INSILICO UK

The Economic Impact of *In-Silico* Technology on UK and its Lifesciences Sector

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Main Findings

In this report we found

1	By 2025, a $109 billion global market is predicted for medicines and medical devices developed using *in-silico* methods, which will grow at 16% CAGR.
2	By 2025 25% of new pharmaceuticals and 50% of all new medical devices will utilise *in-silico* technology in their R&D lifecycle.
3	The UK will purchase ~£654 million in drugs in 2025, and at least £400 million of medical devices will have used *in-silico* methods throughout their Research & Development (R&D) lifecycle.
4	*In-silico* technologies will impact the UK's entire £88.9 billion life science sector.
5	*In-silico* technologies offer a step-change to the productivity of drug and medical device development such that By 2025, *in-silico* methods will enable 30% more new drugs and 30% more new medical devices to be brought to market annually By 2030, *in-silico* methods will enable 60% more new drugs and 30% more new medical devices to be brought to market every year.
6	Demand from medical device and pharmaceutical developers will grow the open market for *in-silico* software tools and services to $5.0 billion globally by 2025 and 9.2 billion by 2030, with the UK share of this being at least 5%.
7	*In-silico* technologies will be critical to the future of the 111,200 directly employed in 2,010 UK manufacturing sites in the Pharmaceutical and Med-Tech sectors.
8	By 2025 at least £2.6 billion worth of Pharma and Med Devices underpinned by *in-silico* methods will be made in the UK, even at our current share of the global manufacturing.
9	By 2025 the UK will export at least ~£800 million of pharmaceuticals underpinned by *in-silico* methods annually.

1. Introduction

Building back better a resilient economy and healthcare system: the COVID19 legacy.

The unfolding pandemic highlighted the fragility of the world's most powerful economies and the crucial roles of world-class and responsive innovation ecosystems, digital and interconnected data, and well-streamlined regulatory processes. COVID19 offers a learning platform and an opportunity to build back a better resilient healthcare ecosystem.

The pandemic also demonstrated that it is possible to deliver medical products in a responsible, patient-sparing way that balances the desire for certainty in their performance whilst limiting the delay in patient access associated with gathering increased certainty. However, today, medical products must regularly progress through lengthy, expensive clinical trials before gaining regulatory approval. Failure rates are high and can be extremely costly. Over 30% of drugs entering Phase II studies fail to progress, and over 58% fail in Phase III.

The UK Med-Tech sector comprises ca. 90% of Small and Medium Enterprises (SME), highlighting the UK's innovative strength and vulnerability as this is the stage with the highest risk of commercialisation failure. When medical devices fail at later stages, financial losses can be very large (high-risk Pre-Market Approval (PMA) device costs can average £74m, of which £54m are spent in Food and Drugs Administration (FDA)-linked regulatory stages over an average of 4.5 years). Three primary trends dominate medical device development:

a) A shift in initial product launches from Europe to the United States;
b) An increase in Software as Medical Device products (e.g. digital health, AI software or hybrid soft-ware/hardware technologies); and
c) An increase in in-vitro diagnostics (IVDs) from lab-developed tests.

The EU Medical Device Regulations (MDR)/IVD is currently perceived to be more demanding than the FDA regulatory clearance process and is therefore creating a trend of product launches occurring first in the United States and then in Europe. According to the EU MDR's new rules, all medical devices must be on 26 May 2024 to be authorised under the new regulation to remain in the European Market. However, by the end of 2024, it was estimated that around 22,000 certificates would expire, of which 4,000 would expire during 2023. To address the concerns sparked by these deadlines and the potential for widespread shortages of medical devices, these deadlines were extended by 3 years to May 2027. The main reasons for concern are the work involved in obtaining certification from an accredited body and the lack of capacity. At least 22% of IVD tests on the market today will be discontinued for the IVD Regulation. Many more IVDs will be lost if no urgent solutions ad-dress the existing transition issues to the IVD Regulation. In July 2021, certificates had not yet been issued for 88% of devices. The effect is also felt in the UK due to an inadequate regulatory system that needs modernising and streamlining.

The UK's medical devices sector faces similarly unprecedented challenges with soaring R&D costs and the need to generate sound safety and performance evidence to comply with the additional UK MDR/IVD, which will be the primary regulation in force from the second half of 2023. Additional challenges could result from products obtaining independent approvals in the UK and the EU. If there is no incentive to get regulatory approval in the UK first (e.g. due to excessive costs or regulatory complexities), some companies may choose not to access the UK market or do it much later than in other geographies, effectively reducing the available therapies and diagnostic technologies to the detriment of UK-based patients.

For many innovative companies, particularly start-ups and SMEs, adopting these new regulations is prohibitively expensive, time-consuming and often even unachievable due to the lack of notified bodies certifying their devices. Meanwhile, the UK's health system is under immense strain from the pandemic, with hospital waiting lists coming from an all-time high period. Rapid innovation must meet both challenges. COVID19 demonstrated the capability of the UK regulatory environment to adjust quickly to a rapidly evolving situation. For example, the Medicines and Healthcare products Regulatory Agency (MHRA) was the first to approve vaccinations for distribution. The approval was based on a rigorous assessment of clinical evidence, yet the processes applied facilitated continuous reviews with experts and a collaborative engagement with the industry.

Brexit offers the opportunity to create an agile regulatory system that widens the positive learnings from the pandemic. An innovation-friendly regulatory system that retains and attracts R&D from pharmaceuticals and medical device manufacturers to the UK. A reduced cost associated with regulatory certification stimulates these industries to carry out clinical trials in the UK first, thanks to supporting infrastructures and regulations to generate regulatory evidence. Beyond boosting the economy, improved regulations will major impact healthcare quality: innovations available to UK patients first and without delays and backed by solid evidence gathered efficiently in the NHS and at scale.

Safer, faster, cost-effective innovations for patient benefit.

This report explores the impact on some aspects of the UK's economy of an emerging approach to innovation and the generation of regulatory evidence. *In-silico* technologies can support areas currently held back by the incumbent regulatory framework, such as virtual or *in-silico* trials studies performed in virtual populations via computer simulation using engineering and science principles. Computational Modelling and Simulation (CM&S) are omnipresent in almost every industry sector relying on engineering and science (e.g. automotive, aerospace and microelectronics) but only to a limited extent in pharma and med-tech.

