



Multifiscale Complex Genomics



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Executive summary

In this document we explore the options open to the MuG consortium that will allow their project results to survive independently from project funding.

From a stock-take of project results, a preliminary service catalogue has been developed. The candidate services identified have been built into a business model and this has been tested against the market models that have also been developed through detailed market analysis activities. We find that there is a huge potential market for the MuG platform, where revenues, are easily able to support the running and development of the platform and also to guarantee the support organisation around it. The business and market modelling also revealed that although there would be very low revenues in the first phase of organisational operations there would be sufficient funds to cover the modest start-up costs and to grow the organisation organically. Preliminary business planning activities have taken these issues into account.

The need to create and deploy an organisation to support the sustainable operations of the MuG platform was agreed early on in the project and many options were discussed. Informal organisations were discounted and formal structures were favoured. Outright commercial activities did not sit comfortably with some partners so a not-for-profit organisation was favoured. However, upon greater exposure to this model we discovered that there may be operational constraints placed upon the organisation that harmed sustainability. We are currently in the final phases of decision-making about the legal entity type we will establish to support the sustainable operations of the MuG platform. We also discussed the possibility of licensing the MuG platform to a third-party organisation. This is still an option.

We consider two main business models. The first is the formation of a distinct legal entity that will grow a business around the MuG platform in order to support it in the long term. The second is the sale of rights the commercial exploitation of the MuG platform to a third-party legal entity. Partners, in general, favour the first (legal entity) option as it gives them more control over the platform and how it evolves, and how it can be constrained especially in relation to profit making activities: partners are more comfortable supporting a not-for-profit entity but there are problems still to resolve here. A third option is also considered where the first (legal entity) option is supported for a period through continued project funding. This is the most likely model moving forward and partner exploitation plans reveal a strong commitment to supporting this approach. The EOSC initiative is considered a likely source of such funds.

The activities reported in this deliverable demonstrate that there is a real opportunity to deploy the MuG platform and operate it in a sustainable manner. However, there are competitors. MuG has the lead in terms of time to market and also in performance and utility. We intend to capitalise on this advantage in order to establish a global market, able to support our ambition to make the MuG platform available to researchers, wherever they may be.



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1 INTRODUCTION AND BACKGROUND

The Multiscale Genomics (MuG) research project is funded by the EU Horizon 2020 research and innovation programme under grant agreement No 676556.

Experiencing exponential growth, the area of 3D and 4D genomics represents one of the greatest challenges for biology and biomedicine in the next decade. Understanding how the genome is organized in space and how this affects gene regulation will be instrumental in developing a full understanding of the time-dependent connection between genome and phenome. MuG has successfully moved the State of the Art in genomics away from static 1D and 2D models that are difficult and time consuming to construct, into a place where dynamic 3D and 4D models are easy to construct, destruct and reproduce.

Specifically, the MuG project has developed tools and services that address the following challenges:

- Preventing the decline in 3D/4D genomics field, due to an inability to manage the computational problems originated within massive sequencing experiments and simulations.
 - MuG has brought the software tools commonly used in the genomics community and prepared them for efficient Exascale operations on High Performance Computing (HPC) infrastructures. All data handling issues are addressed through the development and integration, within the MuG VRE, of a common genomics data infrastructure. To ease access to the newly standardised data MuG has created the first ever multi-resolution genome-browser with visualization tools able to move from 1D genomics, to low- and high-resolution 3D/4D levels.
- Organisation of the 3D/4D genomics community, bringing it closer to the HPC and Big Data worlds.
 - MuG has stimulated and actively engaged the growing biology community to encourage improved interactions with the HPC and Big Data communities. It has achieved this through the development and deployment of user oriented solutions, where new standards in software tools and data have been defined and an efficient and sustainable, HPC-optimized infrastructure has been created. The sustainable infrastructure will foster research in the 3D/4G genomics field for years to come.
- Developing an integrated three-dimensional picture of the genome.
 - Through pilot studies, MuG has proven the strength of the developed methodology and has improved understanding of chromatin structure and dynamics and other biologically relevant topics through the development of complex multi-dimensional data structures accessible and visualise-able within the genome-browser.

2 EXPLOITATION OF PROJECT RESULTS

In this section we discuss the exploitable results of the project and how they may be best able to reach a market.

2.1 Stocktake of Exploitable Results

The primary exploitable result and the main focus of this business plan is the MuG Virtual Research Environment (VRE). The MuG VRE is a platform that helps those working in the expanding field of 3D/4D genomics. The platform offers services that link existing genomics tools in a manner that improves consistency and the speed at which workflows can be deployed, connecting the various tools required in each experimental pipeline. With more consistent pipeline configuration and improved navigation, the quality and consistency of data output are also improved when sequencing 3D/4D genomics data.

Deliverable D6.2 has provided a detailed analysis and justification for tool integration into the MuG VRE. The analysis has structured the tools under four main headings: Feature prediction, Structural analysis, Docking and Affinity analysis, Motif Discovery and Binding Site prediction. The tools described here are not the focus of the business and sustainability plan; however, the IP of some of the tools are owned by the participants in the project and these will be exploited independently by them when the project concludes. For this reason and other reasons connected with the protection of market opportunity, great attention will be given to the licensing conditions attached to the tools, when MuG services are offered to users of the VRE, once sustainable operations commence. This is to ensure that there are no constraints placed on the sustainable VRE by these same licences. For completeness, D6.2 is enclosed at Annex A to this report.

The primary result is an open source, free to access service, made by scientists for scientists. The basic version of the primary result will always be freely available for use by the scientific community. However, its deployment and support must be provided for somehow. To this end the sustainable MuG entity reserves the right to develop tools and services to run on or become part of the basic offer and these may be charged for. Furthermore, a number of ancillary services have also been identified, these are associated with the primary exploitable result and add value to the value already derived from the primary result itself. These services look likely to deliver sufficient income to support the deployment and sustainable operation of the MuG VRE platform. These ancillary services are discussed later in Section 2.5.

2.2 Market Analysis

The ultimate MuG VRE target market is global in nature. Initially, it is composed of researchers working in the genomics research community in both the academic and pre-competitive industrial research contexts, thereafter we plan to target the global diagnostics market. However, for a number of factors related to the current maturity of the VRE, we plan to initially grow slowly and organically and for this reason, our first target market will be composed of EU academic genomics researchers, thereafter EU pre-competitive genomics researchers. By the time we have adequately addressed these market needs, we are confident that the VRE will be sufficiently mature to launch globally.

The overall global genomics market is huge and segmented along several dimension, under four main headings: Application, Product, Technology and Region. The next level of market decomposition reveals the following:

- Application market
 - Research market
 - Diagnostics market
 - Drug discovery market
 - Personalised medicine market
 - Agriculture market
- Product
 - Instruments market
 - Consumables market
 - Services market
- Technology
 - Polymerase Chain Reaction market
 - Deoxyribonucleic Acid (DNA) sequencing market
 - DNA microarray market
 - Nucleic acid extraction and purification market
- Region
 - North America market
 - Europe market
 - Asia Pacific market
 - Rest of World market

Given this level of decomposition, we estimate that the most likely targets for MuG VRE marketing is in the Research and Diagnostics areas of the Application market. However, although these markets already exist, they are populated by a vast number of independent tools (which are further considered below in Section 2.4); the MuG VRE is not a direct competitor of such tools but rather offers an enhancement of them, improving their performance in a number of important ways, which are explored in Section 2.5 below. For this reason, we must create a new market for the MuG VRE within these two existing markets.

Meaningful data about the global market in genomics applications are very difficult to come by, mainly because they are locked behind very expensive paywalls. However, some sample data have been extracted from a sample report by Grand View Research¹ and validated against other available open sources². These data have been used to ground and calculate the data employed here. All data are available in Annex B at the end of this document and we encourage the rest of this section to be read with the Annex data at hand; however, we summarise them here. NB No data are taken directly from either source referenced in order to comply with the copyright restrictions placed on the reports cited, the sources have been used merely to validate and test the calculated data.

¹ Genomics Market Analysis And Segment Forecasts To 2020. Published privately in 2016 by Grand View Research, Inc., 28 2nd Street, Suite 3036, San Francisco, CA 94105, USA. If full data are required in future, they can be purchased through: sales@grandviewresearch.com.

² Baranick B and Vadas A, Genomics 2020: Research and Clinical Trends to Watch, in Executive Insights Volume 18, Issue 43. Published privately in 2016 by L.E.K. Consulting LLC

We find that the global genomics market had a value of nearly \$11B in 2014 and this overall market is forecast to grow to nearly \$24B in 2022, with an annual market growth rate of 10.2%. As already mentioned, the overall market value can be segmented by: Application type, Product type, Technology type and Geographical region. From this segmentation, we find that the EU genomics research market was valued at nearly \$280M in 2014 and is expected to grow to just over \$591M in 2022.

Of this market we cannot expect the MuG VRE platform element to be a significant feature until much later in its operation, for this reason we cap the reachable market at 10% of the whole EU genomics research market. This leads to the revelation that the possible market that the MuG VRE is initially aiming at will be capped at approximately \$28M (if we had launched in in 2014) and at \$59M in 2022. However, the MuG VRE will not immediately be able to reach these market targets, it has to grow from a market introduction base, which because of the difficulty we anticipate in “selling” research results in conjunction with the fact that the “value added” aspects of the platform are expected to be intrinsically difficult to sell (initially), we have set the preliminary reachable market for MuG VRE market introduction at 1% of the overall possible market share and have assigned a low 1% annual growth rate for our projections (starting at the 2014 baseline).

We have used these very conservative predictions in the modelling, in order to stress-test the viability of the MuG VRE business case under harsh conditions. So, assuming that the MuG VRE enters the market in 2018, under the model just described, we foresee an initial attainable market for the MuG VRE to be approx. \$500K in 2019, growing to approx. \$600K in 2022.

2.3 Customer Segments

The market aimed at by the MuG VRE is very flexible and dynamic. By this we mean that the market is new and is arguably being created by the introduction of the MuG VRE. Initially we plan to focus on the EU scientific community in the academic and industrial sectors. However, once this small market is established we plan to grow organically into the Global research market and from there into the global diagnostics market. As the MuG VRE develops and new regions are penetrated, language localisations are planned in the user interface but we do not anticipate the need to take localisation further down as the language of genome research is international in nature.

