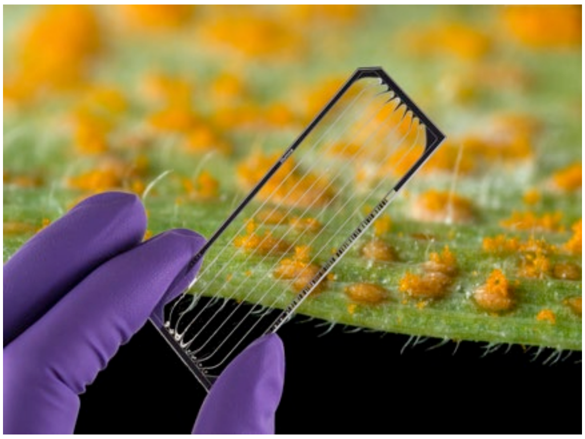
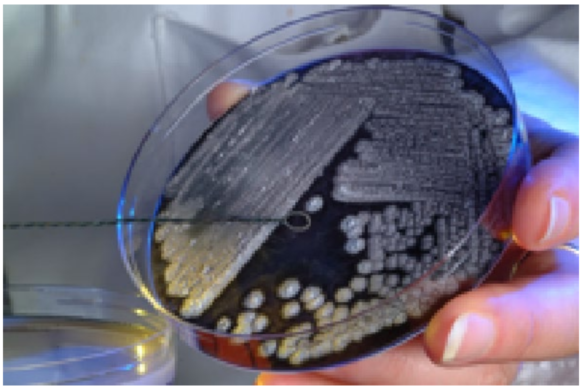
Impact of the John Innes Centre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Executive Summary

Brookdale Consulting was commissioned by the John Innes Centre (JIC) to produce an updated socio-economic impact assessment of the Institute, the last one being in 2013.

JIC is one of eight institutes strategically aligned to BBSRC. These institutes focus on long-term world class strategic bioscience research with the aims of contributing to UK and global socio-economic growth, sustainable food supply and improved health outcomes; as well as positioning the UK as a leader in science, knowledge and innovation.

JIC has a wealth of historic research which is generating ongoing impacts around the world. Examples include discovery of the wheat dwarfing gene, which improves yield in global commercial wheat crops, and antibiotic discoveries, which have contributed to development of new drugs.

JIC continues to invest in fundamental research to support new discoveries, with a particular focus on agri-tech for food security, health and wellbeing as well as innovation in natural and new to nature chemicals. The focus of this report is on JIC's ongoing research and its emerging impacts. Since the 2013 report JIC has enhanced its commercialisation activity through a number of start-ups, spin-outs, license agreements and inward investment. Its return on investment has increased as shown below.

On-going Impacts
JIC's operating impact (from staff and supplier spending) supports 724 jobs and generates £39.5m of Gross Value Added (GVA) across the UK economy per year.

JIC's extensive education and training activities range from schools' activities including the Youth STEMM Award and Year 10 Science camp through to international summer schools, year in industry programmes, PhDs and post-doctoral training. At any one time JIC is training approximately 100 PhD students. Over the next 10 years JIC's training and visitor spend is estimated to contribute £41m GVA - £23m to the UK economy and a further £17m GVA to the wider global economy.

Research Impacts[1]
A sample of JIC's research has been assessed for impacts. Two impact assessments have been undertaken, using different methods

- **Method 1**: An assessment of the impacts of a sample of research case studies, including a Return on Investment calculation (RoI) based on

[1] See Appendix 1 for assumptions.

associated research grant and operating costs. This method is similar to that used in the previous report (2013) allowing comparison.

- **Method 2:** An assessment of the impacts of all research projects plus operational, training and visitor impacts, including an RoI-based on all grant and operating costs[2].

Method 1 – Results

This report identifies research impacts of £300m GVA at the UK level over 10 years and a return on investment of £14.22 per £1 invested. This is based on the sample of projects reviewed and the research costs associated with them plus overheads.