The UK is falling behind in exploiting the advantages and benefits of in-silico trials due to uncertainty in the regulatory frameworks about accepting regulatory evidence. Meanwhile, the Food and Drug Administration[1] in the USA and the European Medicines Agency[2] in the EU have stated the importance of CM&S in regulatory science and innovation. They made steps towards modernising their regulatory policies and embracing computational and model-based evidence in their regulatory processes. The industry-led Medical Device Innovation Consortium[3] in the USA and the Avicenna Alliance[4] in Europe embraced this approach. They got ready through nurturing internal regulatory science and driving related standards (e.g., ASME V&V40[5] or www.eu-stands4pm.eu[6]). In January 2021 (with updates in 2022), FDA published their Advancing Regulatory Science at FDA: Focus Areas of Regulatory Science (FARS)[7], offering an excellent starting point. More to our specific proposal below, FDA Published a recent report showcasing the use of Modelling and Simulation at the FDA[8]. Following the March 2022 public kick-off[9] of the InSilicoUK Innovation Network (www.insilicouk.org[10]), which counted with Ministerial Presence, we are in the process of publishing several reports on various aspects of in-silico technology in the UK, the first of which is a recent InnovateUK-Beahurst Report on In-silico Medicine[11] on UK entrepreneurial activity, venture capital and start-ups.

Towards a Centre of Excellence for In-silico Regulatory Science and Innovation. This document provides further evidence of the benefits of creating a national capability on in-silico technology for the life sciences that enables and accelerates innovation, provides thought leadership and technical support to UK regulatory agencies, and produces best practice guidelines and standards to unleash practically the potential of innovation-friendly regulatory frameworks for the med-tech and pharma sectors. Such capability will build upon the success of and complement existing UK capabilities like, for instance, in artificial intelligence (Alan Turing Institute[12]), digital health data (Health Data Research UK[13]), high-performance computing (HPC-UK[14]), and UK networks like the Medicines Discovery[15], Digital[16] or High-Value Manufacturing[17] Catapults.

We believe a faster pace in the transition to in-silico methodologies would benefit patients and the health system by:

- Bringing new, innovative pharmaceuticals and medical devices to market faster;
- Modelling devices over decades, which is not feasible for real-life patient studies;
- Extending the trial cohort to rare, extreme or difficult-to-recruit patient phenotypes;
- Directly comparing two alternative treatments in the same virtual population;
- Evaluating devices under practically challenging physiological conditions that could represent extreme but plausible applications (off-label use);
- Reducing the number of humans and animals required in clinical trials;
- Reducing the number of failed clinical trials – in-silico trials provide more certainty for companies.

Economic Growth through Regulatory Innovation – The economic impact of in-silico technologies in the life sciences.

There are also enormous economic opportunities for in-silico trials. For example, an "Amazon marketplace" type system could provide pre-approved catalogues of algorithms or tools for modelling various devices or drugs. After undergoing regulatory assessment as Medical Device Development Tools (MDDT)[18] by FDA, these tools can facilitate device development, timely evaluation of medical devices, promote innovation, and support regulatory submissions and associated decision-making. This would create a vibrant new industry and stimulate the UK's med-tech and pharma sectors.

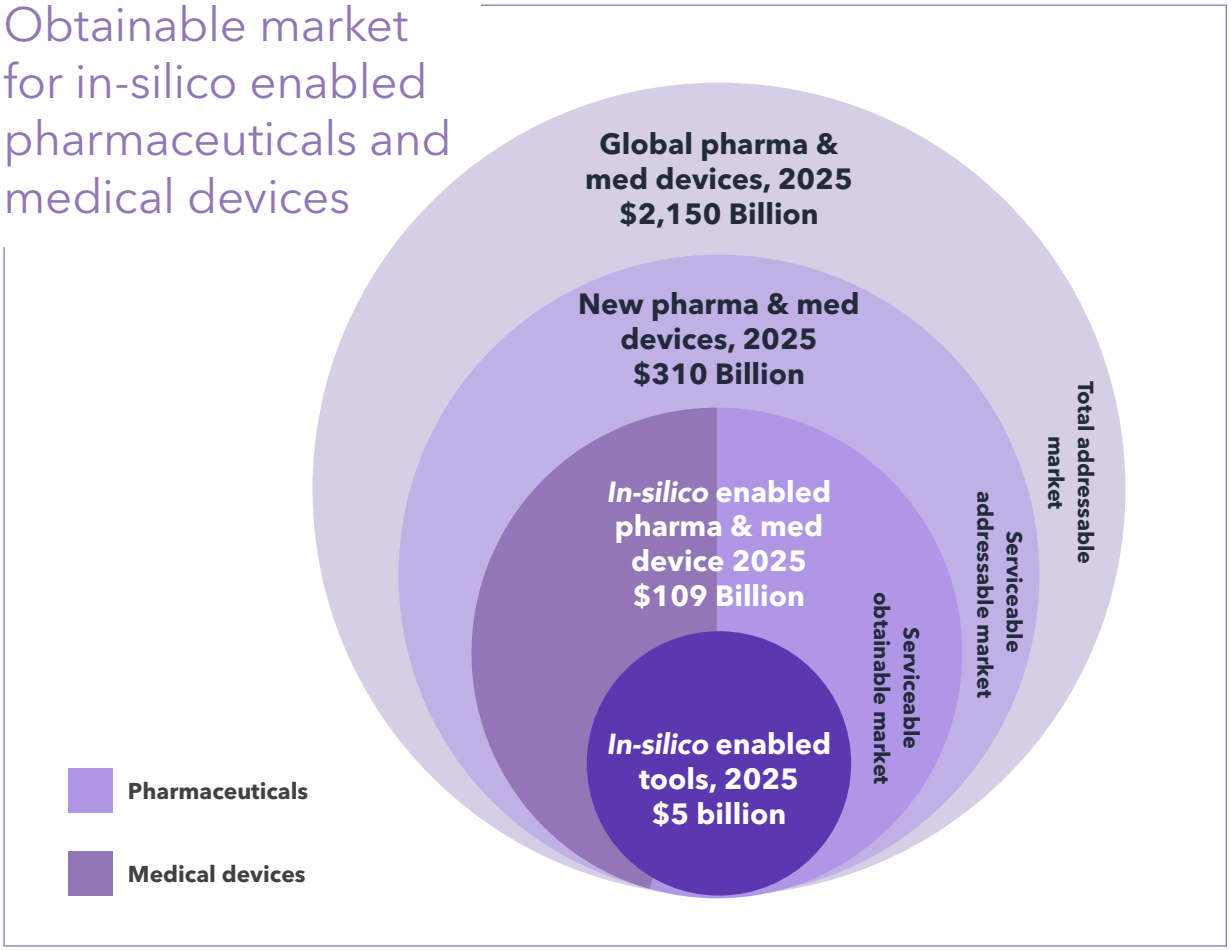
For the first time, this report evaluates the direct contribution *in-silico* technologies can bring to the UK economy and life sciences sector, highlighting the breadth of its impact. The analysis provides key demand and supply metrics and economic impact, including the revenue associated with *in-silico* technologies, the size of the affected workforce that will have to deal with these new essential skills, and the Gross Value Added (GVA) to the UK economy. The analysis is based on a proven methodology for quantifying the impact of transformative industries, which accommodates the diverse nature of the sector and accounts for the fact that *in-silico* technologies will be embedded within large, diversified companies.

