
Predictive computer-based model
Post marketing drug surveillance
Medical devices
Tiered testing methods
Micro-dosing
In vitro endotoxin
Clinical Trials
Stem cell research
DNA chips
'Six Pack' Toxicity
The rise of the NAMs
Cell culture chambers
In vitro pyrogenicity
Human-on-a-chip
3D tissue models
Human- patient simulators
New imaging technologies
Pumps and accessories
In Vitro carcinogenicity
Computational bioinformatics
In vitro genotoxicity/mutagenicity
High-throughput screening methods

This snapshot focuses on Non-Animal or Alternative methods and technologies of testing in the context of a deeply rooted reliance on animal testing.

It provides a glimpse of the impressive and largely underfunded centres of work around the world in 2022, by comparison with the colossal investment in testing using animals.

The Rise of the NAM's

Around the world there are many significant changes happening in the alternatives to the use of animals in testing. Some of the hundreds and hundreds of current businesses and organisations engaged and successfully implementing alternatives.

The talent and skills are astonishing and wonderful to see.

Consider the fate of the animals in laboratories too.

Add in the industrial scale side businesses that surround animal testing of animal housing, technicians and providers of animal food and bedding then you can easily see the resistance to embracing this period of convergence and innovation.

The parallels with the fossil fuel industry and climate change are significant.

What could the UK do now to accelerate the use of NAM's and change animal testing for the better TODAY?

1. Insist all researchers provide evidence of their search for alternatives with the project licence. This can be checked and verified **before** signing off the project licence. Like this:
   https://www.nal.usda.gov/legacy/sites/default/files/altwksht_jan2020.pdf/

2. Use a searchable standardised database for all toxicology work. In the absence of one provided by the UK government for researchers to use, here is one that is a database of a database. It's a global list of 78 toxicology databases.
   Turn it into an App!

   https://norecopa.no/search?fq=type:%22Databases%22&sort=name_s%20asc&q=*&facet.limit=125

3. The Government can ensure that their departments and the related agencies responsible for animal testing in research, collaborate to produce a single gateway to reduce the barriers to accepting non-animal methods for toxicity testing. Some government departments and agencies already hold or provide access databases for toxicity testing and to databases of chemicals but currently is there is **no single access point to all of them.**

   This single action would unlock enormous potential for innovation and development in the UK research industry. It would synthesize opportunities for a whole range of industries and businesses and would immediately provide a framework that the regulators could use to ensure there is no needless and pointless testing on animals.

   The contribution to the economy would be significant. This would bring the UK alongside the USA and the EU in the ambition to update the science of product safety, drug and medical device development so it is truly world leading and not trailing behind.

   Non-Animal Alternatives Testing Global Market Report 2022
   Source: Globenewswire

   "The non-animal alternatives testing market consists of sales of non-animal alternatives testing products and services that do not involve testing on animals to determine the safety and efficacy of products and ingredients used in any industry sector. On-animal alternative testing technologies include: in-vitro human cell and tissue cultures, organs-on-chips (OOCs), computer simulations and modelling (silico models), 3D bio-printing of tissues, and synthetic skin substitutes as well as studies with human volunteers.

   These technologies replace animal testing in end-use industries including pharmaceuticals, medical devices, chemicals & pesticides, food, and others.

The main methods of non-animal alternative testing are cellular assay, biochemical assay, in silico, and ex-vivo. A biochemical assay is an in vitro analytical process used to detect, quantify, and/or investigate the binding or activity of a biological molecule, such as an enzyme.

The various technologies used include cell culture technology, high throughput technology, molecular imaging, omics technology, and other technologies. These are utilized by industries such as pharmaceutical industry, cosmetics & household products, diagnostics, chemicals industry, and food industry.

North America was the largest region in the non-animal alternatives testing in 2021.Western Europe was the second-largest region in the non-animal alternatives testing market."

Researchers have created "organs-on-chips" that contain human cells grown to mimic the structure and function of human organs and organ systems.