The users of the MuG VRE are most likely to be researchers engaged in genomic research. They might be employed in universities or in companies working on pre-competitive research. Some specialist SMEs may even be dual classified also as competitors, for example see the references to Dreamgenics, EpiDisease in the following section 2.4. In such complex subject area markets, these kinds of dual relationships are not uncommon and we will deploy measures to ensure that “Chinese walls” are erected between those parts of MuG service delivery and MuG competitive positioning to ensure that information does not leak between the two areas when a single entity features in both processes.

Such users will be attracted to the MuG VRE by its ease of use, its ability to increase the speed they generate results and the quality of those results. The price-point chosen for access to the enhanced version of the MuG VRE and for the ancillary services around both the basic and enhanced versions of the VRE will be set at a point which will not only result in the generation of a sustainable income stream

for the legal entity but also at a point which will be easily justified by the user in terms of the performance increases through improvements in the speed and quality of their work as well as the inherent ease of use built into the VRE.

When marketing the MuG VRE we anticipate that we will easily reach our user community through our existing genomics research networks; however, our users do not usually hold purchasing powers and for this reason the marketing offer will be constructed and developed in a manner that it addresses the concerns and needs of all the different communities of interest that we need to engage with, including researchers, laboratory or facility managers, directors and trustees, purchasing departments, finance departments, etc. Eventually we will also target the relevant departments at biotech and pharma companies.

2.4 Competitor Analysis

The market that the MuG VRE will address is an emerging one. There are very many tools available to genomic researchers and these tools independently carry out an enormous range of specific tasks in the analytical and other workflows. Such tools are listed and compared in a wide range of scientific websites³ and are also addressed in many review papers⁴. In these papers, it can also be discovered that one of the areas of inefficiency in genomics research lies in the fact that there is no single or even coherent set of tools that can perform the kinds of complex analyses that are now required. There are some existing related academic services accessible online, such as the

- HiC Explorer service, which is build on top of the Galaxy analytical workflow engine, focussing on the analysis of Chromatin conformation.
- 3DGenome browser, focussed on some aspects of Chromatin interaction analysis.

However, both of these services offer functionality that is much more limited, through their binding to specific tools and features, than the MuG VRE and they are not available to support commercial activities. Therefore, we assess that there currently exists no platform that is able to automate the connection of tools, workflows and data: except the MuG VRE. This is its unique market signature (its unique selling point), and where it offers a very attractive proposition to genomics researchers (increased speed of execution and quality of results, and improved ease of use). Currently, there is no competing offer in the market.

On the other hand, it is worth mentioning other strongly funded initiatives or partial solutions that have the potential to develop a similar product in the short to mid term:

³ For example: OMICTOOLS at <https://omictools.com/genomics2-category>, ONLINE ANALYSIS TOOLS for MOLECULAR BIOLOGISTS at <https://molbiol-tools.ca/Genomics.htm>, and GenomeTools at <http://genometools.org/>

⁴ For example: Dovichi N.J. and Hummon A.B. "The Tools Behind Genomics", in the Analytical Scientist, Issue 0113, Section 4, Article 401. Published online by Texere Publishing Limited, available at: <https://theanalyticalscientist.com/issues/0113/the-tools-behind-genomics/>. Accessed 28/08/2018.

- Under the NIH **4DNucleome** initiative several projects have been funded^{5 6 7} including the development of the 4DN network portal, which aims to include interoperable data management, retrieval, analysis and visualization. Although the MuG VRE has a time advantage and unique multidisciplinary know-how, there is a risk that discontinued funding of MuG at the stage in which it needs to be scaled up might compromise its acquired competitive advantage.
- **Qiagen Bioinformatics:** Provide individual solutions for sequencing data analysis and visualization and for the interpretation of datasets. If some of their provided partial solutions were to be merged, the solution might be comparable to MuG VRE.
- Smaller companies developing Sequencing data analysis platforms and consultancy services (e.g. Dreamgenics⁸, EpiDisease⁹, ...) could eventually become competitors as well, although in being young companies they could also be regarded as potential collaborators (e.g. end users of MuG tools in combination with their in-house solutions).

While, in one sense, it is an advantage to have no direct competition; in another, it is a disadvantage. We must build the market we will operate within from the ground up. In order to achieve growth from this kind of starting point, we plan to grow organically, through:

- leveraging the capacity of our existing scientific networks.
- engaging the tool supplier networks in a collaborative stakeholder development exercise. Through collaboration with the MuG VRE, the tool providers will have the benefit of increasing the profile of their own tool and the MuG VRE will benefit from the marketing power of the tool's own user network.

Overall, the genomics tool market is global in nature and contains a diverse range of supplier organisations. Many of the tool providers we plan to collaborate with are academic institutions and access to the tools they offer depends upon continued public funding for their availability. It is our intention to explore mutually beneficial ways of working with these collaborators that not only increases our own resilience but theirs as well. Other tools are owned by commercial organisations and in these cases we will discuss various licensing and collaboration models in order to also allow such tools to operate in the MuG VRE. Given that commercial tool suppliers will have already deployed some kind of sustainable business model, we do not plan to seek mutually beneficial relationships with these suppliers, instead we will develop commercial arrangements where access to the MuG VRE is licensed on a commercial basis.

2.5 Value Proposition

The MuG Platform offers a set of services that are unavailable anywhere else at this time, anticipating to a necessary change of paradigm in the study of genomic data. As already stated, the MuG VRE has no direct competition and must build its own market. The other operators in the wider genomics tool market offer targeted solutions to solve single problems. While there is a vast array of genomics tools to choose from, they are not easy to compare because very few try to solve exactly the same problem.

⁵ https://projectreporter.nih.gov/project_description.cfm?projectnumber=1U01CA200059-01

⁶ https://projectreporter.nih.gov/project_description.cfm?projectnumber=1U01CA200060-01

⁷ https://projectreporter.nih.gov/project_description.cfm?projectnumber=1U01CA200147-01

⁸ <https://www.dreamgenics.com/en/>

⁹ <http://www.epidisease.com/servicesproducts/>

Those that do, employ techniques that have external dependencies that restrict the freedom of choice in the user community (e.g. computer hardware and software configuration, data structures, etc.), effectively reducing the choice to one or nothing. It is for this reason that many genomics researchers feel that they spend too long designing experimental workflows and selecting the right tools instead of generating and analysing data.

The MuG VRE will ease these problems and it is for this reason that the MuG VRE will view the tool providers as potential collaborators rather than competitors. By working together, everyone can benefit. The prices attached to these tool offers varies alarmingly; from free to many thousands, even hundreds of thousands, of US dollars (the tool market is profiled in US dollars). The nature of our collaboration will vary depending upon the fees associated with each tool. As previously mentioned, we aim to develop mutually beneficial synergies with the free to use tool suppliers and commercial relationships with the fee-based tool suppliers. The benefits to the tool suppliers in working with the MuG VRE are to be found in the increased uptake of their tools by users of the MuG VRE, who will in turn (regardless of the benefit of each individual tool) benefit from the increased number of tools available within the VRE, leading to an enrichment of the overall MuG VRE market offer.

The modelling we have carried out shows that the cost-base of the legal entity required to support the MuG VRE can be kept low and this means that the offer of the commercial services it plans to provide can be kept correspondingly low. In a market where commercial services can not be accessed without accepting fees of many hundreds of thousands of US dollars¹⁰, the MuG service fees will be seen as relatively low. In the more constrained world of academic research, the MuG service fees will be recognised as fair and reasonable, offering good value for money in terms of the comparison between the fee itself and the opportunity benefit of the time gained by researchers and the improved quality of the results they generate when running their experiments in the MuG VRE.

- For the **Basic MuG VRE**, access and use will always be free to those using it for academic research and pre-competitive industrial research.
- For the **Enhanced MuG VRE**, two fee levels (which have yet to be set) will be established to enable academic and industrial researchers to access improved platform features and services for fees that reflect their associated financial situations. Preliminary fee levels have been established in the modelling that is included at Annex B to this document.
- For the **Ancillary services** we will deploy around the MuG VRE in both its Basic and Enhanced versions, two fee levels (which have yet to be set) will be established to enable academic and industrial researchers to use them. The services will be offered through a catalogue and will be charged for independently, enabling all users to select the right level of support service for them. A preliminary catalogue is discussed later, in Section 2.7.2, and the associated initial fee levels have been established in the modelling that is included at Annex B to this document.

¹⁰ The size of the global market for genomics tools and services is measured in US dollars. Converting to Euros would introduce variance that is not helpful when assessing the scales of opportunities and threats. To avoid brittleness and potential inconsistencies introduced through converting the US dollar prices to Euros, this report retains the US dollar market values.

2.5.1 Technical Maturity

The MuG project has implemented, deployed and run the VRE in a number of pilot projects which have verified the platform in the areas of: Chromatin reorganization during senescence, a Multi-resolution dynamic mapping of the Yeast chromatin, and in exposing the Physical properties of DNA and protein-DNA complexes. Given the validation in industrially relevant areas, we determine that the MuG VRE has achieved TRL6 according to Annex 5 of the General Annexes to the H2020 Work Programme. See Figure 1 below for a wider context of TRL and how they decompose technology evolution into a discrete number of finite steps and decision points. According to this figure, MuG is at the threshold with TRL7, having passed the go/no go decision point.