2. Study Summary

The global market for pharmaceuticals and medical devices whose innovation or regulatory lifecycle has benefited from Computational Modelling and Simulation (CM&S, aka *in-silico*) techniques will grow at 16% per annum to reach $109 billion by 2025. These new pharmaceuticals will make up 43% of this market and 57% of the medical devices.

In-silico methods (and the derived *in-silico* scientific evidence) are predicted to have a major transformative role in increasing pharmaceutical and medical device development efficiencies. Experts estimate that by 2025, at least 25% of all new pharmaceuticals and 50% of new medical devices will use *in-silico* technology at some point in their ideation, design, development, production, regulatory approval or post-market surveillance.

Obtainable market for in-silico enabled pharmaceuticals and medical devices



This report may refer to those abusing the notation as *in-silico* pharmaceuticals or *in-silico* medical devices. Likewise, we will refer to *in-silico* tools or technology to the enabling software platforms, services or products that enable the conception, design, development, assessment, regulatory approval or post-market surveillance of any medical products.

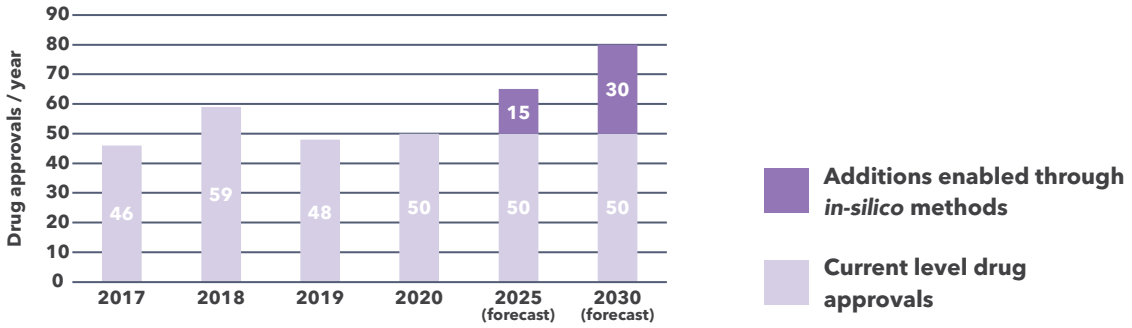
In-silico technologies are predicted to enable the following:

- average pharmaceuticals and medical device development costs to be reduced by up to 40%
- 30% more new pharmaceuticals and medical devices to be brought to market annually using *in-silico* techniques by 2025, rising to 60% and 30% more, respectively, by 2030

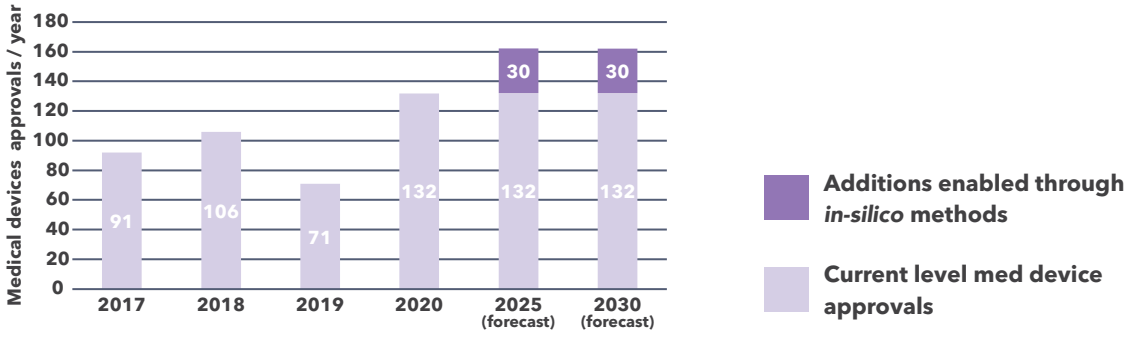
Developing any new pharmaceutical or medical device uses a wide range of often complex techniques and processes applied across the development and approvals process. Unusually *in-silico* evidence is predicted by all analysts to have an impact throughout the development process, with 40% of the impact in discovery, 29% in refinement & engineering, 20% in pre-clinical testing and 11% in clinical trials. This breadth of impact will drive significant disruption in medical product innovation and enable 60% more drugs and 30% more medical devices to be brought to market annually by 2030.

In-silico techniques will therefore be a key innovation enabler for the pharmaceutical and medical devices markets, sized at $1,260 billion[19,20,21,26,27] and $425 billion[22,23,24,25] respectively in 2020 and forecast to grow to $1,600 and $550 billion respectively by 2025.

Impact on the number of in-silico enabled pharmaceutical brought annually to market



Impact on the number of in-silico enabled medical devices brought annually to market



As *in-silico* methods can revolutionise pharmaceutical and medical device development, from identifying potential drug candidates to using digital twins in device approvals, *in-silico* evidence and methods will impact the entire £89 billion UK life science industry[28]. By 2025 at least £2. 6 billion worth of pharma and med-tech devices developed using *in-silico* methods will be made in the UK, even without increasing our global market share of medical product manufacturing. With a domestic market of ~£0. 8 billion, the UK will be a net exporter of the next generation of pharmaceutical and medical devices developed using *in-silico* evidence and methods.

UK Supply Side Impact	Pharmaceuticals	Medical devices	Total
UK pharma / med-tech manufacturing employment (2020)[28]			**111,200**
UK pharma / med-tech manufacturing sites (2020)[28]			**2,010**
UK pharma / med-tech manufacturing output (£ million) 2020[28]			**£ 31,700**
UK pharma and med-tech manufacturing (£ million), 2025 forecast[29]	**£ 24,300**	**£ 16,300**	**£ 40,600**
UK manufacturing *in-silico*-enabled medical *products* (£ million), 2025 forecast	**£710**	**£1,850**	**£2,560**
UK pharma / med-tech employment (2020)[28]	**129,900**	**138,100**	**268,000**
UK pharma / med-tech employees working with *In-silico* technologies, 2025	**32,500**	**69,100**	**101,600**

By 2025, it is predicted that 100,000 people in the UK life science sector will be working with *in-silico* technology daily. This is equivalent to 40% of all the people employed in biopharma and med-tech sectors in the UK[28], reflecting the research and development intensity of the life science sector and the demand for *in-silico* innovations to improve the efficiency of pharma and medical device innovation.

Demand from medical device and pharma developers will grow the open market for *in-silico* software tools and services to $5. 0 billion globally by 2025 and $9. 2 billion by 2030[30,31,32,33], with the UK share of this being at least 5%. This will form a key part of the global $110 billion market[34] for drug discovery technologies in 2025.