This compares to the previous report (2013) which identified £224m of GVA at the UK level over 10 years and a RoI of £11.99 per £1 invested.

GVA impacts	NPV - 10 yrs
UK	£300,547,839
Rest of the world	£5,710,377,341
Total	£6,010,925,179

Attributable research costs	**NPV - 10 yrs**
Total	21,135,554

RoI (GVA leverage)	NPV - 10 yrs
UK research benefits divided by total research costs	14.22
Rest of the world research benefits divided by total research costs	270.18
Total research benefits divided by total research costs	284.40

[2] Uses the latest figures and assumes JIC's income and expenditure remains stable over the period.

Method 2 - results

JIC is estimated to generate a total of £1.8bn GVA at the UK level over the next 10 years, taking account of (a) operating impacts (b) education and training impacts (c) visitor spend and (d) the anticipated economic impact of the full portfolio of current research/commercialisation projects (of which 21% has been sampled and analysed).

This represents a RoI (impact divided by total operating costs) of £4.25 per £1 invested over a 10-year period, rising to £7.10 per £1 invested, over a 25-year period (allowing for the maturing of impacts of a number of the research projects).

GVA impacts	NPV - 10 yrs	NPV - 15 yrs	NPV - 25 yrs
UK	1,847,434,408	3,451,899,803	6,108,251,211
Rest of the world	26,933,888,548	121,146,239,004	249,964,390,361
Total	28,781,322,956	124,598,138,806	256,072,641,572

Operational cost	NPV - 10 yrs	NPV - 15 yrs	NPV - 25 yrs
Direct costs	434,409,232	601,599,983	860,894,777

RoI - total benefits divided by total costs	NPV - 10 yrs	NPV - 15 yrs	NPV - 25 yrs
UK	4.25	5.74	7.10
Rest of the world	62.00	201.37	290.35
Total	66.25	207.11	297.45

1. Introduction

Brookdale Consulting was commissioned by the John Innes Centre (JIC) to produce an updated impact assessment of the Institute for 2018.

This report highlights the range of quantitative and qualitative impacts generated by the ongoing research and activities of JIC. The report reviews and updates the impacts from the previous report of 2013 as well as highlighting the wide range of new areas that JIC is actively researching.

JIC receives three quarters of its revenue from BBSRC and supports BBSRC's vision to deliver world-class bioscience to support:

- **Food security** - feeding nine billion people by 2050. *Work to improve wheat and oilseed rape yields, and alleviate the need for vernalisation in brassicas are examples of JIC contributions here.*
- **Industrial biotechnology, chemicals and renewable materials from bioscience** - *The potential to make new high value products from plants and microbes such as adjuvants or drugs, to improve sustainability of extraction or to increase oil content in oilseed rape are examples.*
- **Enhancing lives and improving wellbeing** - through fundamental bioscience, particularly as the proportion of UK society living beyond 65 continues to increase dramatically. *Molecular pharming, enriched broccoli, resistant starch, antibiotics and other high value compounds are all examples here.*

JIC also supports the UK's industrial strategy as its work is fundamental to growing the UK's bioeconomy. JIC has around 100 PhD students at any one time and runs a Masters course in plant genetics and crop improvement with the University of East Anglia (UEA). JIC works in partnership and encourages innovation in all its science and outreach programmes. There are numerous examples of JIC's innovation such as Youth STEMM awards, dealing with algal blooms in Norfolk and new spin-outs or start-ups.

The structure of the rest of the document is as follows:

- Section 2 - sets out the operating impact of JIC
- Section 3 - presents the impact of JIC research through a series of case studies
- Section 4 - presents wider impacts of JIC's KEC effort
- Section 5 – identifies future potential impacts
- Section 6 - summarises the findings of the report
- Annexes contain supporting material and data.

Brookdale Consulting acknowledges the significant contribution of JIC staff in working with the team to produce this final report.