The chips can be used instead of animals in disease research, drug testing, and toxicity testing and have been shown to replicate human physiology, diseases, and drug responses more accurately.

Blizard researchers showcase animal-free cancer research methodologies in Parliament. Based in the Blizard's Centre for Cell Biology and Cutaneous Research, Animal Free Research UK-funded scientist Dr Adrian Biddle is leading research in New Approach Methodologies. The Biddle Lab is concerned with the question – how can diverse cancer stem cell phenotypes best be modelled in vitro, in order to accurately predict cellular behaviour and response to

https://www.labskin.co.uk/

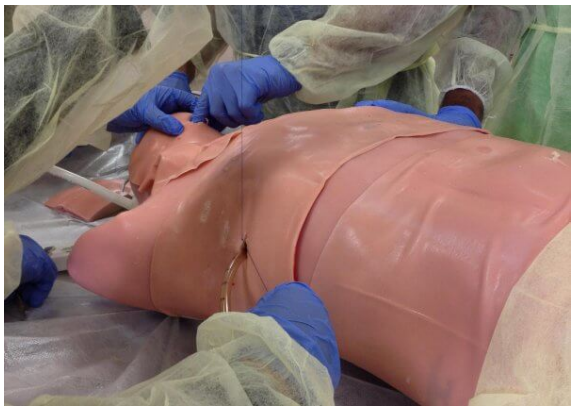
Labskin has a 12-year pioneering track record of developing human skin models.

Labskin is the only commercially available lab-grown full thickness human skin model that naturally mimics the skins microbiome.

- **Real human skin equivalent**
- **Thousands of industry tests**
- **Meet ethical, regulatory and competitive standards**

All medical schools across the U.S., Canada, and India have completely replaced the use of animal laboratories in medical training with simulators as well as virtual reality systems, computer simulators, and supervised clinical experience. (2016)

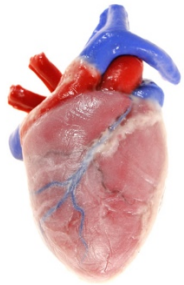
https://www.washingtonpost.com/news/animalia/wp/2016/06/30/one-last-u-s-medical-school-still-killed-animals-to-teach-surgery-but-no-more/

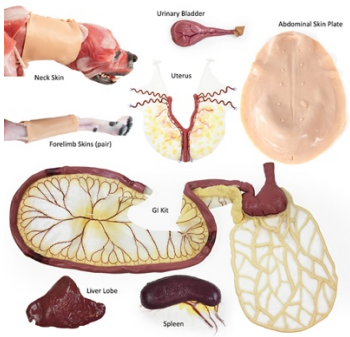


If your experience and life skill is based upon testing with animals, however poor the failure rate is, you are unlikely to easily develop the full range of skills, expertise and understanding of replacement methods that involve these areas, after years of working the same way.

Most learning institutions including pharmaceutical research laboratories, are led by experienced and senior researchers with single subject backgrounds so the problem is compounded.

SynDaver manufactures the world's most sophisticated synthetic human and animal tissue analogs, body parts and full bodies. Our SynDaver Synthetic Human and SynDaver Surgical Canine can bleed and breathe, and both employ hundreds of replaceable muscles, bones, organs and vessels that are made from materials that mimic the mechanical, thermal and physicochemical properties of living tissues. This validated technology is used to replace live animals, cadavers and human patients in medical device studies, clinical training and surgical simulation.





SynDaver, the advanced bio-technology company known for their creation of synthetic human and animal simulators for educational, medical testing and training.

The development of a new synthetic feline surgical training model is now available, which has been designed for use in veterinary colleges. The feline surgical model allows students to learn how to perform a spay on a synthetic cat as opposed to a live patient.

The SynDaver® Surgical Canine is a revolutionary high-fidelity surgical trainer. It provides an unparalleled platform for repeatable surgical procedures. Featuring customizable pathologies integrated with complete vasculature, the system affords veterinary students and surgeons an incomparable experience in surgical situations commonly faced in the operating room.

