maternal development (maximum length) and reproductive capacity (fertility, embryo survival, and larval accumulation).

Multi-phenotypic analysis: Paraquat



Paraquat caused significant maternal adverse effects at high doses (NOAEL: 2.5 mM) and pronounced reproductive toxicity at lower doses (NOAEL: 0.16 mM).

Multi-phenotypic analysis: 5-FU



As expected, 5-FU exhibited no maternal adverse effects at the tested doses but demonstrated strong reproductive toxicity at intermediate doses (NOAEL: 50 µM).

Conclusion

These case studies illustrate the advanced capabilities of accurate prediction of reproductive toxicity of Nagi Bioscience's SydLab™ One platform. Furthermore, the platform enabled precise quantification of compounds dose-dependent effects.

Nagi Bioscience's DART solution empowers researchers to obtain reliable, high-quality *in vivo* data more efficiently and with fewer resources than conventional methods. By streamlining complex workflows and reducing the need for manual intervention, SydLab™ One offers an affordable and practical option for DART studies, ultimately contributing to safer therapeutics and consumer products.

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APPLICATION NOTE

Explore our technologies and research solutions

Discover the capabilities of SydLab™ One with the Discovery Pack experience

Let's connect

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