Technology Readiness Levels

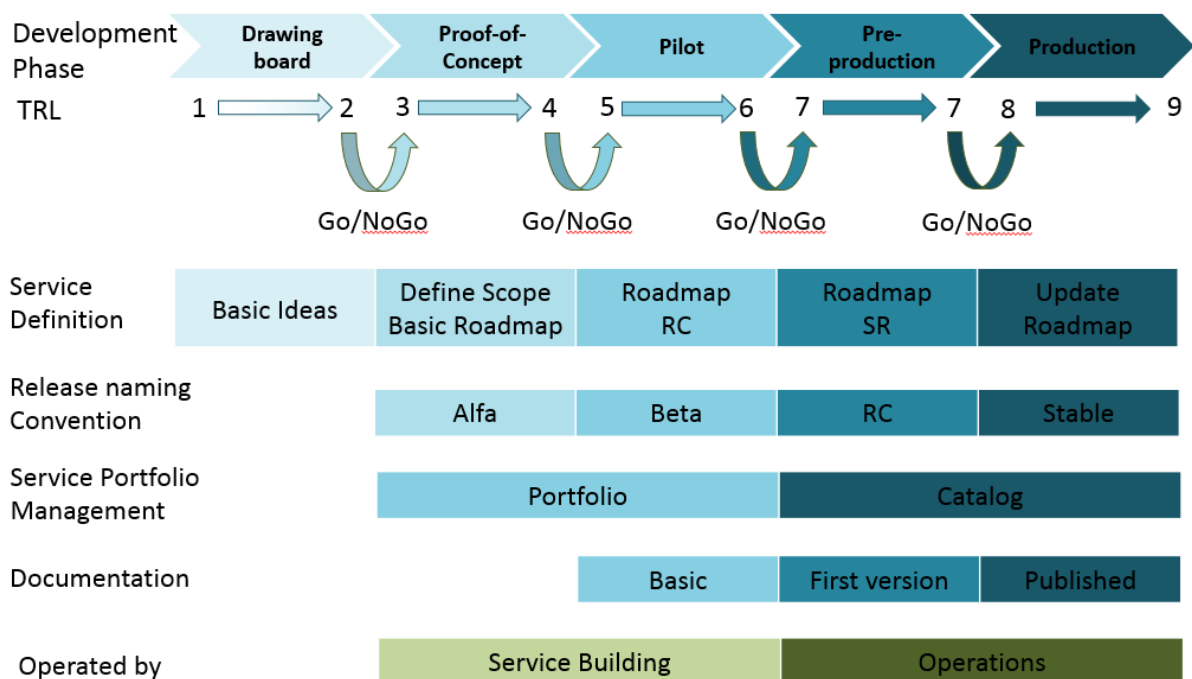


Figure 1: TRL in a Wider Context

(Source: Mark van de Sanden. EUDAT)

During the three years of the project's life (the project commenced on 1 Nov 2015) the MuG project has significantly extended the current State of the Art. As of 31 Aug 2018, the platform now:

1. allows the connection of 1D to 3D/4D genomic data within a single data paradigm. This allows the users of the MuG VRE to navigate through different genomic scales using the appropriate model at each scale.
2. enables the visualisation of complex genomic machinery through a 4D multiresolution picture. The MuG VRE now provides an integrative simulation capacity to model entire chromatin at different levels of resolution.
3. provides for the modelling of chromatin re-organizations, linked to the different needs and/or pathological states of the cells.
4. offers a new paradigm for synergistic collaborations between experts in the 3D/4D genomics community, including a new scheme for interaction with the HPC world.

2.5.2 Further Developments

Clearly, the MuG VRE is still far from being a commercial offering at the moment, and supporting the maturity enhancements will require additional funding. This is another reason we have chosen to initially focus on organic growth: we need the time. During the first phase of sustainable deployment we intend to further mature the MuG VRE with a target of TRL7 before attempting to penetrate the global market, as the EU academic research community is most likely to tolerate our services being made available at less than industrial strength. In order to achieve the required uplift we intend to further enhance the resilience of the infrastructure and continue to develop the user interface to make interactions with the platform even easier than they already are. The engine that supports the automation of workflow integration (between supported tools) will also receive attention during this period. In the next phase of growth we will aim for the global industrial research and academic research communities. While these markets for the MuG VRE are being developed we will focus our efforts on enhancing service stability and infrastructure availability, with the intention of achieving TRL8 before launching the MuG VRE in the global diagnostics market, where it will naturally mature to TRL9 over the first year of operation at that level. We anticipate this duration of the total MuG VRE enhancement phase will be approximately seven years.

See figure 3 in Section 6 for a timeline illustrating these milestones.

2.6 Market Introduction and Commercialisation Plans

Access to the MuG VRE will be achieved through direct licensing of users. We foresee the need to create individual and institutional licensing. We will not employ floating licenses¹¹ as these are too difficult to manage without specialised infrastructure, which would place an additional burden upon the early stages of growth. Licensing will be managed centrally but agents will be appointed to territories, once the MuG VRE reaches specified stages of deployment. Agents will be recruited through a specific stakeholder marketing initiative and will become a second order network, managed by the MuG legal entity.

This specific marketing activity will structure the MuG VRE market by geographical regions as well as by research area, with the number of regional agents depending upon the number of regions covered and the density of research areas funded within each one. These agents will work through their own networks and will be compensated through commissions earned on all licenses sold. Free licenses for academic users of the Basic platform will not attract a commission but agents will be rewarded through preference schemes run by the legal entity: such agents are most likely to be academic researchers acting as champions for the MuG VRE within their field of expertise.

¹¹ A normal (individual) licence entitles a single named user to run the corresponding application. Multiple / bulk/ corporate licences for applications are often purchased by companies, these entitle all of the employees to use the application as if they had an individual licence but only so long as they work for the licenced company. A floating license is allocated to a number of authorised users, any one of whom can use it but only one at once. Two floating licences can be used by the same team members but only two at once, etc. So, when an authorised user wishes to run an associated application they request a licence from a central licence server, adding a burden to the vendor's infrastructure.

The MuG VRE website will attract users to sign up for a user licence directly and we will strenuously market the website through various social media as well as directly through our own networks. We have no plans to offer white label or local deployments of the MuG platform; however, if a commercial entity expresses such interest, bespoke activities can be contracted through our consultancy services for a fee to be negotiated on a case by case basis.

All enhancement of the MuG VRE as well as all maintenance activities will be handled in house by our developers, who may be directly employed (eventually) or may be employed by the partner institutions (see Section 3.3 for partner Exploitation Plans) who allow effort to be deployed in support of the MuG VRE in return for considerations which will also be negotiated on a case by case basis. Such negotiations will be encapsulated within the articles and memoranda governing the formation of the legal entity.

Where necessary, we will engage with the policy-maker community in order to ensure that our routes to market are not handicapped by changes to policy or regulation.

To sustain the position of the MuG VRE in its market and to develop the platform in order to grow the user-base in that market, the licence fees will be annually renewed. Additional fees will also be charged for ancillary services. All income from fees will be used to develop and maintain the platform and to compensate those individuals and institutions contributing to those development and maintenance activities. No profits will be accumulated, unless expressly associated with strategically important and specifically planned activities, such as accumulating the funds necessary to launch and market the platform in a new region or in a new research area.

Although we plan to manage the commercialisation of the MuG VRE through the sustainable legal entity which we will establish, there is also the possibility that the rights to the MuG VRE will be sold or leased to a private entity, with the specific purpose of this entity taking over commercial operation. Such an approach has been successful in the past, especially in the tools domain. However, we anticipate that this offboarding route to market will be more difficult to achieve for the MuG VRE, given that it embraces an abstract concept and encapsulates indirect benefits. Moreover, the VRE requires significant HPC infrastructure for its deployment and this fact alone will raise the access barrier above the limit of what a specialised SME might be able to tolerate and it is such SMEs that represent the most likely entity for the offboarding route.

2.7 MuG VRE Business Model

In this section we consider the conditions under which the MuG VRE will operate in order to determine its viability as a business opportunity.

2.7.1 Business Objectives

The purpose of the MuG VRE is to help researchers improve the performance of their experiments and to increase the quality of their results. The VRE presents a set of preconfigured tools to help new users and gives them access to a set of support services to help them customise the tools or to integrate new tools.

OBJECTIVE 1. From technical perspective, the MuG VRE business will function to speed up scientific discovery through the automation of existing manual processes.

OBJECTIVE 2. From the business perspective the MuG VRE legal entity will function only to attract sufficient revenue to sustain itself and to continue developing the MuG VRE.

It is not a business objective to make profit in order to distribute dividends to shareholders, any profit will be accumulated only so far as it is necessary to support continued growth. All other revenue, after running costs are deducted, will be allocated to VRE development.

In order to measure how progress is being made against OBJECTIVE 1, technical and operational performance indicators will be established, for example: a 200% reduction in the time taken to generate results, or a 50% increase in the quality and consistency of analytical results. In order to measure how progress is being made against OBJECTIVE 2, business and financial performance indicators will be established, for example: A 100% increase in the number of Users, a 10% annual increase in the number of services in the MuG VRE Service Catalogue, a \$250K budget for Global marketing.

2.7.2 Revenue and Cost Models

2.7.2.1 Revenue

All revenue generated by the added-value features and services offered by the sustainable legal entity, supporting the MuG VRE, will be used by the entity to support itself and its mission, this includes investing in internal development of these added-value services to enhance the service portfolio. Here we have to re-emphasise the value that the open-source nature of the code. While the successful open-source ecosystem is an emerging business concept, we fully intend to continue developing the core MuG services this way. We anticipate that this approach will allow the rapid growth of user communities around the MuG core and that these communities will provide a ready-made market within which to promote the added-value MuG commercial services. In this model we foresee the symbiotic benefit of running open-source and commercial services side by side.

The preliminary formation of a service catalogue is outlined below through the use of a number of [non-exclusive] service options, namely:

1. Membership and Membership Services
 - a. Academic use of the basic platform is free and always will be free.
 - b. Academic use of enhanced platform services (to be directly developed within the sustainable entity e.g. workflows, or which indirectly accrue around the platform e.g. publicity) will be made available for a fee, the level of which will be set to benefit the user as well as MuG.
 - c. There are two options for commercial use of the platform:
 - i. The code for the MuG platform will be licensed to commercial service providers which operate their own platform for Business users. The

commercial service provider will be able to develop features independently, according to their own client needs.