WHY DO SO MANY PROMISING COMPOUNDS NEVER BECOME DRUGS?

The 3R's principles describe the testing for safety and efficacy of drug development set up in the 1950's. The present and immediate future is all about convergence of life sciences, mathematics, technology and physics and inevitable rise and use of non- animal methods of testing.

The Government, and animal rights activists, have asserted the higher failure rate of testing using animals as did the editor of British Medical Journal:

https://www.bmj.com/content/348/bmj.g3387

This is not acceptable for the students and researchers who will work in the industries requiring testing, for the next 50 years, let alone the general public. There is increasing and growing discontent about how universities who are linked to the pharmaceutical businesses through funding, are operating.

Innovative scientists in the healthcare, clinical, medicine field have created alternative courses for students accessible world-wide on evidence-based toxicology

Dr Thomas Hartung at the John Hopkins Bloomberg School of Public Health is one such scientist:
https://www.coursera.org/learn/evidence-based-toxicology/

"Over the recent years, there has been an increasing recognition of the weaknesses that pervade our current system of basic and preclinical research. This has been highlighted empirically in preclinical research by the inability to replicate the majority of findings presented in high-profile journals. The estimates for irreproducibility based on these empirical observations range from 75% to 90%. These estimates fit remarkably well with estimates of 85% for the proportion of biomedical research that is wasted at large".

The Convergence of Technology, Life Sciences, Physics, Engineering and Mathematics has disrupted this way of working especially since the Genome Project in 2003 and the world changing innovations in technology.

We have scientists doing stem cell research who do not need to test on animals today. We no longer need to test on cosmetics anywhere.

We have household products have never been tested on animals ever.

These animal free standards exist, are commercially viable or in research terms acceptable. The responsibility for ensuring they are COMPULSORY lies with the government and the regulators.

The regulatory standards applied to non-animal methods of testing are equivalent or higher and are produced in ways that counter much of the current slow science.
The range of methods and devices are increasing significantly every week.

Here is a link to a database in English and Norwegian and supported by the Norwegian government listing 1000 plus entries of alternatives for students and researchers.

https://www.nat-database.org/

We do not have a database like this in the UK for our students and researchers and no expectation that they will check before applying for licences.

FACT
The resistance to new ways of testing that significantly reduced animal testing was overturned during the initial phase of the Covid pandemic. The regulators **APPROVED** the running of animal tests alongside human tests with volunteers, micro-dosing and monitoring in 8 months.
Normal time for vaccine development is 8-15 years.

This is unprecedented.

In the world's largest experimental vaccine trial – many animal trials stopped and hence many animals were saved.
"In a move to accelerate the discovery of a COVID-19 vaccine, the International Coalition of Medicines Regulatory Authorities (ICMRA) has advised that the usual animal tests for the effectiveness (efficacy) of potential vaccines is not required before proceeding to human clinical trials."
https://www.animalfreeresearchuk.org/covid-19-open-letter/

If the whole world is not a sufficient model then what is?

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it is interesting to note that that the advances in PCR and gene sequencing in assays, all non -animal methods, were significant in the development of the Covid 19 vaccine. The vaccine development jumped the normal regulatory rules and will **undoubtedly be used again should the need occur.**

The pharmaceutical industry is known for innovation and developing life-saving products. The industry is also known for a reluctance to embrace change, new technologies and methods in medicine production. This is largely due to a long and document heavy field of regulation.

Yet they have demonstrated they can overcome that, by sharing population level big data sets between ten of the biggest, after the initial phases of the pandemic. This gave them all excellent core and reliable data at a level that makes it reach weight of evidence standards, particularly following the Covid-19 pandemic and the race to provide vaccines.

https://www.europeanpharmaceuticalreview.com/news/89540/ten-big-pharma-companies-collaborate-on-data-sharing-ai/

They did this within months of the rollout of the Covid-19 vaccine.
No animals used as the data was already there and proven.
Where the pharmaceuticals lead, the regulators follow.