2. Operating Impact of JIC

The operating impact of JIC relates to the on-site running of the Institute, such as expenditure incurred and staff employed, plus the knock-on effects as these expenditures ripple through the UK economy and support further activities. The total economic impact of operating JIC therefore encompasses three distinct elements:

1. Direct impact: output generated and persons employed in the day-to-day operation of the Institute in Norwich;

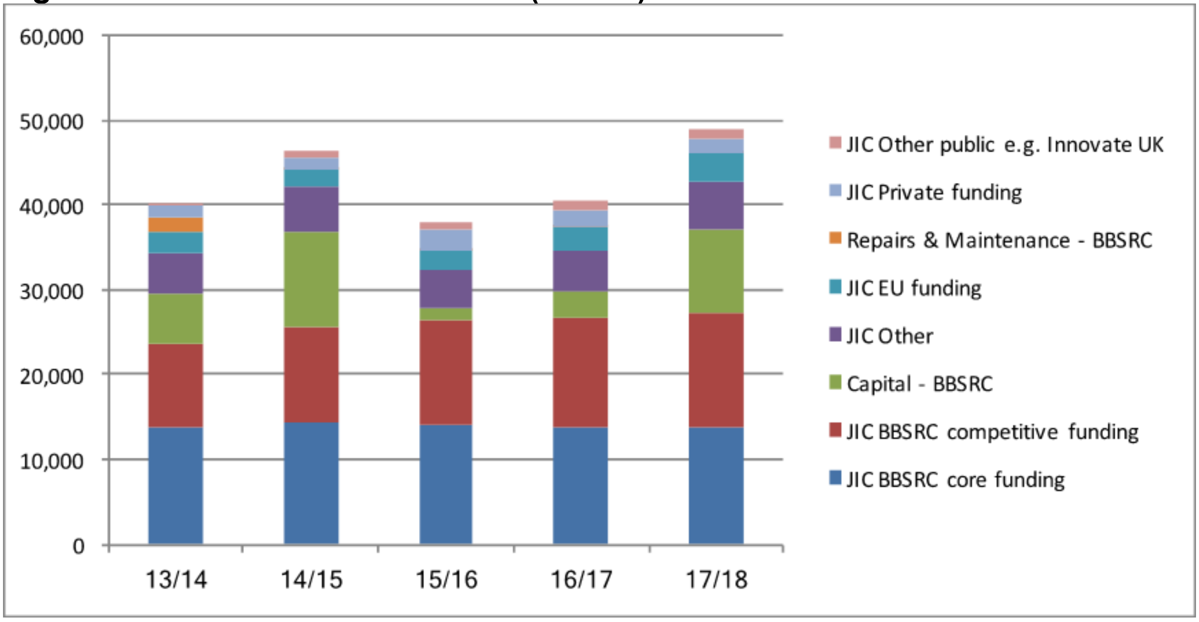
2. Indirect impact: output and employment created in the businesses which supply the inputs or materials used by the Institute; and

3. Induced impact: output and employment created when workers employed directly or indirectly spend their income in the local economy.

2.1 Direct Impact

JIC's income in 2017/18 was £49m. Figure 4.1 illustrates JIC income by source over the last 5 years. Income has steadily increased over the last 3 years, largely due to increased capital expenditure, having dipped in 2015/16. Between 2013/14 and 2017/18, total revenue income has increased by £8.7m and capital funding has increased by £3.7m. The main sources of the increases in funding have been BBSRC competitive funding and BBSRC capital.