- ii. Business use of the platform will be managed on a single MuG platform, where commercial access fees will be set at levels commensurate with similar commercial services. For the commercial access fees, higher levels of support and consultancy will be bundled. Any features developed to meet commercial user needs will be made available to both the commercial and enhanced academic user communities at the relevant fee levels. The same arrangement will also hold for the commercial use of features developed for enhanced academic users.
2. Support Services
 3. VRE Training
 4. Subject Matter Training
 5. Consultancy
 6. Technical Services
 7. Separating the VRE into commercial and academic where the commercial one is “sold” to a 3rd party company that operates it, develops it more for industry and sells services and training around it. Original partners get revenue share or a lump sum fee

The point of these services is *not* to solely benefit MuG by increasing the access cost to MuG services for the academic community but to *reduce the overall costs* they face when encountering novel environments, tools and services. Doing this in a manner that benefits both the wider academic community and MuG itself, ensures the continued survival and (ideally) the continued enhancement of the MuG platform. Everyone benefits.

The nominal set of options described below distinguish between:

Users and Members. Everyone using the MuG platform is a User. Those academic entities using only the free MuG services are Standard Members. Academic entities paying an annual fee to MuG for the use of additional services are Enhanced Members. Commercial entities paying a commercial annual fee to MuG for the use of all services are Industrial Members.

Academia and Industry. Because of the public funding behind MuG, academic users and members have wider access opportunities at lower cost than industrial members. Industrial users will pay commercial membership fees and are able to use the MuG services *only* for pre-competitive research purposes.

Fee levels for all services are to be set, by the consortium, at a level the partners are comfortable with and which can be demonstrated to benefit the sustainability plan through modelling: see Annex B for the levels selected for the modelling carried out in this report.

2.7.2.2 MuG Membership Services

The MuG VRE offers a set of services that allows for the connection of genomics tools. The manner in which the connection mechanisms function allow for easier and richer connections to be made

between those tools. These easier and richer connections allow for complex relationships to be developed not only between the tools but also between the data they consume, share and produce. In analogy, we therefore consider the MuG platform to be the “Facebook of genomics tools.” Continuing with the Facebook analogy, we also note that the tools are “on the platform” but it is the Users who use the platform and they need to communicate as well, to share: ideas, concepts, problems, solutions, etc. In order to support this level of communication, we plan to “bundle” the VRE with a human communication tool to facilitate the development and support of a MuG user community, e.g.: Briar, Jabber/Conversations, Keybase, Riot.im, Signal, Tox, etc. This additional service will be bundled with all levels of membership and will be available to all relevant users, who will be required to register and qualify as part of the access protocol of the MuG VRE.

Additionally, we will offer “app store¹²” services to our tool/app collaborators. The “app store” function for third party apps/tools will be strongly managed. All code will be verified. Verification service is free for apps and tools that are free to use but a fee is payable if a fee will be charged for use of the app/tool. Open Source is encouraged but Closed Source is allowed, so long as code is supplied for verification (all rights will be respected).

Standard Membership

Access to the Basic VRE and to other MuG offerings (e.g. community communication and app store) at this level remain free and can be used at any time by all academics. Standard membership is not open to Industrial entities.

Enhanced Membership

In addition to accessing and using the VRE and other MuG offerings, academic membership at this level gives the member an opportunity to participate in the design and delivery of future MuG services and to benefit from any income they might generate. This level of membership is accessed through the payment of an annual membership fee.

Industrial Membership

This type of membership makes access and use of the VRE and other MuG offerings available to industrial users for pre-competitive research use only. The industrial member is also able to participate in the design and delivery of future MuG services and to benefit from any income they might generate. This level of membership is accessed through the payment of an annual membership fee. [NB This fee will be set at commercial levels]

2.7.2.3 VRE Support Services

All MuG VRE Support Services will be delivered against a predefined SLA that describes each level [standard | enhanced | comprehensive] of service and which sets out the service delivery aspects and standards for that level of service.

¹² This is a metaphor, the MuG “AppStore” we describe requires users to have more technical ability than that of being able merely to click a link allowing a piece of software to download and install itself. However, they are conceptually the same and they offer the same kind of functionality.

Standard Services

All services at this level remain free to access and use at any time by all academic researchers. Dual licensing could make these services casually accessible also to those industrial users, which are not already industrial members, for a fee.

Enhanced Support Services

Services at this level offer support to users and contain advanced features. Such services are developed in a manner that increases productivity, flexibility and reduces the overall cost of use for the community. These services are accessible for a fee and are selected from a list of optional advanced services. Examples of services: User help desk, technical support, fault reporting, advanced analysis tools, tools pre-integrated into “product” workflows, etc. Enhanced services are available to Industrial Members.

Comprehensive Support Services

Like those at the enhanced level, these services contain advanced features, which are developed in a manner that increases productivity and flexibility, reducing the overall cost of use for the User. These bespoke services are accessible for an additional fee; however, this comprehensive level includes all enhanced services. Comprehensive services are available to Industrial Members.

2.7.2.4 VRE Training

Standard VRE Training Services

These training sessions are built at low cost from existing MuG resources and knowledge assets. They are freely available to academic users in virtual sessions and at cost when delivered face to face; for academic members they are freely available to academic users in virtual sessions and when delivered face to face in scheduled slots. They are available to industrial members in virtual sessions and face to face at cost; for industrial users both the virtual and face to face delivery models attract delivery fees.

Bespoke VRE Training Services

MuG is able to design, develop and deliver bespoke VRE training sessions for all types of user. Fees for such training services are negotiated and invoiced beforehand.

2.7.2.5 Subject Matter Training

Standard Subject Matter Training Services

Like the VRE training, these training sessions are built at low cost from existing MuG resources and knowledge assets. They are freely available to Standard Members in virtual sessions and for a fee when delivered face to face. For Enhanced Members and Industrial Members they are freely available in virtual sessions and also when delivered face to face in scheduled slots. They are available to Enhanced

Members and Industrial Members for a fee, when face to face delivery is required outside of the training schedule.

Bespoke Subject Matter Training Services

These training courses are developed and delivered as required by the community and also other research communities [success depends on performance of outreach activities] e.g. How to use the MuG **multi-resolution genome-browser** and the new visualization tools in novel environments (Genomics is not the only domain struggling to view complex data and the tool may find considerable application opportunities outside this domain).

2.7.2.6 MuG Consultancy

VRE Consultancy

VRE Consultancy services are defined as required through discussion with the client. Costs and payment schedule are negotiated and agreed with each client before work commences.

Subject Matter Consultancy

Subject Matter Consultancy services are defined as required through discussion with the client. Costs and payment schedule are negotiated and agreed with each client before work commences.

2.7.2.7 Technical Services

General Tools Supporting the Community

Those tools and infrastructure access points developed in the project remain free to use for all academic researchers. Dual licensing will make these tools accessible to industrial users for a fee.

Definition and Deployment of an API

The development, deployment and support of a MuG VRE API, enabling the remote integration of third party tools and services in the MuG VRE is a major undertaking. Work on this feature has already started in the project and we currently have such a feature that enables technical integration¹³ and this has been successfully tested within the consortium and with a limited number of lead users. However, further work in this area is on the MuG roadmap and we have set app-store-like functionality as our target. Such work is probably best done in a follow-on project (if available), or if there are resources available through fee-paying services delivered elsewhere, it could also conceivably be developed in house within the sustainable MuG entity if sufficient profits can be generated and the decision is taken to focus on this area over other areas. Once fulfilled, this feature could become the de-facto means of ensuring the HPC-ready simulation tools / analysis workflows and the software and data standards defined during the project are followed and adopted as it fundamentally creates a “path of least resistance”. Training and consultancy services could be developed around this concept, to maximise the opportunity. Access to the VRE API could be made available for free (to academic and

¹³ See: <https://www.multiscalegenomics.eu/MuGVRE/policy/>

industrial members) for a fee (to industrial users) and for a fee, or some other contribution in kind, to academic users.

Some of the tools in MuG were previously developed and are commercialised by external companies (e.g. in the case of pyDock, this was developed by BSC for protein-protein and protein-DNA structural modelling, and is now in the process of being transferred to a local company). The integration of such tools into the MuG VRE can be offered as a technical service, in agreement with these external companies, on a specific tool by tool basis.

Bespoke Integration Services

Such activities are negotiated and delivered as required with each client. Deployment of the skills and resources required to integrate third party tools and services into the MuG VRE will be managed by the MuG sustainable entity. Fees for such integration services will be negotiated and agreed before any technical or integration work commences. Alternatively, speculative deployment within the MuG sustainable entity itself could be undertaken to exploit identified market opportunities, such as developing the multi-resolution genome-browser so that it will function in other research domains.

2.7.2.8 Revenue Forecasts

Some very limited market possibilities have been described in Section 2.2 above. In terms of the scope for commercial activity within the new legal entity, these translate into relatively low level initial activities with accompanying modest increases in staffing levels. We anticipate seven revenue streams (see above in this Section), combining membership income with different types of training and consultancy services and these will support a staff level which will begin with just one member of staff, growing to four in 2022. Nominal fees for these services are:

- | | | |
|---|----------|-------------------------|
| ● Enhanced Membership fee | \$500 | (annually per member) |
| ● Industrial Membership fee | \$5,000 | (annually per member) |
| ● Average Support Service costs | \$1,000 | (annually per member) |
| ● Average VRE Training costs | \$250 | (per person session) |
| ● Average Subject Matter Training costs | \$500 | (per person session) |
| ● Average Consultancy costs | \$10,000 | (per consultation) |
| ● Average Technical Services costs | \$15,000 | (annually per contract) |

Over time the income streams will diversify (e.g. charging developers of paid tools for the privilege of promoting their tools on the MuG platform) and grow (we assume an internal growth rate of 12% as it fits well with other aspects of this model), leading to more members of staff. Within this model, we have used a conservative take up mix of the above offer and have arrived at a cumulative income in 2019 of \$327,500.00 and in 2022 of \$460,113.92. The mix can be seen in greater detail at Annex B to this report.

Within this very modest anticipated growth model, we aim to end the 2022 business year achieving 93.4% of the growth possible under our conservative initial attainable market prediction, this will result in a balance of \$260K in the bank account after modest internal costs (which are mainly accounted for by salaries) but not taking into account: tax, depreciation, interest and amortisation because we are not yet sure where the entity will be established (See Figure 2).