This open market is only a small fraction of the value of *in-silico* tools developed internally by pharmaceutical and medical device manufacturers for their internal use. This is illustrated by the number of companies, especially in drug development, built around a foundation of applying *in-silico* techniques, exemplified by the UK's Exscientia, which reports supporting the development of 25 new drug candidates with a workforce of only 210 people[38]. Whilst many other drug development technologies are bought in, a growing trend would appear to be the internal development of *in-silico* modeling and simulation expertise, reflecting the value companies put on this technology as a key enabler.

In-Silico Tool Market	2025	2030
Global open market for *in-silico* tools, software and contract services[30,31,32,33]	**$ 5. 0**	**$ 9. 2**
Fraction of drug discovery tech market (for scale)[34]	**5%**	**5%**
Fraction of the high throughput drug discovery market (for scale)[35,36,37]	**21%**	**26%**
UK market for *in-silico* tools, software and contract services (£ million)	**£ 187**	**£ 351**

Definitions

Pharmaceuticals

The definitions of Pharmaceuticals (including biopharmaceuticals) used is based on the WHO definition[39]: "any substance or pharmaceutical product for human or veterinary use that is intended to modify or explore physiological systems or pathological states for the benefit of the recipient" defined in more detail and regulated by the UK government[40]. The terms drug, medicine, and (bio) pharmaceutical are used interchangeably.

Medical Devices

Medical devices refer to the definition by WHO[41]: a "medical device can be any instrument, apparatus, implement, machine, appliance, implant, reagent for in-vitro use, software, material or another similar or related article, intended by the manufacturer to be used, alone or in combination for a medical purpose" and defined in more detail and regulated by the UK government[42].

In-Silico Technology

***In-silico* evidence and methods refer to using Computational Modelling modelling and Simulation (CM&S) in medicine (or *in-silico* medicine). In this context, the term' *in-silico* clinical trials'[43] refers to developing patient-specific models to form virtual patient cohorts upon which to test for the safety and/or performance of new drugs and new medical devices. Predictive CM&S approaches vary, ranging from pure data-driven, phenomenological modelling to knowledge-driven, mechanistic simulations. In the context of in-silico medicine, it is generally favoured, where possible given the available knowledge, the use of mechanistic over phenomenological CM&S as this provides usually beter generalisation than purely data-driven methods.**

***In-silico* methods and evidence are yet to consolidate their positioning in medical product innovation and regulatory pathways, but their impact is expected to be broad and staged. The initial focus will likely be on how *in-silico* methods and evidence enhance evidence regulators currently receive and how evidence-free gaps (paediatrics, rare diseases, combination devices, incremental innovation, etc.) can be filled.**

In this study, we have taken a liberal approach to the intended use of *in-silico* evidence throughout the R&D lifecycle of medical products. That is, we will equally include uses in ideation, design and pre-clinical testing (where *in-silico* methods can provide more realistic design and testing conditions than a bench or animal test), *in-silico* clinical trials (e.g. as a sifting tool of real clinical trials for which there might be sufficient CM&S grounds to believe they will lead to negative results) or relevant as parallel arms to post-market registries (e.g. using *in-silico* models that get updated with post-marketing surveillance data to anticipate risks on marketed products before they materialise).

3. Survey Results

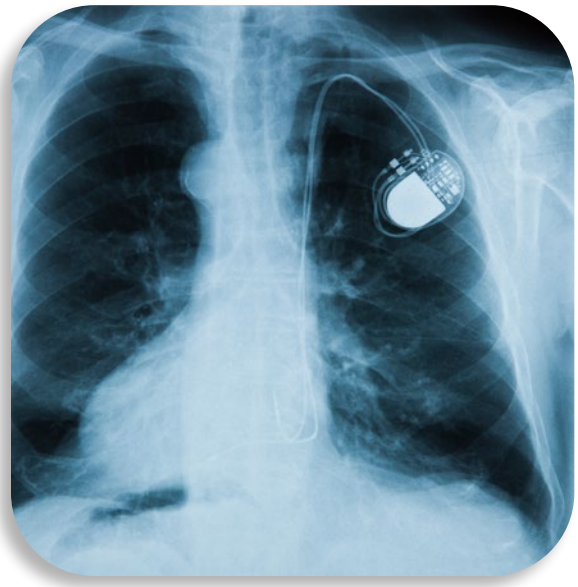
The community were surveyed to gain expert input on the fraction of new pharmaceutical and medical device that would use *in-silico* techniques at some point in their development and the impact on pharmaceutical and medical device productivity.

3.1. Pharmaceuticals

Survey results	Median response
Fraction new pharmaceutical drugs approved between now and 2025 developed using *in-silico* techniques	25%
Additional pharmaceuticals approved per year in 2025 with *in-silico*	15
Additional pharmaceuticals approved per year in 2030 with *in-silico*	30