The inefficiency and exorbitant costs associated with animal testing makes it impossible for regulators to adequately evaluated the potential effects of the hundred thousand plus chemicals currently in commerce let alone study the effects of myriad combinations of chemicals.

In contrast, computer modelling techniques are lightning fast, and many cell-based *in vitro* methods are amenable to "high throughput' automation using robotics.

The cost is much lower and more consistent than testing on animals.

That is why it is a growing and valuable market for research.

Decades of the same studies using animals endlessly, the massive increase in the use of genetically altered animals and still **THE CHALLENGE for ALL** successful drug development remains.

The true validation and intended target of any drug development, is confirmation that at the molecular level is the cause of the human's disease and the drug's intended efficacy

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If the alternatives were pointless and useless and only to save animals from cruelty then the amount of work going on to replace animal testing would be unexplained. It would not be clear why governments are committing to ending animal testing and also why there is a drive to find better ways to produce drugs using new technologies.

The assertion that is often made is about drug safety that until the drug is made available to the public are side effects (Adverse Drug Reactions) encountered.

They are not rare as asserted though:
"The health and financial implications of ADRs are significant: about 6–7% of hospital admissions in the UK are due to ADRs."
https://cks.nice.org.uk/topics/adverse-drug-reactions/

https://www.thompsons.law/support/charities-and-support-groups/sling-the-mesh

This business is all about the vested interests. There are so many side industries built on the supply of products that the welfare of the animals used will always be second to that whatever anyone says. They are seen as products to be used and are referred to as stock. That way they can be added as a line on a financial statement and not a waggy tail in sight. The cost of animals will increase as the numbers needed decline as they surely will, given the technology being used and how.

There is an endless call upon the public purse via the NHS and public donations to medical charities for billions of pounds annually for research for ongoing treatments not cures.

This appetite for funding with the level of secrecy in the animal testing business and the criminalisation of whistle-blowers in section 24 of the 1986 ASPA has resulted in a massive unease and concern in the general public. The reality of the conditions and treatment of Animals in Science will be even more of an issue as costs rise and the pressure to sustain profitability from a declining business model will rise with it.

Warehousing hundreds and hundreds of sentient beings in conditions that reflect the issue of profitability versus standards of care as non- animal methods of testing accelerate and become massively viable and profitable in pre-clinical, clinical, medical and surgical areas as well as drugs development should have already been addressed and planned for.

It is unreasonable to continue to expect that the numbers of animals used every year in procedures or let's call them what they are 'experiments' will remain at the same level or increase.

This is the "Canute effect"

Alternatives innovation, embedding into practice is happening,
It is increasing and is cost effective.

Add in the lack of cruelty factor, it's a win- win and public opinion counts

https://www.ipsos.com/en-uk/public-attitudes-animal-research-2018

Key findings:

- Key measures of the acceptability of animal research are at similar levels to 2016. However, public acceptability is contingent on the purpose and context of the research.
- However, animal welfare is becoming a bigger consideration for some members of the public and the link between animal research and human health appears weaker.
- Public trust in the regulation of animal research in the UK remains at levels recorded in previous years.
- Public awareness of government work on the "three Rs" of animal research remains low.
- Two thirds of the public do not feel well-informed about the use of animals in research, while interest in finding out more about work to find alternatives and improve the welfare of animals in research is high and has risen.
- Views on the acceptability of protest and demonstration formats are unchanged. The primary characteristic the public attribute to animal research organisations remains "secrecy".

There are over a hundred laboratories across the world who specialise only in non-animal methods of testing and medical devices. There are hundreds more, who are in the crossover period between only animal testing to an increasingly non- animal methods base. These businesses are already producing billions for the economies of the world and are heavily invested in and often bought out by large pharmaceuticals and research companies. Of course, they are, it is already a lucrative market.