This means that a sum of slightly less than this will be available for investment to grow MuG VRE sales in an increased market share across many potential market sectors. Greater initial market impact and faster growth, is possible only under conditions where investments are made in the fledgling entity. While this is possible, and measures are being taken to explore this possibility, we assume that investors will remain shy of the MuG VRE until a positive track record can be demonstrated regarding its performance in the market. For this reason, we plan to answer calls in suitable future funding instruments as a source of external support for the initial growth of the MuG VRE.

The size of the global market we finally aim at is at least 17 times the size of the market we initially aim at, we see no reason why the growth of the legal entity will not continue to grow in the longer term, with a long-term target of achieving a revenue of \$14.5B being reachable by 2029.

Cost Forecasts

Initially the costs centres will be few and relatively small. We have modelled only:

- Average personnel cost per Person Month
- Office costs per Month
- Equipment Cost per person per Annum (depreciated over 3 years)
- Consumable costs per Month
- Average operational costs per Month

As the business grows we anticipate having to add organisational and operational costs into this mix, such as Human Resource management, administration, marketing, management, etc. and the costs of these will be met from the predicted growth in the strengthening revenue streams. A priority factor in all spending decisions will be to ensure that the business is receiving sufficient revenue to support the new process or function.

The balance between revenue and costs as well as the cumulative reserve can be seen in Figure 2.

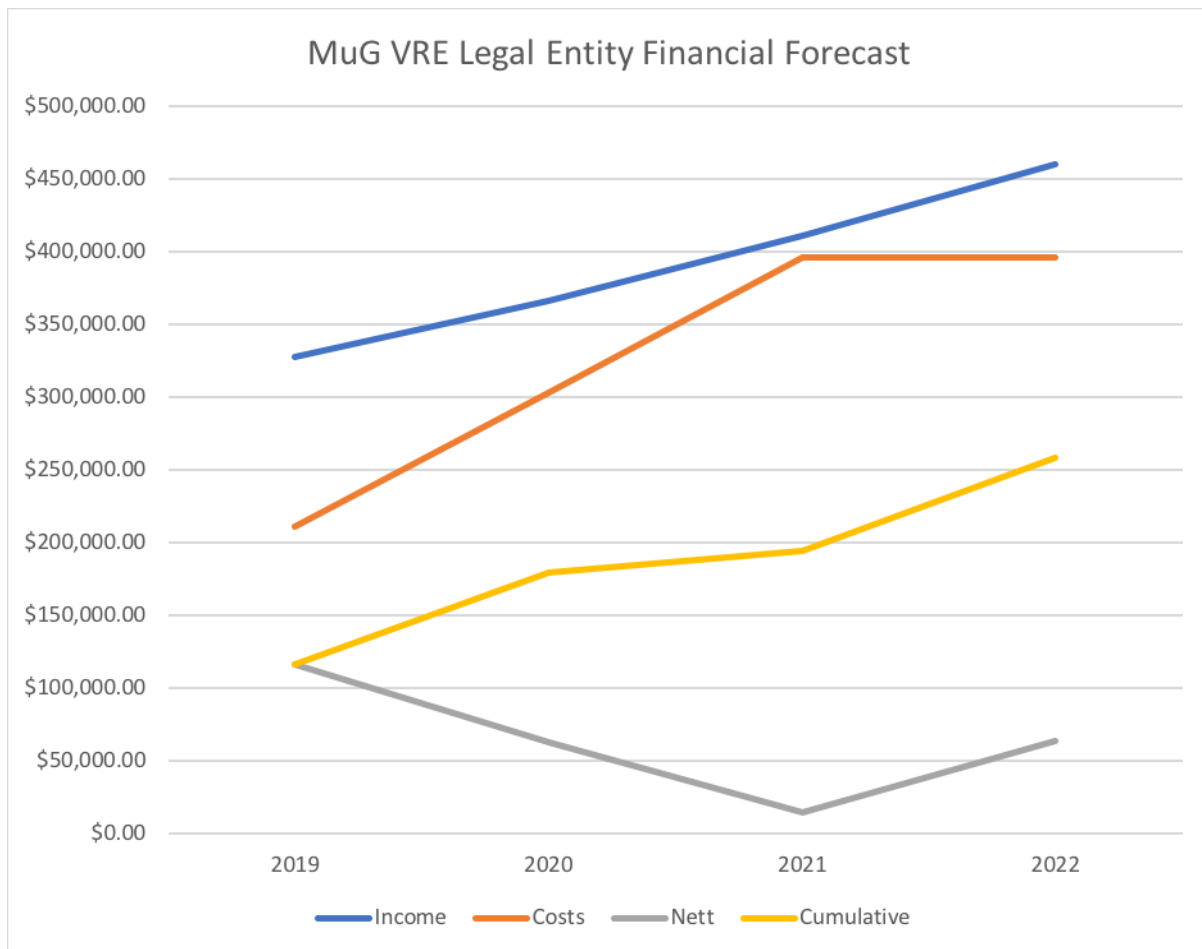


Figure 2: MuG VRE Legal Entity Financial Forecast

It should be noted that if it becomes possible to achieve investment, then this model could be heavily revised to reflect more up-front spending on activities that will accelerate market take up, where we would expect to reach the ten-year target much more quickly. In this case, the start-up phase of business development will take on the commonly recognised negative nett and cumulative balance trends. The positive balances illustrated here are only possible because we limit our market opportunities and growth potential in order to ensure sustained organic growth within the anticipated revenues.

2.7.3 Legal and Regulatory

It is a feature of deploying anything into a market that issues far away from the lab bench have to be considered. Not least of these are those related to various forms of compliance, the most important of which are discussed below.

2.7.3.1 *Freedom to Operate, IPM and KM*

We have performed searches of the EU and US patent offices^{14,15} and can find nothing there that interferes with our Freedom to Operate. This is hardly surprising as it is not possible to patent software in the EU and as the MuG VRE has no direct end user in mind, it will be very difficult to patent in the USA. For this reason our IP is treated as an industrial secret, with all necessary agreements in place (NDAs and model confidentiality clauses).

However, all of the code that underpins the MuG VRE is available as open source. Despite this, the code is still owned and is licenced for certain classes of use under a number of different licences. The MuG legal entity will establish a detailed repository to track IP ownership and to ensure that licence conditions are not infringed. It will also use this repository to manage its own IP, when this is developed.

There is nothing on the market that our searches have discovered that can be considered as a threat or competitor to the MuG VRE, so we are currently pioneers and must maintain access to the specialised knowledge and skills that created it. Knowledge management principles will be established in the legal entity articles and memos of incorporation to ensure that it always has access to the necessary knowledge and skills base.

2.7.3.2 *Licensing and 3rd party Licensing Requirements*

The underlying IP is owned by the partners in the current project consortium. Before the end of the project an agreement will be signed that either transfers IP into the new legal entity, or grants it a perpetual exclusive licence to the MuG VRE IP. Compensation obligations, on the part of the legal entity and benefiting the originator, will form part of the agreement.

Any improvements to the underlying Basic MuG VRE code-base will continue to be carried out by the originators of the IP and will continue to be freely available to all qualified users. It is possible that, with the agreement of the originators, a dual licensing scheme may be applied to the Basic code-base, allowing the legal entity to offer commercial access to industrial users more easily than it might otherwise be able to do. Any modifications made by the MuG legal entity and funded from commercial income will be made available under a licencing scheme that is suitable to protect commercial activity. In such a case, that part of the code-base may not be released as open source software.

2.7.3.3 *Standards and Regulations*

Many standards and regulations exist in relation to the application of the results of medical and biological research. Ethical considerations also overlay the working practices of the research process itself in these areas. Many of the tools that are directly involved in such research can be categorised as medical appliances. However, we can find no such limitations or constraints that are placed upon the platform that connects the tools. At the moment, we are confident that there are no operational obligations that the MuG VRE must accept; nevertheless, we will constantly keep this understanding

¹⁴ The European Patent Office:

Espacenet service at: https://worldwide.espacenet.com/advancedSearch?locale=en_EP

¹⁵ The United States Patent and Trademark Office: PatFT and AppFT services at: <https://www.uspto.gov/patents-application-process/search-patents>

under review by monitoring changes in the regulatory and standards landscape. Despite this claim, we do note that the data transferred between the tools within the MuG VRE are subjects of various standardisation activities. It is incumbent upon us to ensure that the MuG VRE does nothing to interfere with this type of compliance. The MuG VRE does not itself manipulate protected data.

2.8 Feasibility Assessment

Considering all of the above factors, we consider that **the business is viable**. We have established that the need for a platform such as the MuG VRE is present in the market. While recognition of this need is not strong at the moment, the VRE concept is new and our conservative modelling indicates that it will be possible to grow interest and develop a new market. We have demonstrated how the business can develop organically and still achieve revenue growth through careful management of costs. We have established that there are no IP blocking or interfering with our freedom to operate in our target markets. We have also demonstrated how parallel commercial and free-to-use services can be deployed alongside each other in a symbiotic manner that benefits both without infringing any dual financing restrictions or state aid rules.

3 LONG-TERM SUSTAINABILITY of MuG

Previously in this document we have discussed the market opportunities for the MuG VRE and have modelled its potential to generate income sufficient to secure its sustainable operation. In this next section we consider the entity that will be formed to administer and manage these operations. Normally the steps discussed here are already addressed when business planning takes place; however, we are considering taking the MuG VRE to market in a relatively short space of time and for this reason the business planning and sustainability planning are being undertaken in parallel.

Fundamentally, there are two main options to consider when planning the means by which the business model can be deployed. The question is: should the MuG VRE be held close to the development teams and managed through a new entity they establish to execute their wishes, or should the operation of the MuG VRE be sold, or leased, to a third party which will deploy the MuG VRE independently of the development teams. There is no right answer to this question. In this section we consider both options in light of the modelling already carried out and summarised above. We first consider the formation of a dedicated legal entity and we then consider the licensing of the VRE to another already established legal entity.

3.1 Legal Entity Option

There are many types of legal entity when the full variety of options across all EU nations are taken into consideration. They range from entities that are explicitly non-profit to the limited liability profit-making companies; from national, through cross-border to international in scope; and from publicly held, through privately held to partnerships and sole traders.