3.2. Medical Devices

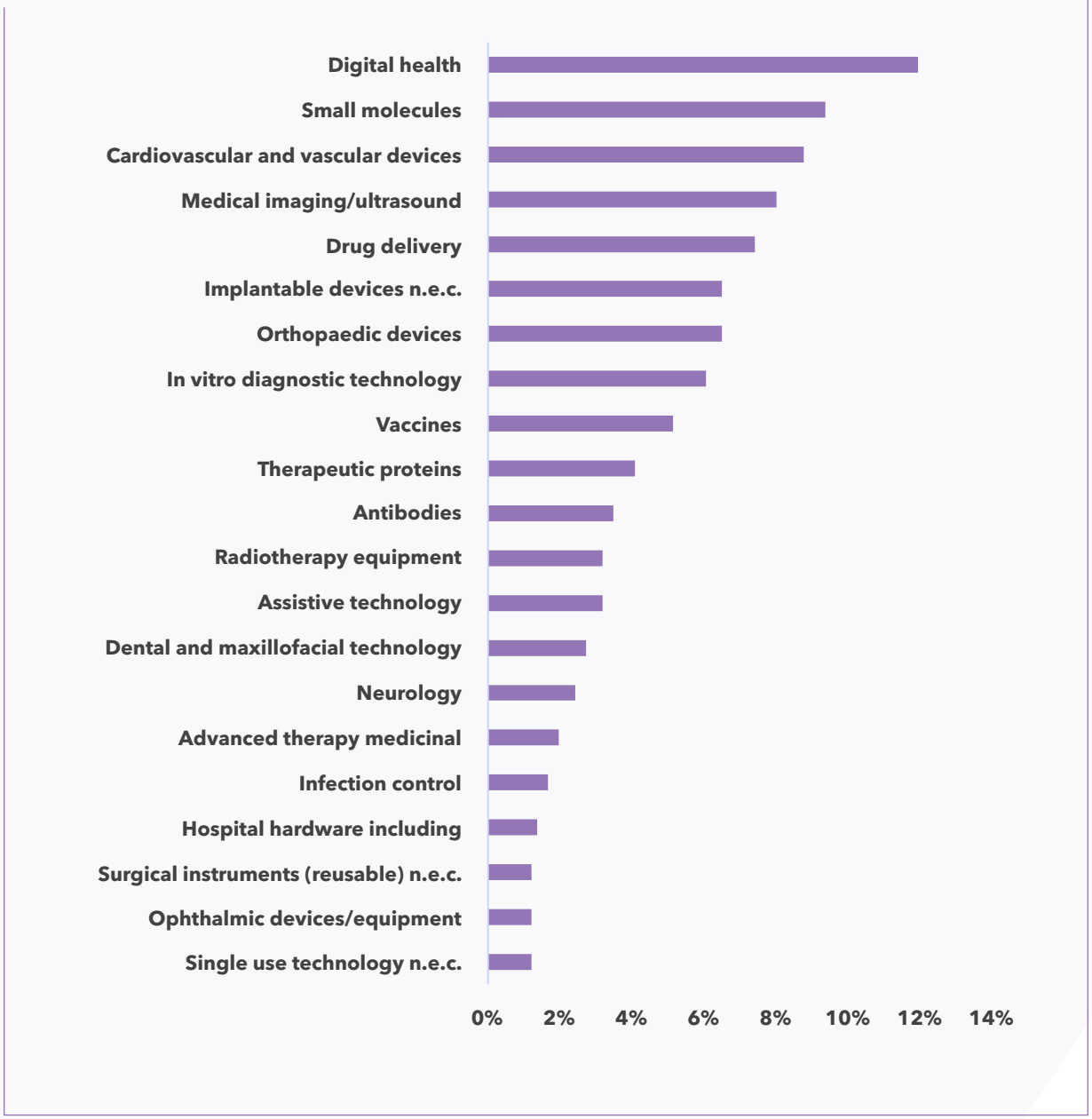
Survey results	Median response
Fraction new medical devices approved between now and 2025 developed using *in-silico* techniques	50%
Additional medical devices approved per year in 2025 with *in-silico*	30
Additional medical devices approved per year in 2030 with *in-silico*	30



3.3.
Impact Per Life Science Subsector

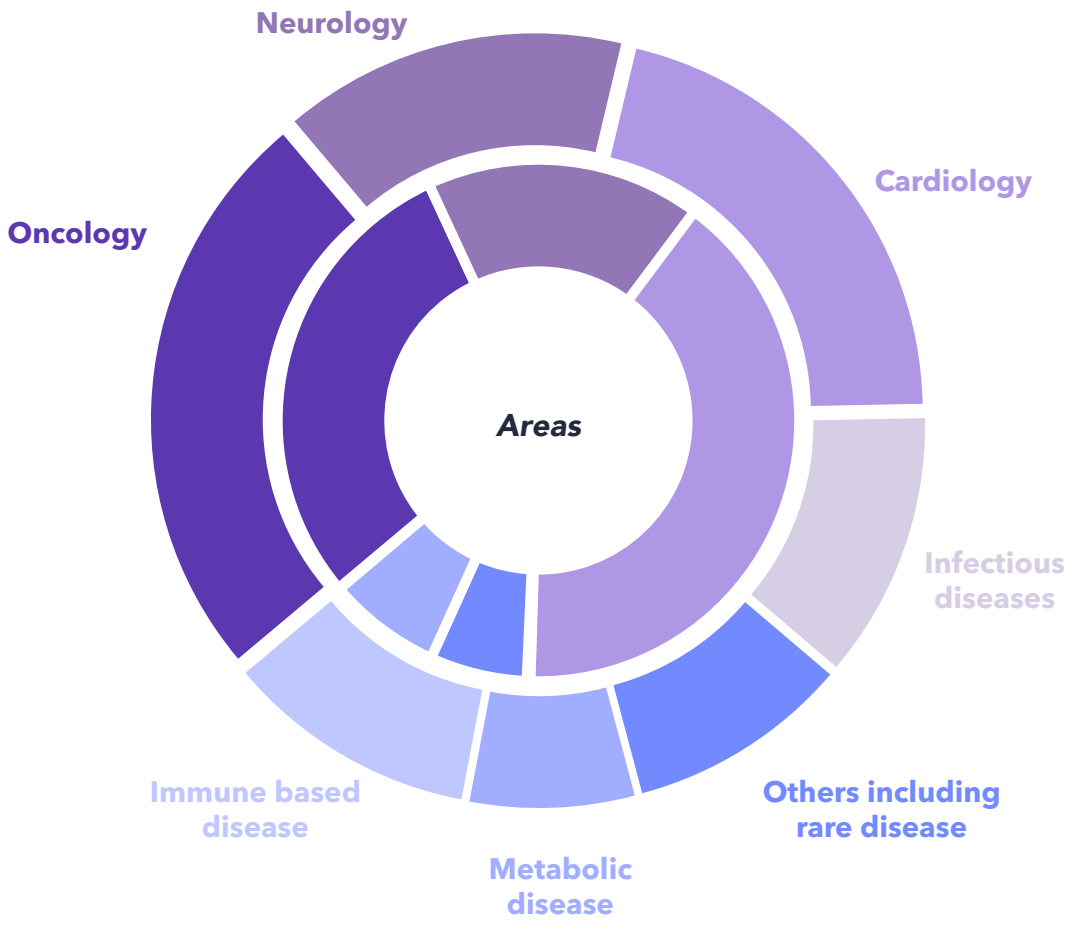
Based on our respondents, the primary life science subsectors impacted by *in-silico* techniques will be:

Products where *in-silico technologies will have an early impact first*



3.4.
Impact Per Therapeutic Areas

Therapeutic areas impacted early by adoption of in-silico technologies across the lifecyle - pharma and med devices



Outer circle Crowd-sourced predictions of areas of early therapeutic impact across various product lifecycles according to our survey.

Compared to

Inner circle Predictions of areas of early therapeutic impact according to previous analysts[30,32].

The comparison shows that there is common agreement that the major impact of *in-silico* technologies will first be in cancer, cardiovascular and neurodegenerative disease treatment. The greatest variation is seen around the potential treatment of infectious diseases.