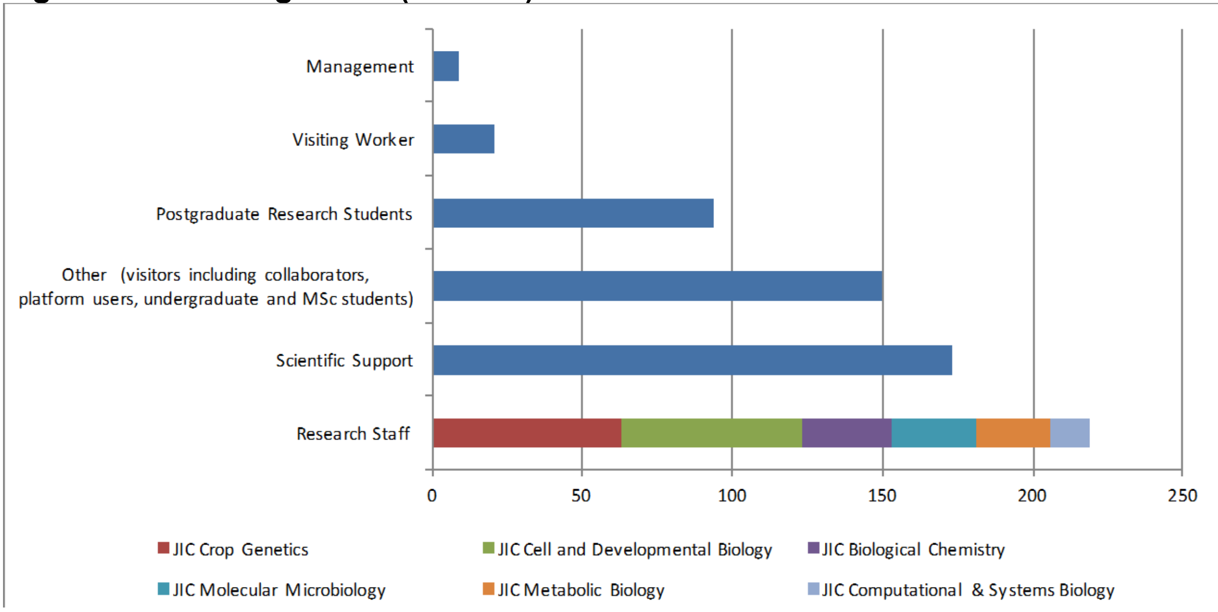
Figure 4.1: Sources of JIC Income (£000's)



Source: JIC Management Accounts

JIC directly employs 422 staff comprising 219 (209 FTEs) in research, 171 (141 FTEs) in scientific support, 8, in management, 3 (2 FTEs) students and 21 (19.5 FTEs) visiting workers. JIC had an additional 87 students and 147 visiting scientists in 2017/18. The students receive a stipend that varies according to the sponsor. Visiting scientists are supported by their host institutions, or by EU funding for training purposes – see Figure 4.2.

Figure 4.2: Staffing at JIC (2017/18)



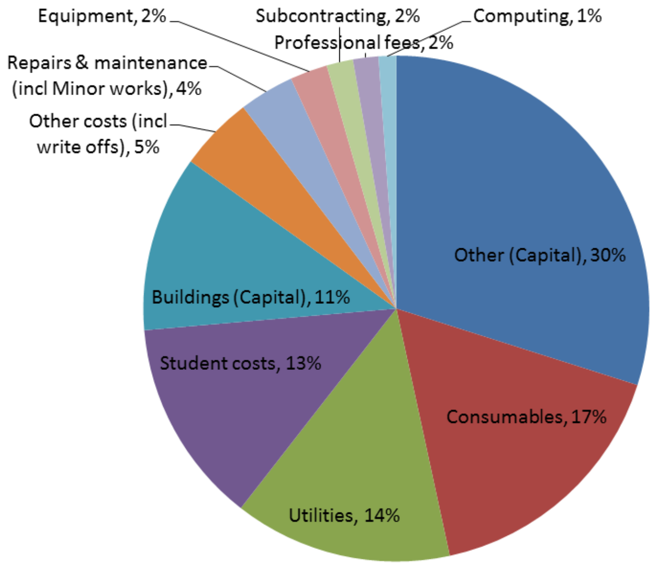
Source: JIC

Back office support is provided to JIC via NBI Partnership, a shared services organisation used by all institutes on the Norwich Research Park (NRP).