BLUESCREEN™ ANIMAL-FREE (BS-AF)

BlueScreen™ Animal-Free (BS-AF) is a non-regulatory human cell-based test, free from any animal-derived components. Unlike the current* in vitro *regulatory methods for genotoxicity, BlueScreen™ Animal-Free detects all three major classes of genotoxin (mutagens, clastogens and aneugens) in a single test. The test is ideal as a rapid, cost-effective early screen in product development & to generate supporting information in a weight-of-evidence approach to safety assessment.

XCellR8
Redefining testing

The Quasi Vivo® systems provide a significantly more human relevant research environment and enable the use of human cells/tissue slices in 2D or 3D constructs (scaffolds, gels or spheroids) in long term toxicology, mechanistic and metabolic studies. https://www.kirkstall.com/

CN-BIO

Single and multiorgan microphysical systems to generate clinically translatable data to enhance drug development.
Cells, tissues and multi organ chips.

https://www.labskin.co.uk/

Labskin has a 12-year pioneering track record of developing human skin models.

Labskin is the only commercially available lab-grown full thickness human skin model that naturally mimics the skins microbiome.

- **Real human skin equivalent**
- **Thousands of industry tests**
- **Meet ethical, regulatory and competitive standards**

COMPUTATIONAL BIOINFORMATICS - BIG DATA

Computational biology and bioinformatics develops and applies computational methods to analyse biological data, such as genetic sequences, cell populations or protein samples, to make new predictions or discover new biology. Many human patient studies contribute to the information stored. Data is obtained, collated and studied or treatments given with permission. This allows population level data to be used for conditions and diseases

You will see many pharmaceutical companies, organisations responsible for healthcare, medical research charities investing heavily into this area.

Research is more relevant using data around actual human conditions than mimicking the disease in an animal.

This powerful and available alternative substantially offers the opportunity to alter and remover the very worrying trend of trying to recreate human diseases and conditions in genetically modified animals.
The number of GM animals has risen exponentially year on year in testing.

biobank uk
Enabling scientific discoveries that improve human health

'Researchers, particularly from industry, are enhancing the resource further (for example, by funding cohort-wide assays) in order to augment their own research aims, while at the same time benefiting the wider research community as the enhancements are shared with all researchers after a limited exclusivity period, which is now set at a fixed period of 9 months.

Examples of this include cohort-wide assays of whole exome sequencing, whole genome sequencing, telomere length and NMR-metabolomics."

https://www.ukbiobank.ac.uk/learn-more-about-uk-biobank/about-us/our-funding

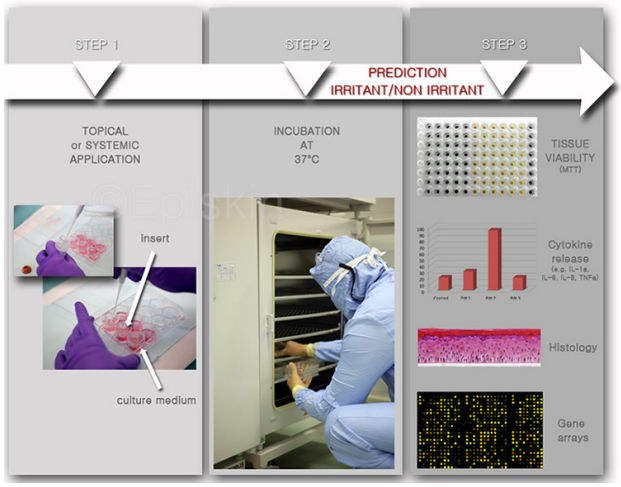
Training our young researchers across all the universities in how to question, interrogate and refine their research skills using a resource like this should be part of any initial syllabus for the Life Sciences sector.