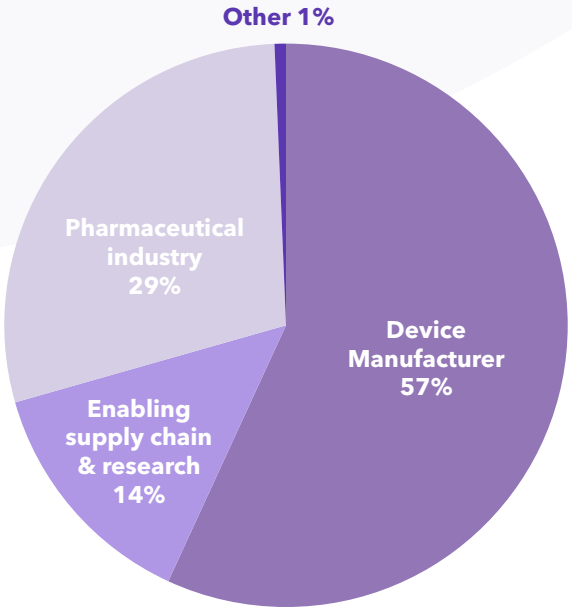
3.5.
Survey Respondents Profile

One-third of the 165 surveyed respondents identified most strongly with the pharmaceutical sector and three-fifths with the medical device sector.

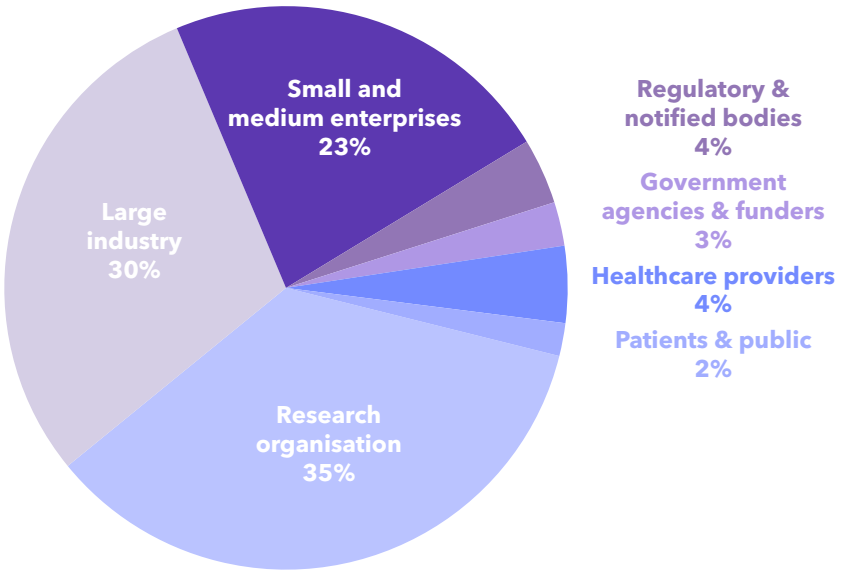
Respondents were fairly uniformly split between research organisations, and large and small industries, with a slight bias toward research organisations.

Relative to this report's preliminary versions, significant additional input was received from the pharmaceutical sector.

Per sector



Per organisation type



3.6.
Survey Response Distribution

The lack of crossover knowledge (i.e. pharmaceuticals vs medical devices) of *in-silico* technologies impact was indicated by the fraction of respondents who selected they were unable to provide input on the fraction of pharmaceutical drugs that would leverage *in-silico* in their development but could be for medical devices or vice versa.

Whilst the median response to the question about the fraction of new pharmaceutical or medical products leveraging *in-silico* method in product lifecycle was 25% and 50%, respectively, there was a wide distribution of responses. There were many respondents indicating the impact in pharmaceuticals could be 75% or more, as those indicating that it would be 10% or less.

Given the strong representation of research organisations, survey data was checked for correlations between organisation type and the impact of *in-silico* methods. No correlation was seen evidencing that those working in research organisations or industry, respectively, are more or less likely to indicate their views on *in-silico* technologies update will have a high or low impact.

In-silico technologies will lead to increased amount of new products by 2025

4. Methodology

4.1. Total Addressable Market

Pharmaceutical and medical device markets are subject to extensive analysis and forecasting, with multiple reports estimating the current size and growth of these key global industries[19,20,21,22,23,24,25,26]. Due to the impact on these key markets, there are also several reputable market forecasts for *in-silico* software and services[30,31,32,33]. The *in-silico* industry is also relatively new and rapidly growing, with many of the most significant players developing their in-house tools and applying these to pharmaceutical and med device development rather than putting them on the open market.

The methodology applied here to quantify the economic impact of *in-silico* technology has therefore sought to:

- Leverage the best quantitative information available from wide reputable independent reports and a range of analysts.
- Combine historic data and projections from various reputable sources into consistent estimates and assumptions.
- Combine these estimates with community estimates where historic data or published forecast are unavailable.

The starting point was to form a consensus on the overall pharmaceutical and medical device markets in 2020, 2025 and 2030. Where published market reports used different base years, these were transposed using the compound annual growth rate associated with each forecast. In combination, these form the Total Addressable Market (TAM).

4.2. Total Serviceable Addressable Market

A significant fraction of the pharmaceutical market relates to the sales of previously developed and approved products and generic medicines. Fully approved and in established production, existing products are not forecast to be significantly impacted by *in-silico* developments. Therefore, the fraction of the pharmaceutical and medical devices markets related to new drugs or devices coming to the market was identified as forming the total Serviceable Addressable Market (SAM).

In the pharmaceutical market, forecasts for the market for new brand drugs are widely available, enabling separation from the overall pharmaceutical market[19]. The number of new drug approvals per year is also widely reported over several years, with a median of ~50 per year evident.

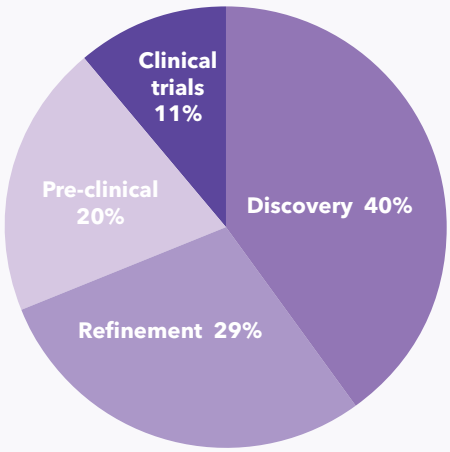
The value of new devices approved annually is less clear for medical device data. Therefore an approximation is used that the market growth over 5 years is equivalent to the value of the new device launched over that time. This assumes that the market for existing medical devices is static, and all growth comes from new launches. The market for a new device may be greater or less than this, depending on how many new devices take sales from existing solutions or if there is substantial growth in older devices. As a balance between these two, it is a fair working assumption and not significantly different from the dynamics seen in the pharmaceutical sector. A consensus view of ~100 medical device approvals per year was used as a base, although, as with pharmaceuticals, this is acknowledged as open for disruption.