2.2 Indirect Impact

JIC spent £24.4m with suppliers in 2017/18, of which £23.3m was with UK based suppliers. This supplier expenditure forms the inputs for calculating the indirect operating impact of JIC. Figure 4.3 illustrates the supplier expenditure by type.

Figure 4.3: JIC Expenditure by Type



Source: JIC Management Accounts

In 2017/18 'other capital' was a major element of the expenditure. Consumables, utilities and student costs were also high.

This profile of supplier expenditure supports output and employment amongst supplier industries, and their suppliers in turn. The extent of this impact can be estimated using the UK National Accounts published by ONS, estimating the level of expenditure required to support a FTE job in each supplier, and their knock-on expenditure.

In total for 2017/18, JIC's supplier expenditure is estimated to **generate a total of £47.2m output for UK industries, supporting 358 jobs**. This comprises 242 FTEs in those UK companies directly supplying JIC, and a further 116 employed through further supply chain effects (i.e. as JIC's suppliers purchase inputs in-turn from their suppliers, which is still attributable to JIC's initial demand).

2.3 Induced Impact

Total salaries and associated costs paid to JIC staff amounted to £17.5m for 2017/8. There was a further £3.2m of student costs. The salaries paid to staff working within the JIC supply chain are estimated at £7.4m. In total, this £28.1m of direct and indirect salaries accrues to households to be spent on a profile of consumer goods and services, generating further economic activity in the UK. This forms the basis for JIC's induced impact.

Modelling this household income using an average consumer profile, indicates that the direct and indirect salaries will lead to increased spending of £8m and will support a further 60 jobs across the UK economy. While these induced impacts can be attributed to JIC, they will largely occur in sectors in consumer industries such as retail and recreational services.

2.4 Summary of Operating Impacts

Figure 4.4 summarises the direct, indirect and induced impacts of JIC highlighting the 840 jobs and £39.5m of Gross Value Added (GVA) across the UK economy.

Figure 4.4 Summary of JIC Operating Impacts

	Output (£m)	Employment (jobs)	GVA (£m)
Direct	50.5	422	17.4
Indirect	47.2	358	20.4
Induced	8	60	1.7
Total	**105.7**	**840**	**39.5**

3. Impact of JIC Research

This section sets out the calculation of actual and potential impacts arising from JIC research through a series of case studies under the following headings:

- Wheat
- High Performance Brassicas
- Oilseed Rape
- Healthier Wheat and Peas
- Industrial Biotechnology and Synthetic Biology
- High Value Products from Plants

Alongside the case studies there is an economic model that calculates the impacts arising from the research in a consistent manner – see Appendix 2 for the methodology.

3.1 Wheat

JIC continues to research in wheat at fundamental and applied levels. Growing world populations, the threat of climate change, new pests and diseases and the withdrawal of certain crop protection products mean that there is an ever more pressing need for more productive food crops. Recognising this need, the UK has developed the Designing Future Wheat Programme with JIC having the leading role alongside other partners.

UK farm gate turnover of wheat was £2.0bn in 2011[3], with 1.8m hectares grown and an average yield of 8.3 tonnes per hectare; down from a peak of 9 in 2015, but well up on 2016.

At the European level, production in 2016 was 250m tonnes at 4 tonnes per hectare, while at the global level, yields have increased consistently since 2013 to reach 3.4 tonnes per hectare in 2016 producing 749m tonnes over 220m hectares (FAOSTAT). The difference in yield figures across world regions shows that even in current production systems there is substantial scope to improve productivity.

3.1.1 Improving Wheat Productivity

JIC's historic discoveries in wheat are well-documented and included in previous impact reports. The main historic impact is of wheat dwarfing genes which are still key to most commercial varieties. These genes remain important to commercial wheat crops around the world so can be considered an ongoing impact of the work of JIC, other institutes and industry. **In 2018, using the same assumptions as previous reports, the gross value of these benefits globally is estimated to be £4.9bn**.