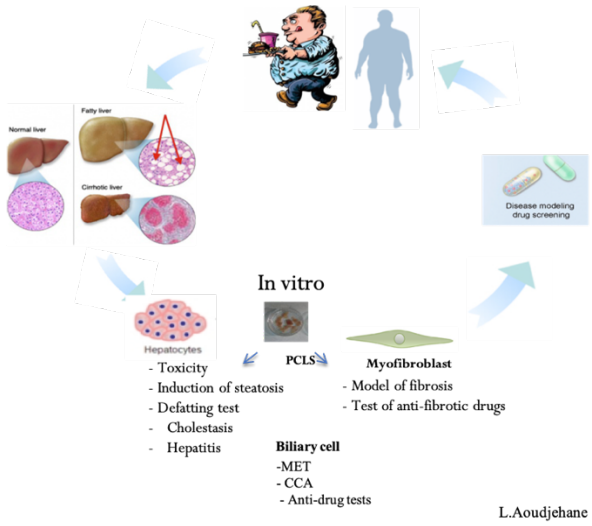
SOME OF THE MANY NAM LABORATORIES & TECHNOLOGIES WORLDWIDE

CollPlant
Pioneering Regenerative Medicine

Our revolutionary plant-based technology is the only commercially viable technology for mass production of recombinant human Type I collagen (rhCollagen), which is identical to the collagen produced by the human body. This makes our rhCollagen the ideal building block for regenerative medicine. Leveraging on the unique properties of rhCollagen and biomaterial know-how, we are developing a pipeline of products aimed at 3D bioprinting of tissues and organs and medical aesthetics.

EPISKIN, world leader in tissue engineering, offers Human Reconstructed Tissues to the global scientific community - academic and industry - to support research and development activities in Safety and Efficacy.
https://www.episkin.com/





The ICAN BioCell Human Liver Biology Platform aims to produce primary human liver cells (hepatocytes and all non-parenchymal cells) and to develop primary cultured liver models in 2D or 3D (thin slices or spheroids) to study chronic liver diseases and in particular fibrosis and NASH

IHU ican Foundation for Innovation in Cardiometabolism and Nutrition

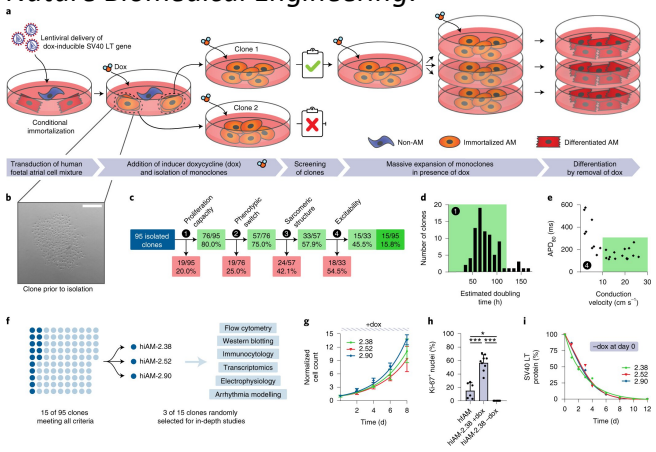
SOME OF THE MANY NAM LABORATORIES & TECHNOLOGIES WORLDWIDE

LABORATORIO DE INVESTIGACIÓN ALTERNATIVA | LIALT

MEXICO

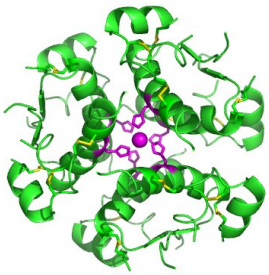
The Alternative Research Laboratory (LIALT) was born in 2017 in response to the mistreatment, suffering and death of animals used for the toxicological evaluation of all types of products that we use daily such as: chemicals, medicines, cosmetics and household products. LIALT replaces the use of animals through the use of three-dimensional tissues in conjunction with i internationally recognized protocols that provide more specific information on the mechanisms of toxic action than that obtained in animals, offering a solution to the aforementioned problem.

Researchers at the Leiden University Medical Centre (LUMC) have managed to culture human heart muscle cells on a massive scale. This is an exceptional achievement because it is very difficult to replicate heart muscle cells outside the body. Using a special technique, the researchers have now created a sheer inexhaustible source of human heart muscle cells offering many new opportunities for research into heart diseases. The results were published in *Nature Biomedical Engineering*.