4.3. Serviceable Obtainable Market

Whilst *in-silico* techniques can be applied to a wide range of processes through the lifecycle of product development, from discovery to approvals, they will not be used in all cases. The Serviceable Obtainable Market (SOM) was therefore taken as the fraction of new pharmaceuticals or medical devices that will use *in-silico* techniques at any point in their discovery, development and approval. This critical impact information is not available in published reports and was taken from an expert survey of the community, who were asked, in separate questions, what fraction of new pharmaceutical and medical devices would be brought to market with *in-silico* techniques in 2025. The median of survey results was applied to the SAM for new pharmaceuticals and new medical devices to give the SOM in each case and summed up to give the total forecast market for *in-silico*-based pharmaceuticals and medical devices. Responses where 'No idea or impossible to guess' were selected were ignored in calculating the median.

The UK market share (demand/consumption as distinct from production) was based on the European and UK share of the global market for new pharmaceutical and medical devices. This is notably less than the proportion of new pharmaceuticals as a fraction of the global market, attributed by analysts to differing global reimbursement regimes and healthcare structures.

In-silico technologies impact across the product lifecycle



4.4. Productivity Efficiency

One of the greatest potential impacts of applying *in-silico* techniques is to increase the productivity of pharmaceutical and medical device developments. The community were, therefore, also asked for input on how many additional drugs or medical devices per year would come to market with the application of *in-silico* techniques. Relative to the current reported number of annual approvals, this additional survey output was used to estimate the productivity increases in drug and medical device development due to the application of *in-silico* predicted for 2025 and 2030. As noted below, an increase in the absolute number of products coming to market does not necessarily correspond to the growth in the market value of these products.

4.5. UK Market & Manufacturing Value

The SOM for *in-silico* pharmaceuticals and medical devices establishes demand and the global potential for *in-silico* in medical products, but not the potential for UK manufacturing and impact on productivity in the UK life science sector.

The potential for *in-silico* to impact UK manufacturing was estimated, assuming the UK's current share of pharmaceutical production will remain constant. It is also estimated that the UK's share of new drug manufacturing is the same as the global share of the total market and that the share of those new drugs made in the UK developed with *in-silico* is the same as the global share. The same logic was applied to the medical device sector. The simplification in these assumptions is acknowledged and should be considered with caution given that the value of UK pharmaceutical and med-tech device manufacturing in the UK is reported by the UK Office for Life Sciences, Bioscience and Health Technology as declining at ~2. 4% per year[28].

4.6. UK Employment

Given the wide variety of stages in the development and approvals process, *in-silico* techniques impact medical product innovation, and the high fraction of the market impacted, as illustrated in our survey, *in-silico* will impact the entire life science sector in the UK. Their launch will impact even those not working with new *in-silico* products as they re-position existing products and adapt supply chains. The number of UK jobs impacted and employees needing to be familiar with *in-silico* technology is therefore taken as the product of the predicted fraction of new pharmaceuticals or medical devices developed with *in-silico* in 2025, obtained from the survey, with the total employment in the UK BioPharma and Medical technology sectors in 2020 respectively[28]. This assumes that UK biopharma and med-tech employment will not significantly change over the next 5 years. This assumption is open to disruption but consistent with the principle impact of *in-silico* on development productivity (below). This also implies a need for significant and rapid retraining of the life science sector in *in-silico* technology to ensure it is fully leveraged in the UK.

4.7. *In-Silico* Software as Enabling Technology

In developing new pharmaceuticals and medical devices, *in-silico* techniques will naturally drive growth in the demand for *in-silico* software tools, services and contracted research involving such tools. Published long-term forecasts for the open market of these tools vary in their coverage, i.e. tools for medical devices and pharmaceuticals or just drug discovery[30,32,33]. The current market for *in-silico* tools is $2.7bn (2020), rising to $9.2bn (2030) based on the consensus that includes applications in both areas and is also within that forecast for the use of digital twin in healthcare[31]. Forecasts of the UK market share remain constant at 4. 7-5% over ten years. The same forecasts indicate where *in-silico* techniques will be used within pharmaceutical and med device development where a 50:50 split is common vs the 60:40 split from the current survey.

4.8. Life Science Subsector Analysis

The survey asked respondents to select up to three subsectors or areas where *in-silico* will be first applied. The survey asked respondents to select up to three subsectors or areas where *in-silico* evidence and methods will be first applied. The list of subsectors was derived from a combination of the bio pharm and medical tech subsectors identified in the UK official Bioscience and health technology sector statistics 2020[28]. Subsectors were given a score of 1 if selected and 0 if not. The total scores across all respondents were summed to provide the priority list of subsectors impacted.

4.9. Analysis per Therapeutic Areas

The survey asked respondents to select up to three therapeutic areas *in-silico* with first impact, with no priority request between the top three. The area was given a score of 1 if selected and 0 if not. The total scores across all respondents were summed to provide the priority list. Total scores were then normalised to 100 to give the percentage split for comparison with other analysts' forecasts.

Unlike other analysts, no timescale was requested for when this first impact will occur. The question was also specific to which areas of evidence on safety and performance would first have an impact.

5. Study Assumptions

When valuing the pharmaceutical market, we have not considered the impact of off-invoice discounts and rebates in certain markets. Industry analysts note these can impact reducing the effective market size in some geographies but are not uniformly applicable and, therefore, not considered here.

The consensus value used here for the *in-silico* tools market supporting pharmaceutical and med device development ($5 billion in 2025 and $9. 2 billion in 2030) is within the optimistic scenario given by BIS Research[33] for *in-silico* tools used in drug discovery alone. Assuming that *in-silico* tools will be applied ~60:40 between drug discovery and medical devices, this implies a potential upside market for *in-silico* tools across med devices and pharm of up to $15 billion by 2030.

5.1. Productivity Vs Market Growths

The methodology separates the impact of *in-silico* on the value of the market and the number of new product approvals. Alongside medical product markets, many analysts consider spending in these areas and healthcare in general as a fraction of the Gross Domestic Product (GDP) in countries across the globe. Given the very high percentage of GDP directed to healthcare and the significant fraction already spent on pharmaceuticals and med-tech devices, it is assumed that it is not viable for *in-silico* to drive significantly higher value growth in these markets than already forecast. Therefore current forecasts of market growth and new product introductions are used with *in-silico* products taking an increasing fraction of these, but not necessarily creating the inflexion in value growth that may be expected in other markets on introducing such a disruptive technology.

Rather *in-silico* will make the development of medical products much more efficient, increasing the number of products brought to the market per year, driving a significant inflexion in the number of different medical products available, as indicated in the efficiency impact figures. This should provide a major societal impact by enabling the treatment of a wider range of conditions with a wider range of medication and medical devices better matched to individual needs. Disrupting development efficiency should also lower development costs per product, enabling lower costs per product and more treatments for the same budget assuming productivity gains are passed to healthcare providers. Enabling a step-change in development productivity also offers the potential for much greater security in the life science sector by spreading new product income among a greater variety of products reducing the impact should a single drug or medical device not be successful in the market.