[3] All Defra references in this section are from the publication 'Agriculture in the United Kingdom 2017' unless specified otherwise.

JIC is one of eight institutions in the Designing Future Wheat (DFW) Programme[4], the UK's National Wheat Research Programme. DFW aims to develop new germplasm with the traits needed by plant breeders to develop new wheat varieties.

In addition to co-ordinating the whole programme, JIC is leading two of four work packages in DFW: 'Added Value & Resilience' and 'Germplasm - development for trait dissection' as well as contributing to the remaining two work packages[5]. This programme is likely to lead to productivity enhancements for UK wheat.

Alongside DFW, JIC is also researching other aspects relating to wheat productivity. For example, JIC discovered the DA1 and DA2 genes which control seed size by affecting the shape of the seed as it develops. JIC has patented these genes which can be used to increase 1,000 grain weight, a key determinant of high yielding plant varieties. Plant breeders are already using this IP under licence in wheat, and research is ongoing for its application to rice and maize.

Only 10% of the diversity available to wheat breeders is currently exploited in breeding programmes. The recent discovery of the ZIP4 gene will allow transfer of useful traits from wild relatives into wheat. Magnesium treatment increases the level of exchange and ZIP4 mutants are now being used in breeding to improve the efficiency of transfer of wild relative traits into wheat.

For every 1% increase in wheat yield at the UK level, the additional revenue to the farming industry will be £20m per year (assuming all other factors such as inputs and price remain constant). As the plant breeding industry is constantly introducing new lines, the research will not increase costs to the industry.

JIC's **Germplasm Resources Unit** (GRU) curates germplasm collections of a wide range of cereal and legume crops and their wild relatives. It is a National Capability for the research community, which is unique for the UK and is formally registered under the International Treaty of Plant Genetic Resources for Food and Agriculture operated through FAO. Access to extensive genetic variation in the GRU is useful for identifying traits to cope with climate change, disease resistance and improved productivity for

[4] Other partners are Rothamsted, NIAB, EBI (the European Bioinformatics Institute), Earlham Institute and the Universities of Bristol and Nottingham.
[5] WP1 'Increased efficiency and sustainability' and WP4 'Data Access and Analysis'.

crops. It is vital to JIC ongoing research and is also being exploited commercially – see New Heritage Barley case study.

The impact of research coming out of DFW can be attributed to the partnership as a whole both the research partners and the plant breeding industry. As a major partner in DFW we assume 30% attribution for JIC. On this basis, **for every 1% increase in yield achieved, the JIC share of impact will be £4m at the UK level.**

Given the significance of this work and the international nature of plant breeding, it is likely that the resultant yield improvements will also influence EU wheat production, and possibly wider global production (except in areas where other factors such as water may restrict production). Therefore, **at the EU level where wheat production was 250m tonnes in 2016[6], a 1% increase would generate 2.5m tonnes of additional wheat at £131 per tonne[7] generating £327m, the JIC share of impact being £65.5m at the EU level.**

3.1.2 Reducing Wheat Diseases

The previous report highlighted JIC's major contribution to tackling wheat diseases. Globally, direct yield losses due to pests and diseases are estimated to be 20-40%[8]. There is a strong rationale for ongoing investment in this area, particularly as chemicals are withdrawn. As new challenges emerge, JIC's work is important in supporting the delivery of durable resistance and highlighting potential trade-offs between resistance to initial target pathogens and other traits such as yield or resistance to other pathogens.

For example, JIC's work in yellow rust resistance is focused on understanding its genetic basis. According to AHDB, yellow rust can lead to yield reductions of 10-20%. There are two types of resistance genes. Firstly, those that confer strong resistance through all stages of plant growth. This strong resistance can often be defeated quickly in-field. Secondly, those genes that offer partial resistance, for example, only at the adult stage. These genes are harder to identify but potentially offer longer term persistent resistance. One example of this type of gene is YR36.