We are in the final stages of selecting the type of legal entity we will use but no final decision has yet been made. What is the best option for the MuG legal entity has been determined from an analysis of the partner requirements, as well as their needs and constraints. For many academic entities a non-profit structure is preferred, however, this type of instrument can severely curtail possible future choices, so a long-term view is taken in the decision-making process. This is the reason the final

decision has not yet been made, satisfying the needs of the non-profit community and the for-profit community is difficult but not impossible.

As part of the incorporation process, all partners will be invited to join the company (as shareholders/trustees, etc.). Some members may not want to be directly involved and will need to be compensated in return for their contributions. Those partners not wishing, or those unable, to participate directly in running the business will be given the opportunity to define the kind of relationship they want with the company and their rights and obligations will be defined in a contract. Other partners wishing an even looser relationship can enter into an ad hoc relationship as defined in a memorandum of understanding (MoU). Such an MoU will define what each party will expect from the other.

All revenue generated by the sustainable legal entity supporting the MuG VRE will be used by the entity to support itself and its mission, this includes investing in internal development of services to enhance the service portfolio. In order to deploy the MuG VRE sustainable entity must agree terms with the IP and other rights holders of the MuG VRE. Some may become shareholders in the sustainable entity and benefit directly; others may choose to remain outside the sustainable entity, in which case suitable compensation packages will be agreed.

3.1.1 Legal Entity Selection and Initiation

In selecting the appropriate type of legal entity is appropriate for the MuG VRE, we will analyse all of the different types of legal entity, matching their characteristics against the needs of the partners. The suitable entity types (those that enable the business objectives to be met) will then be shortlisted and presented to the project management board for a decision to be made. The decision will consider the needs of all of the consortium members.

Once a decision is made, the necessary legal steps can be taken to incorporate or establish the business. The contents of the articles and memoranda will be decided by the members and will define the roles of directors / trustees and consider powers of shareholders (if appropriate). Structural operational matters will also be settled during this phase of initiation, when management structures, personnel roles and responsibilities, terms of reference, etc. will be created and a library of appropriate reference material will be created.

3.1.2 Business Plan for Legal Entity Option

The business plan for the sustainable MuG VRE legal entity is presented in Section 1 and Section 2.

In addition to implementing the business plan, and in order to support initial stages of organic growth, the legal entity will also seek public funding through submitting project proposals into suitable funding instruments. As such, the legal entity would be effectively acting as a kind of “agent” for the participants in this project, especially those directly involved in the sustainable activity. We identify the EOSC programme as being one such source of funding and have identified INFRAEOSC-02-2019 as being a call of possible interest to us. Please note that the MuG VRE is liaising with eInfraCentral to be included in their Common Service Catalogue, which is the service catalogue that is being designed for use by EOSC. Furthermore, partners in the MuG consortium maintain close relationships with the EOSC community: notably BSC - CNS (through the ELIXIR and EOSCLife projects along with The Global Alliance

for Genomics and Health (GA4GH) organisation) and EMBL-EBI (also through ELIXIR and directly through key personal working within both the EMBL-EBI and the EOSC communities). We will use these relationships to ensure that we are always ready to participate here, whenever we are able. However, we are aware that the restructuring of work in this area, under the EuroHPC JU, is likely to result in the published calls being revised and we will monitor the situation as it develops.

3.1.3 Financials for Legal Entity Option

A combined revenue and cost model is presented in detail at Annex B and is summarised in Section 2. The model demonstrates that the business is viable, regardless of the tax and accounting requirements in whichever EU territory is selected for incorporation.

3.2 Licensing Option

The licensing option will be seen by some partners as an easier route to achieving sustainability for the MuG VRE, than the creation of a dedicated legal entity. However, it is important to consider that control over the VRE will be lost if this route to market is selected. The sale or leasing of the MuG IP is also not a straightforward process. It is very likely that a post project consortium will have to be created and a lead partner will need to be elected. The partners will then need to vest all interest in their IP into that new consortium. The proportion of IP being vested will carry a “compensation” weight and this will be used to determine the ratio governing the internal distribution of any revenue. The lead partner will then act on behalf of the partners and will have the responsibility of conducting the sale negotiations or managing the leasing arrangement.

Once the sale or leasing arrangement is agreed, the lead partner conducts all business-related activities in respect of the sale/lease and distributes any revenue according to the rules specified in the contract that defines the new consortium agreement.

3.2.1 Partner Search and Selection

Before the lead partner can initiate negotiations with the outsourced exploitation entity, such an entity must be found. First of all, the partners will explore their networks for suitable candidates, using pre-defined search parameters and a set of selection criteria; trade registries will also be searched. This process will result in the generation of a long-list of suitable candidate organisations. A short list of potential partner organisations will be created from the long-list by matching the business objectives of the long-listed entities against a set of criteria describing the MuG VRE operational goals. Short listed organisations will be invited to meet and discuss the opportunity. If more than one partner passes through the discussion phase, each one will be invited to make sealed bids to seal the opportunity. The sealed bids will be evaluated according to criteria issued with the competition details which originally invited the bids.

A contract will be exchanged with the successful sales partner. The contract will specify minimum performance requirements, roles, duties and responsibilities on both sides.

3.2.2 Business Plan for Licensing Option

The business plan in the case of sale or leasing of the MuG VRE to a third party will be a matter for the third party itself to determine. The MuG consortium will have no right or opportunity to engage in such planning.

3.2.3 Financials for Licensing Option

Given the potential value of the MuG VRE, modelled in Section 2, it is not unreasonable to anticipate revenue in the order of \$20M in the case of a direct sale. Alternatively, annual licensing fees (in the case of a leasing arrangement) set at \$2M per annum could be similarly justified, once an agreed revenue level has been reached by the external entity. Prior to that it is not unreasonable for the new MuG consortium to take a commission based on actual revenue.

3.3 Outcome of Sustainable Operation Considerations

The consortium favours the option of keeping the IP close to them and it also rejects a pure commercial operation. Not-for-profit business options are being considered and a decision is expected soon. In order to support this new organisation through its initial growth phases, a hybrid model is proposed: one where the legal entity is initially supported by further project funding until such time it is fully able to stand alone in its market.

3.4 Consortium Partners – Individual Exploitation Plans

Here the consortium partners briefly summarise their exploitation plans. Where appropriate they discuss their plans directly in relation to the sustainable MuG VRE and the legal entity representing it.

IRB Barcelona

General Exploitation

IRB Barcelona, as MuG coordinator aims that the MuGVRE reaches the global scientific community and becomes a reference in the field. To this end, IRB Barcelona will put its best efforts in sustaining the platform until the creation of the legal entity to manage MuGVRE's exploitation. Specifically, IRB Barcelona will keep assuming the costs of maintaining of the multiscalegenomics.eu domain. Furthermore, IRB Barcelona will promote the integration of future relevant tools developed in-house into the MuGVRE and contribute to keep the tool offer at the VRE up to date aligned with the demands from the community. It will also do its best to continue providing resources to sustain the infrastructure.

Support to the MuG Legal Entity

Regarding a direct commercial exploitation of MuG, IRB Barcelona does not envision to be directly involved. Nonetheless, it will provide support to the aforementioned exploitation activities, via participation in the legal entity (when created) and on the training/consultancy activities promoted by it.

BSC - CNS

General Exploitation

BSC-CNS have no commercial exploitation plans regarding the MuG infrastructure. The MuGVRE infrastructure will be maintained and offered as a service integrated in the Life Science computational infrastructure, and used as a base for the development of specific infrastructures for forthcoming projects. Eventual improvements and developments in such projects will be adapted to MuGVRE when appropriate. MuG tools and services to developers will be also kept active. In particular, we expect fully adoption of the standards and recommendations by EOSC (through ELIXIR and the EOSCLife project), and by cloud computing group of the GA4GH.

Support to the MuG Legal Entity

BSC-CNS will support the MuG legal Entity through the necessary agreements that would allow the use of the computational infrastructure for development purposes and providing training and technical support in the adoption and installation of MuGVRE by others.

CRG - CNAG

General Exploitation

At present, CNAG-CRG does not envision to be directly involved in the commercial exploitation of the MuGVRE, although it is open to reconsider its position again, once it is established and stable. Nonetheless, it will explore the possibilities of maintaining both TADbit and TADkit updated within the MuGVRE and further integration in the platform of future relevant workflows and tools developed in-house.

Support to the MuG Legal Entity

CNAG-CRG will work closely with the MuG Legal Entity to explore mechanisms to allow the integration in the VRE of the tools developed within the scope of this H2020 grant and of any future tools that could have relevance for the platform. In particular, it will explore adoption of the EOSC standards and recommendations.

EMBL – EBI

General Exploitation

EMBL-EBI has no plans at this point in time to exploit the MuG platform within its infrastructure. However we do state that some components developed within the scope of the H2020 grant award currently licensed under Apache 2.0 may be reused within EMBL-EBI infrastructure to provide additional functionality unrelated to the MuG aims or platform. This would primarily target the data management API (dm-API), REST API bindings and analysis workflows developed as part of WP4 of the H2020 grant. We would continue to develop workflows and tools that could be integrated into the VRE and collaborate with the MuG Legal Entity to ensure the introduction of these tools into the VRE. Our results and involvement would not rely on the results of other partners.

Support to the MuG Legal Entity

EMBL-EBI has the ability to setup support contracts and to draw up consultancy agreements between other legal entities such as the MuG Legal Entity. Under this model the MuG Legal Entity may engage with EMBL-EBI to provide support and development to the platform. This assumes that EMBL-EBI still possess the in-house knowledge to be able to deliver such support.

EMBL-EBI currently has links to EOSC via Elixir and our head of Technical Services Cluster, Steven Newhouse. We are developing methods to interact with the EOSC platform.

University of Nottingham

General Exploitation

The University of Nottingham has no current plans to exploit the MuG platform for other ongoing research projects. However we expect know-how developed during this project related to the design

and construction of virtual research environments will be leveraged for future projects in fields unrelated to multiscale genomics.