5.2. UK´s Share of Global Market

Analysts predict the UK share of the global market for pharmaceuticals and medical devices enabled through *in-silico* technologies and the market share of the *in-silico* tools global market to be highly consistent over time. Such consistency is normally a sign of an evolutionary market not subject to significant disruption. The application of *in-silico* techniques offers significant disruptive potential. Thus whilst consistent market share assumptions are applied in this methodology, they are potentially subject to change according to how *in-silico* is adopted.

Timely application of *in-silico* techniques has the potential to disrupt a number of the assumptions both on the UK share of manufacturing and the UK market for new medical products. Whilst the choice of manufacturing location, especially for pharmaceuticals, is often based on the type and chemistry of formulation, it can also efficiently transfer new products to manufacturing close to the development site. The emergence of pure-play *in-silico* pharma development companies, such as the UK's Exscientia, who intend to make extensive use of sub-contracted manufacturing[38], may also change the geographic manufacturing distribution as a result of the indirect impact of accelerating product pipelines and driving demand for additional capacity for the manufacture of a wider range of products.

If the significant shifts in medical product development productivity translate to lower costs and increased product diversity. In that case, this may also impact adaption rates for such new products in the UK, which analysts note is lower in the UK and Europe than, e.g. North America, potentially increasing the UK's share of the global market for *in-silico* products above the £0.8 billion indicated.

5.3. Influence of COVID19

As noted by many analysts, the COVID19 pandemic has significantly impacted had a significant impact on both pharmaceutical and medical devices markets. The device market, in particular, saw a substantial downturn from which it is currently recovering. On the inverse side, the production and sales of COVID19 vaccines had a notable impact on the pharmaceutical market. Analysts generally agree that these effects are short-term (2-3 years) and are already working through the relevant markets. The forecasts and economic impact predictions derived here can therefore be considered valid in the post-COVID world and take short-term disruptions into account.

5.4. Development Tool Mix

Whilst the expert view of the impact of *in-silico* methods is very significant, it should be noted that these tools form part of highly complex development processes using a wealth of additional technologies in which *in-silico* methods works alongside. This is illustrated by the modest finite fraction of the total drug development market and high throughput screening market that all *in-silico* enabled pharma represent.

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Appendix Survey Questions

The request for input on the following questions was distributed to the InSilicoUK Slack Community (insilicouk.slack.com) on LinkedIn and social media starting on 11 March 2022. Responses were collated on the TypeForm survey platform. One hundred sixty-five (165) responses were received by 7 June 2022.

Pharmaceuticals

1) What fraction of the ~250 new pharmaceutical drugs* forecast to be approved between now and 2025 will be developed using computational modelling & simulations in at least one stage of their discovery, development, manufacturing, and regulatory approvals.

a) 1%,
b) 5%,
c) 10%,
d) 25%,
e) 50%,
f) 75% (select one of them).

* new pharmaceuticals being taken as drug formulations of any type applied for any treatment approved for use in at least one major market, e.g. USA, Europe, Asia.

2) With the application of CM&S at any point in discovery, development and regulatory approval, how many additional drug formulations will be approved per year in 2025 and 2030, above the current baseline of ca. 50 per year

a) *In-silico*-enabled additions in 2025 - No change, 5 more, 15 more, 30 more, 60, >60 additional approvals (select one of)
b) *In-silico*-enabled additions in 2030 - No change, 5 more, 15 more, 30 more, 60, >60 additional approvals (select one of)

Medical Devices

3) What fraction of new medical devices launched between now and 2025 will use CM&S sometime during their conception, development, manufacturing, and regulatory approval?

a) 1%,
b) 5%,
c) 10%,
d) 25%,
e) 50%,
f) 75% (select one of).

+Applying the broad definition of medical devices from implants to instrumentation approved for use in at least one major market, e.g., USA, Europe, and Asia.

4) With the application of CM&S, how many additional medical devices will be approved per year in 2025 and 2030 above the current base-line of ca. 100 per year

a) *In-silico*-enabled additions in 2025 - No change, up to 15 more, up to 30 more, up to 50 more, up to 75 more, >100 additional approvals (select one of)
b) *In-silico*-enabled additions in 2030 - No change, up to 15 more, up to 30 more, up to 50 more, up to 75 more, >100 additional approvals (select one of)

5) What are the top 3 application pharmaceutical or medical devices developed and approved with the aid of *in-silico* techniques will first be applied to (Pick list – choose 3)

a) Small Molecules.
b) Therapeutic Proteins.
c) Antibodies.
d) Vaccines.
e) Advanced Therapy Medicinal Products.
f) Blood & Tissue Products.
g) In-vitro diagnostic technology.
h) Assistive Technology.
i) Orthopaedic Devices.
j) Ophthalmic Devices/Equipment.
k) Reusable diagnostic or analytic equipment not covered else-where.
l) Medical Imaging/Ultrasound Equipment and Materials.
m) Drug Delivery.
n) Surgical Instruments (reusable) are not covered elsewhere.
o) Cardiovascular and vascular de-vices.
p) Anaesthetic and respiratory technology.
q) Dental and maxillofacial technology.
r) Radiotherapy equipment.
s) Implantable devices are not covered elsewhere.
t) Neurology.

Appendix Survey Questions

6) Which therapeutic area will *in-silico* evidence on safety and efficacy first have an impact (select up to 3)

a) Cardiovascular
b) Neurodegenerative
c) Oncology
d) Orthopaedic
e) Dermatology
f) Rare disease
g) Metabolic disease
h) Immune-based diseases
i) Infectious diseases
j) Other (define)

Respondent Verification

7) What sector do you most closely associate with (select all that apply)

a. Medical device research, development, sales, distribution, manufacture, regulation, or application
b. Pharmaceutical research, development, sales, distribution, manufacture, regulation, or application
c. Supply chain and enabling re-search, technologies, and services (e.g., simulation and modelling software, computer and storage infrastructure, data hubs and providers, contract research organisations, etc.)
d. Other (specify)

8) What organisation are you based in, or do you work for?

a. Healthcare providers (e.g., health and care professionals as defined by HCPC)
b. Research organisation (e.g., High-er education institutions, independent research organisations, public sector research establishments, UKRI-funded Institutes/Units)
c. Industry (Large, >250 employees)
e. Industry (SME, <250 employees)
d. Regulatory and notified bodies, Compliance Testing
e. Government, funding bodies, re-search charities
f. Trade association or other related sector body
g. Patients and Public
h. Other (describe)

9) Any comments on the survey or the economic impact of *in-silico* trials (Free text input, limited to 200 characters)

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