Plant breeders have been selecting for the strong resistance genes for a long time. However, the new varieties produced have not lasted long in the field (only 4-5 years) due to breakdown of resistance. This has reduced the returns to plant breeders as well as creating costs for wheat millers who have to adapt their processes to new varieties.

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[6] Eurostat
[7] Based on FAOSTAT figures for 2016 at Eurostat prices of €157 per tonne changed to £ at €1.20/£1.
[8] Savary, S., Ficke, A., Aubertot, JN. et al. Crop losses due to diseases and their implications for global food production losses and food security. Food Sec. (2012) 4: 519.

JIC has shown that YR36 offers effective yellow rust resistance in the field. Working closely with plant breeders, JIC is identifying molecular markers for key yellow rust resistance genes. This includes YR36 and other genes such as YR5 (one of the few strong resistance genes that is not yet defeated) and YR15 (which offers a different resistance mechanism). In particular, JIC has encouraged breeders to consider the genetic basis alongside the visual appearance of the crop - it may look healthy but be susceptible to yellow rust.

JIC's 'field pathogenomics' programme has made great advances in understanding of the pathogen side of the interaction by using gene sequencing technology in pathogen surveillance. For instance, JIC identified a recent introduction of a diverse set of exotic yellow rust lineages into the UK and showed that these lineages displayed potential seasonal and varietal specificity. By knowing which wheat varieties are susceptible to which isolates, and when those isolates are prevalent throughout the year, provides valuable insights for disease management.

Another example is JIC's ongoing work in Septoria resistance. JIC discovered that the most important gene associated with increased yield in British wheat also increases susceptibility to Septoria. Plant breeders had inadvertently introduced this susceptibility in the 1980s. According to AHDB, Septoria can lead to yield reductions of 20%. There are several other genes that are now being used by plant breeders to deliver Septoria resistance. JIC's work is helping plant breeders to understand the trade-off between yield and Septoria resistance.

JIC contributes to UK crop productivity in other ways. For example, a JIC plant pathologist sits on the AHDB Recommended List Committee to advise on improving methods of assessment, site selection for trials etc. JIC hosts breeders on-site and shares its research widely.

JIC is also researching genes for resistance to biotrophic diseases – those that reproduce on living plant tissue and necrotrophic diseases – those that kill plant tissue or reproduce on dying plant tissue. This research will be of particular relevance to increasing crop productivity in developing countries.

In assessing JIC's ongoing impact in wheat diseases, **we conservatively assume 5% reduced severity of disease outbreaks in years 10 and 17 saving farmers £24.5m at the UK level and £1bn across the rest of the world for each outbreak with 20% attribution to JIC.**

3.2 High Performance Brassicas

JIC has found a way to switch off the natural requirement for vernalisation in brassicas. Vernalisation is a prolonged period of cold temperatures necessary for the plant to flower. JIC has identified the genetic combinations to provide the necessary characteristics, finally patenting its technology in April 2018.

JIC has formed an industrial consortium of 9 partners from farm to retail. JIC's technology has potential application to a wide number of crops but the initial targets are stem broccoli and cauliflower. At the moment, broccoli and cauliflower tend to be grown outdoors in the UK and harvested in the autumn with 16,500 hectares producing 152,000 tonnes in 2017 worth £105m at the farmgate[9]. Out of season requirements are imported with 2017 seeing 136,100 tonnes imported worth £147.5m[10].

It is anticipated that new indoor commercial varieties will be available within 4-5 years and field varieties in 7-10 years. JIC will license use of the technology producing royalty income. More importantly, the technology will vastly improve quality and productivity of brassica production. With no need to wait for vernalisation, growing single stem broccoli in glasshouses will allow up to 4 crops per year in polytunnels or 5-6 crops in glasshouses. The more uniform plants resulting will permit automated harvesting instead of multiple-pass hand harvesting thus saving cost and reducing waste. Stem vegetables are also worth four times the value of field grown crops.