Support to the MuG Legal Entity

Where possible, The University of Nottingham will pursue its VRE research through collaboration with the MuG Legal Entity. In addition, where future research projects lead to the development of data analysis tools that could have relevance to the MuG VRE, we would collaborate with the MuG Legal Entity to integrate them into the platform.

CNRS – IGH

General Exploitation

CNRS-IGH, it will grant permanent access to the data sets generated in the project (once published), as a means of providing a demonstration set for users. In this framework, CNRS-IGH will release these data for public re-use for all potential users as necessary and remain available to address user enquiries concerning these and related data.

Support to the MuG Legal Entity

CNRS-IGH does not plan to be directly participating in commercial exploitation of the MuG VRE, although it is interested in following up its evolution and to reconsider this position if solicited later on.

4 MARKETING FOR MuG (all deployment options)

Here we consider the intangible assets associated with the MuG VRE and tangible assets that need to be created to support them. We then consider the processes that need to be put in place to distribute the tangible assets in order to build the correct view of the MuG intangible assets within the user community.

4.1 Branding

A brand is much more than a logo or a clever name. What is important are the underlying vision and values of the entity being branded. The MuG legal entity will take great care to develop a clear vision and then from this, it will define the operational principles. Then an overall purpose can be developed. Both of these will lead to the identification of the MuG VRE mission. Understanding these high level concepts will make the market positioning easier and actual performance indicators to be developed and established. Only when these conceptual exercises are complete will the design and sense of the logo and any slogans be attempted.

The current project branding and the look and feel of the project website are already very distinctive and will be used as a starting point.

4.2 Online Marketing Channels

4.2.1 Project Communication

At the moment the project website is the primary means of communication and a place where genomics researchers are able to join the MuG community, sign up for newsletters and have access to training materials and other support information. In the future we expect to classify our community members in interest groups and offer more personalized newsletters.

The project maintains an active Twitter feed, which has 212 followers at the moment, and publishes widely in online academic journals (see section 4.3 for more details on impact of publications)

4.2.2 Post Project Activities related to the promotion of the MuG VRE

During the last year of the project, the website has already evolved into something rather more aligned with the products and services on offer rather than it being a venue to talk about project progress. To this end, the MuG homepage has been reorganized in such a way that it focuses on providing information about the services offered by MuG and details on the VRE, as the central product (documentation, access to workspace, infrastructure and tools information, support and other services) while all project information has been compiled under a single menu item, namely “The project”, which gives access to the old project home page. As the VRE becomes a global brand, the website will further evolve into either a suite of localised sites or a portal able to dynamically deal with localisation issues. In addition to the language localisation issues, we find it is important to deliver localised content also.

A more aggressive social media presence is also planned, in addition to the already well received Twitter posts, the social media activity will also include, as a minimum: robust activity on LinkedIn, Facebook, Reddit and research-oriented social media such as those found on ResearchGate and also the chat function to be built around the VRE itself. This social engagement activity will be interactive, we recognise that it is not sufficient to make announcements, the VRE user community must be engaged and be encouraged to engage in return.

4.3 Offline Marketing Channels

4.3.1 Project Dissemination

The project partners already effectively disseminate their results through the usual routes: conferences, papers and posters as well as in selected industry gatherings, through the institutions’ technology transfer offices.

The project has published thirty one MuG-related scientific papers in high-impact journals, including 5 reviews, which have accumulated 326 citations thus far. It is worthy of mention that 3 MuG PIs have co-authored a position paper on 4D nucleome data and model standards with leading worldwide researchers in the field¹⁶, in which MuG is highlighted as a pioneer initiative in establishing 3D/4D

¹⁶ [Marti-Renom MA et al. \(2018\) Nature Genetics 50, 1352-1358. https://www.nature.com/articles/s41588-018-0236-3](https://www.nature.com/articles/s41588-018-0236-3)

modeling standards in genomic data. The paper was driven by MuG PIs and represents a unique opportunity for MuG to position itself and exploit its competitive advantage. During the last year of the project, MuG has also been strongly featured in key international gatherings of the end-user community (e.g. 2017 [EMBO conference on Nuclear Structure and Dynamics](#)) and has taken the lead in organizing the highly successful Barcelona BioMed conference in [Multidimensional Genomics: the 3D/4D organization of chromatin](#), with which the first public release of the MuG VRE was co-located. To enhance the impact of the November 2017 events a video¹⁷ was developed and a press release was issued that yielded great uptake, including radio interviews to organizers. Dissemination through end-user community gatherings has been combined with a strong presence in computer science gatherings and most importantly, EU infrastructures gatherings (e.g. MuG infrastructure was presented at Digital Infrastructures for Research (DI4R), including EOSC pilot workshops. Overall, MuG has been present somehow at ~80 conferences worldwide. Hands-on training activities on the use of the VRE have attracted >200 attendees and have turned out to be one of the most important means of engaging new users and obtaining highly priced feedback. MuG has joined efforts with partner initiatives such as ELIXIR (for promotion of events) or BioExcel CoE (a MoU has been signed including actions aimed at facilitating the long-term sustainability of MuG training activities). Dissemination and engagement efforts have resulted in a community of 90 registered users, 212 Twitter followers and an average of 270 monthly new visitors of the MuG website (70 for the VRE).

4.3.2 *Post Project Activities related to the promotion of the MuG VRE*

As dissemination evolves into marketing as the MuG VRE transitions into a sustainable environment, the spectrum of activities needs to expand. Conventional media outlets (print / TV / radio) will be more actively engaged. MuG presence in relevant industrial sector and trade shows will be enhanced as well as activity in professional networks such as LinkedIn, in which a group has already been generated (<https://www.linkedin.com/groups/8572323/>). Presentations will be made about the benefits of the VRE, and tutorials will be made available, based on the success stories of pilot projects (as end users of the VRE) and tool developers acting as lead users of the tool wrapping API developed to facilitate tool integration. Embracing the initiative of the abovementioned position paper, we expect to exploit complementarity and invest in building bridges with other international initiatives (NIH 4D Nucleome, LifeTime flagship, 4DNucleome.eu, etc.).

In addition to the already existing academic networks maintained by members of the consortium, networks will be expanded to include industrial, commercial and policy-maker communities. Through these expanded networks we will reach out to enrol regional and sectoral champions who will act as multipliers in propagating the MuG VRE message.

5 INVESTMENT READINESS

The modelling undertaken and summarised in Section 2, with details in Annex B, has assumed a slow organic growth that does not require outside investment. However, if it were possible to acquire such investment, we are aware the user-base of the MuG VRE would be able to grow much more quickly.

¹⁷ <https://youtu.be/CG6zaK4-HtY>

There are pros and cons to obtaining investment, one pro is the previously mentioned increased growth in the user-base, another is the rate at which the VRE enhancements can be implemented. A con is the fact that investors require a stake in the business that usually requires repayment at some agreed point. So long as investment is properly planned and managed, the company will benefit from rapidly increasing revenues which are easily able to cover the repayments. Another benefit associated with investment is that they are often made by well-connected individuals and organisations with skills that are often missing in small business. These enhancements further add to the accelerative effect of an investment. It is worth noting that investment is the most common mechanism supporting the growth of companies in all but the most primitive markets.

The MuG legal entity, if it finds a viable investment opportunity, will make the required difficult decisions, based on what is right for the company, not for the benefit of any particular individual.

Investment opportunities can come from many diverse sources. Partner or individual investments are often the easiest to obtain but usually are of low value in terms of the financial and opportunity values. Crowdfunding and Peer-to-Peer Lending are increasingly popular ways of raising money but the investors here are fickle and usually respond best to emotional appeals rather than logic. They also respond usually to offers associated with concrete benefits. The MuG VRE concept is probably too abstract to engage the crowdfunding and Peer-to-Peer Lending communities. Bank loans are always safe because the due diligence process entered into by the banks prior to funds being exchanged is so risk averse that entities seeking such loans have to offer securities that are difficult for a new business to obtain without exposing directors to high levels of personal risk. The MuG legal entity will not be in a position to apply for a bank loan until such a time that it probably will not need the loan at all. However, the partners agree that the legal entity is able to seek project funding in its own right, to support it through the initial growth phase.

Alternatively, European Investment Bank funds are available through various European Innovation Council initiatives and these are applied for through processes very similar to the research grant application process. However, there are big changes being made to the EIC at the moment and these are likely to shift the emphasis away from start-ups, so this route is also unlikely to reap rewards. The final set of investment opportunities are associated with Angel Investors and Venture Capitalists. Accessing investment through either of these types of entity will reap the greatest rewards but come at the highest price in terms of the required return on the investment. Once the MuG legal entity has its finances in order and has two to three years of operational data to support its case, such entities will be considered: if the decision is made to follow this route of growth. Organic growth is still possible.

NB Stock offers are another way of raising funds for a business and this mechanism involves a floatation on a stock market where shares in a business are offered for sale to public investors. Before this can happen the governance and management structures need to be mature and the business needs a solid proven track record. It will be a long time before The MuG legal entity is able to consider public floatation.

6 TIMELINE

The time-line below provides a link between past achievements and future objectives and targets. (See Figure 1, in Section 2.5.1, for explanation of TRLs and their significance in this timeline).

VRE development begins			VRE at TRL6		MuG Legal Entity Launched		VRE at TRL7		VRE at TRL8		VRE at TRL9			
2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029
Focus: VRE Development				Focus: EU Research Community				Focus: Global Research Community		Focus: Global Diagnostics Community				
Public funding				Public funding continues alongside sustainable operations Target revenue of \$600K by end of period				Target revenue of \$2.5M by end of period		Target revenue of \$14.5B by end of period				

Figure 3: MuG VRE and Legal Entity Timeline

NB The three target revenues, indicated in Figure 3, are headline figures and all operational costs, which will massively increase over this period, must still be deducted.