Cell Pro

Stem cell-based implants successfully secrete insulin in patients with type 1 diabetes. The use of human PSCs has made significant progress toward becoming a viable clinical option for the mass production of insulin-producing cells.



USEFUL REFERENCES

Increasing Collaborations & Partnerships to Reduce Animal Testing

Source: TheBusinessResearchCompany

End-use industries including cosmetics, pharmaceutical, medical devices, chemicals, and food companies are increasingly seeking partnerships and collaborations with the organizations involved in developing non-animal alternative testing technologies.

Collaborations of these end-use companies with leading scientists, academic research institutions, government agencies, and non-profit organizations help them better understand the industry requirements and bottlenecks in the deployment of these alternative technologies.

Written Evidence Submitted by the Lord Dowding Fund for Humane Research (Select Committee)

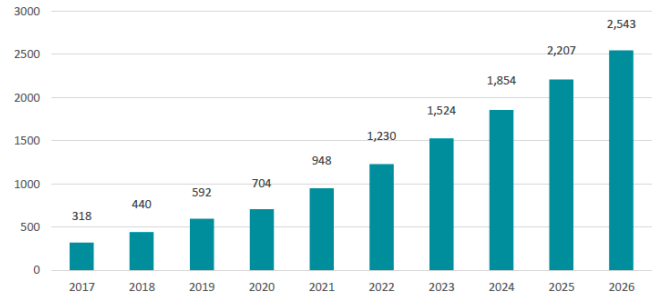
With the international competition in driving forward NAMs in the biomedical sciences, the UK is at risk of falling behind on global developments in this field and missing opportunities for growth of an innovative industry that can also benefit public health and the economy. After the UK's decision to leave the EU, the Department of Business, Energy and Industrial Strategy published a Green Paper, "Building our Industrial Strategy"

With uncertainties around access to EU funds and data/knowledge sharing, the Green Paper reports that it is vital that we "embrace innovation to keep ahead of the competition, create more good jobs, and make sure jobs in the UK are secure", particularly at a time when "the pace of scientific discovery and innovation is quickening across the world". The UK needs to keep "at the cutting edge of new technologies and developing solutions to global challenges".

To be a strong competitor in the global race to create the most innovative and efficient technologies for investigating disease and developing drugs, especially those which contribute to solving global disease outbreaks, it is essential that the UK prioritises its investment in NAMs as disruptive technologies, through dedicated funding. With Governmental support, we now have the unique opportunity to take the lead in biomedical sciences, enhancing the quality of science and industry in the UK. With its world-leading universities and home to some of the largest pharmaceutical companies in the world, the UK is in a strong position to build an economy that can compete with global innovation, reaping rewards for public health.

Source: Animal-Free-Research-UK_Economic Report-2

Figure 10: NAMs industry GVA, actual data 2017-2019, and forecasts 2020-2026, £ million



Source: Companies House, Cebr analysis

Figure 10 displays Cebr's forecast of GVA generated by firms in the UK NAMs industry through 2026. Over the whole period, including both the forecast period and years for which financial data was available, the NAMs industry's contribution to GDP is expected to increase by £2,225 million to £2,543 million (an increase of 700%). Throughout the forecast period, in the seven years through 2026, we estimate that NAMs industry GVA will grow by £1,839 million or 261%.

'OMICS

Overall, the objective of omics sciences is to identify, characterize, and quantify all biological molecules that are involved in the structure, function, and dynamics of a cell, tissue, or organism.

https://www.birmingham.ac.uk/partners/enterprise/news/latest/new-spinout-brings-%27omics%27-to-chemical-safety.aspx

The University of Birmingham has formed new spinout company, Michabo Health Science Ltd, to provide fast, reliable predictions of whether chemicals are potentially hazardous to human health or the environment.

The company will use new methods developed by researchers from the University's School of Biosciences, forming a team with over 20 years' experience in pioneering New Approach Methodologies (NAMs) to assess chemical safety without the need for vertebrate animal testing.