7 Annex A: D6.2 Software tools of protein-DNA interactions

D6.2 Software tools of protein-DNA interactions, is available for download in PDF format at: <https://www.multiscalegenomics.eu/MuG/deliverables/>



8 Annex B: Balance Sheet Projections

8.1 Summary

	2019	2020	2021	2022
EU Research Market Opportunity	\$446.753,56	\$492.429,95	\$492.429,95	\$492.429,95
Income	\$327.500,00	\$366.800,00	\$410.816,00	\$460.113,92
Costs	\$211.200,00	\$303.600,00	\$396.000,00	\$396.000,00
Nett	\$116.300,00	\$63.200,00	\$14.816,00	\$64.113,92
Cumulative	\$116.300,00	\$179.500,00	\$194.316,00	\$258.429,92
Income as Proportion of Opportunity	73,31%	74,49%	83,43%	93,44%

8.2 Income

Growth Rate 12,00%

Income Streams	Fee	Average Cost	Users P/A			
			2019	2020	2021	2022
Enhanced Membership	\$500,00		50	56	62,72	70,2464
Industrial Membership	\$5.000,00		10	11,2	12,544	14,04928
Support Services		\$1.000,00	15	16,8	18,816	21,07392
VRE Training		\$250,00	300	336	376,32	421,4784
Subject Matter Training		\$500,00	75	84	94,08	105,3696
Consultancy		\$10.000,00	5	5,6	6,272	7,02464
Technical Services		\$15.000,00	5	5,6	6,272	7,02464
			\$327.500,00	\$366.800,00	\$410.816,00	\$460.113,92

8.3 Costs

	ANNUAL	
Average personnel cost per PM	6.500,00 €	78.000,00 €
Office per Month	2.000,00 €	24.000,00 €
Equipment Cost per person PA Dep over 3 years	1.500,00 €	1.500,00 €
Consumables per Month	200,00 €	2.400,00 €
Average operational costs per Month	1.000,00 €	12.000,00 €



	2019	2020	2021	2022
# Staff Members	2	3	4	4
Fixed Costs	\$26.400,00	\$26.400,00	\$26.400,00	\$26.400,00
Variable Costs	\$184.800,00	\$277.200,00	\$369.600,00	\$369.600,00
Total Costs	\$211.200,00	\$303.600,00	\$396.000,00	\$396.000,00

8.4 Market Opportunity

Global Genomics Market	
CAGR	10,2%

Market Value Growth	
2013	\$11.090.000.000,00 Data Point (Report)
2014	\$10.991.776.501,29
2015	\$12.112.937.704,42
2016	\$13.348.457.350,27
2017	\$14.710.000.000,00 Data Point (Summary)
2018	\$16.210.420.000,00
2019	\$17.863.882.840,00
2020	\$19.685.998.889,68
2021	\$21.693.970.776,43
2022	\$23.906.755.795,62
2022	\$23.880.000.000,00 Data Point (Summary and Report)

Assumptions	
Market share for platforms is likely to be low	10,00%
Commencement share of market for MuG platform	1,00%
Annual growth rate of market share	2,00%

(2013) Value by:

Application

Value of research market is	\$960.500.000,00	Research accounts for	8,66%	of Global market
Value of diagnostics market is	\$4.034.500.000,00	Diagnostics accounts for	36,38%	of Global market
Value of drug discovery market is	\$2.902.900.000,00	Drug Discovery accounts for	26,18%	of Global market
Value of personalized medicine market is	\$2.102.400.000,00	Personalized Medicine accounts for	18,96%	of Global market
Value of agriculture market is	\$1.089.800.000,00	Agriculture accounts for	9,83%	of Global market

Product

Value of instruments market is	\$3.516.100.000,00	Instruments account for	31,71%	of Global market
Value of consumables market is	\$6.657.100.000,00	Consumables account for	60,03%	of Global market
Value of services market is	\$916.700.000,00	Services account for	8,27%	of Global market

Technology

Value of PCR market is	\$5.429.700.000,00	PCR accounts for	48,96%	of Global market
Value of DNA sequencing market is	\$2.704.400.000,00	DNA sequencing accounts for	24,39%	of Global market
Value of DNA microarray market is	\$1.983.900.000,00	DNA microarray accounts for	17,89%	of Global market
Value of nucleic acid extraction and purification market is	\$971.900.000,00	Nucleic acid extraction and purification accounts for	8,76%	of Global market

Region

Value of North America market is	\$4.105.500.000,00	North America accounts for	37,02%	of Global market
Value of Europe market is	\$3.167.300.000,00	Europe accounts for	28,56%	of Global market
Value of Asia Pacific market is	\$2.460.900.000,00	Asia Pacific accounts for	22,19%	of Global market
Value of RoW market is	\$1.356.300.000,00	RoW accounts for	12,23%	of Global market

Technology market by Region

Value of North America market is	\$1.218.900.000,00	Technology accounts for	29,69%	of North America market
Value of Europe market is	\$978.400.000,00	Technology accounts for	30,89%	of Europe market
Value of Asia Pacific market is	\$825.100.000,00	Technology accounts for	33,53%	of Asia Pacific market
Value of RoW market is	\$493.700.000,00	Technology accounts for	36,40%	of RoW market

Global Population Growth

	2010	2020	
All ages	6.853.000.000	7.770.000.000	13,38%
Over 65 years of age	626.000.000	855.000.000	36,58%

Market Restraints

Cessation of industrial research on RNA inference testing

High price of molecular diagnostic kits

	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
EU Research Market										
Overall Market	\$11.090.000.000,00	\$10.991.776.501,29	\$12.112.937.704,42	\$13.348.457.350,27	\$14.710.000.000,00	\$16.210.420.000,00	\$17.863.882.840,00	\$19.685.998.889,68	\$21.693.970.776,43	\$23.906.755.795,62
Research Component	\$960.500.000,00	\$951.992.906,18	\$1.049.096.182,61	\$1.156.103.993,23	\$1.274.026.600,54	\$1.403.977.313,80	\$1.547.182.999,80	\$1.704.995.665,78	\$1.878.905.223,69	\$2.070.553.556,51
European Research Component	\$274.318.453,56	\$271.888.830,63	\$299.621.491,36	\$330.182.883,48	\$363.861.537,59	\$400.975.414,43	\$441.874.906,70	\$486.946.147,18	\$536.614.654,19	\$591.349.348,92
Completed Years		0	1	2	3	4	5	6	7	8
European platform market	\$27.431.845,36	\$27.188.883,06	\$29.962.149,14	\$33.018.288,35	\$36.386.153,76	\$40.097.541,44	\$44.187.490,67	\$48.694.614,72	\$53.661.465,42	\$59.134.934,89
initial MuG market share	\$274.318,45	\$271.888,83	\$299.621,49	\$330.182,88	\$363.861,54	\$400.975,41	\$441.874,91	\$486.946,15	\$536.614,65	\$591.349,35
Growth of MuG market share			1,020000%	1,040400%	1,061208%	1,082432%	1,104081%	1,126162%	1,148686%	1,171659%
Value of MuG market share		\$271.888,83	\$302.677,63	\$333.618,11	\$367.722,87	\$405.315,70	\$446.753,56	\$492.429,95	\$542.778,67	\$598.277,95
Global Research Market										
Overall Market	\$11.090.000.000,00	\$10.991.776.501,29	\$12.112.937.704,42	\$13.348.457.350,27	\$14.710.000.000,00	\$16.210.420.000,00	\$17.863.882.840,00	\$19.685.998.889,68	\$21.693.970.776,43	\$23.906.755.795,62
Research Component	\$960.500.000,00	\$951.992.906,18	\$1.049.096.182,61	\$1.156.103.993,23	\$1.274.026.600,54	\$1.403.977.313,80	\$1.547.182.999,80	\$1.704.995.665,78	\$1.878.905.223,69	\$2.070.553.556,51
Completed Years		0	1	2	3	4	5	6	7	8
Global platform market	\$96.050.000,00	\$95.199.290,62	\$104.909.618,26	\$115.610.399,32	\$127.402.660,05	\$140.397.731,38	\$154.718.299,98	\$170.499.566,58	\$187.890.522,37	\$207.055.355,65
initial MuG market share	\$960.500,00	\$951.992,91	\$1.049.096,18	\$1.156.103,99	\$1.274.026,60	\$1.403.977,31	\$1.547.183,00	\$1.704.995,67	\$1.878.905,22	\$2.070.553,56
Growth of MuG market share			1,020000%	1,040400%	1,061208%	1,082432%	1,104081%	1,126162%	1,148686%	1,171659%
Value of MuG market share		\$951.992,91	\$1.059.796,96	\$1.168.132,10	\$1.287.546,67	\$1.419.174,42	\$1.564.265,15	\$1.724.196,69	\$1.900.487,94	\$2.094.813,39
Global Diagnostics Market										
Overall Market	\$11.090.000.000,00	\$10.991.776.501,29	\$12.112.937.704,42	\$13.348.457.350,27	\$14.710.000.000,00	\$16.210.420.000,00	\$17.863.882.840,00	\$19.685.998.889,68	\$21.693.970.776,43	\$23.906.755.795,62
Diagnostics Component	\$4.034.500.000,00	\$3.998.766.663,16	\$4.406.640.862,80	\$4.856.118.230,81	\$5.351.442.290,35	\$5.897.289.403,97	\$6.498.812.923,17	\$7.161.691.841,34	\$7.892.184.409,15	\$8.697.187.218,89
Completed Years		0	1	2	3	4	5	6	7	8
Global platform market	\$403.450.000,00	\$399.876.666,32	\$440.664.086,28	\$485.611.823,08	\$535.144.229,04	\$589.728.940,40	\$649.881.292,32	\$716.169.184,13	\$789.218.440,92	\$869.718.721,89
initial MuG market share	\$4.034.500,00	\$3.998.766,66	\$4.406.640,86	\$4.856.118,23	\$5.351.442,29	\$5.897.289,40	\$6.498.812,92	\$7.161.691,84	\$7.892.184,41	\$8.697.187,22
Growth of MuG market share			1,020000%	1,040400%	1,061208%	1,082432%	1,104081%	1,126162%	1,148686%	1,171659%
Value of MuG market share		\$3.998.766,66	\$4.451.588,60	\$4.906.641,28	\$5.408.232,22	\$5.961.123,56	\$6.570.565,07	\$7.242.344,12	\$7.982.840,80	\$8.799.088,63