Another benefit will be to plant breeders as the technology shortens generation time, and in some instances will remove the biannual nature of seed production allowing 2-3 seed crops per year. This will enable breeders to create new varieties much more quickly. There is also the potential future application of the technology to oilseed rape in the next 15-30 years.

A summary of the benefits (Table 3.1) has been calculated as part of the project drawing on expert input. This shows that application of JIC's technology to the current crop in the UK could add £27-£30m if fully adopted. A high level of adoption is likely as brassica growers tend to be large and specialist. It is likely that the technology would displace imports to the UK and could support new forms of robotic indoor farming close to major population centres. It would also reduce the dependence of farmers on migrant labour, which is in increasing shortage.

Table 3.1 Summary of benefits of JIC's technology in broccoli and cauliflower at UK level

Crop	2017 area (ha)	Extra yield value (£per ha)	Automated harvest saving (£per ha)	Retail waste reduction (based on 2.5% of farm gate value)	Total additional value

[9] Defra Horticultural Statistics 2017.
[10] HMRC Trade Statistics Code 0704 Cabbages, cauliflowers, kohlrabi, kale and similar edible brassicas 165,500 worth £172.6m. Defra import statistics suggest 136,100 tonnes cauliflower and broccoli which is 84% of volume is, the target crops here.

Field Broccoli	7,236	£740-£1,224	£107.50	£1.55m	£7.68m-£10.46m
Field Cauliflower	9,255	£1,120	£160	£1m	£12.85m
Stem Broccoli	2,000[11]	£561	£2,808	£0.24m	£6.52m
Total					£27m-£29.8m

Source: Defra horticulture statistics, AHDB Project FV368 and NIPPY project grower base data

The technology would also benefit European production of 135,254ha in 2016 (FAOSTAT) at up to £157m based on field production only (the level of stem broccoli is not disclosed in the statistics). This is based on full adoption and taking the mid-point of field grown benefits from Table 3.1 as £1,159 per ha (the broccoli and cauliflower area is not split out at European level).

3.3 Oilseed Rape

3.3.1 Oilseed Rape – Reducing Pod Shatter

JIC continues to work on premature pod shatter in oilseed rape (OSR). This is a major problem in oilseed rape (OSR), resulting in average yield losses of between 10-25%[12]. JIC has identified the genes responsible and demonstrated the ability to control pod shatter in the greenhouse. The next stage is field experimentation.

JIC's patent in this area has been taken up by a major plant breeder for field testing and potential breeding into its own varieties. The previous impact report (2013) estimated 4-6 years for new varieties of OSR to reach market. It is likely that another 5 years will be required to fully commercialise the benefits, which include:

- increasing OSR yield by an average of 10-20%
- improving production efficiency by reducing the need to spray or swathe the crop; and eliminating the need to spray fields of subsequent crops to eliminate rogue OSR caused by pod shatter

JIC is also collaborating with a group in Oslo to identify the genes that mediate seed attachment tissue in the pods. This is potentially a second line of defence so that if pods do open in the field, the seeds will not drop. Proof of concept is being developed in a diploid brassica before transferring to OSR itself.

[11] Industry estimate.
[12] Bruce, D.M. & Farrent, J.W. & Morgan, C.L. & Child, R.D.. (2002). PA—Precision Agriculture: Determining the Oilseed Rape Pod Strength Needed to Reduce Seed Loss due to Pod Shatter. Biosystems Engineering. 81. 179–184. 10.1006/bioe.2001.0002.

JIC continues to use a non-GM approach suitable for UK and EU markets. Assuming JIC's technology is bred into commercial crops in the UK and EU, it is likely to be adopted widely. **Assuming an increase in OSR yield of 15% would equate to a UK farmgate increase of £115m based on 2017 prices[13] or £1.1bn if implemented across the EU-28[14]. There will also be environmental benefits from reduced need for spraying.**

3.3.2 Oilseed Rape – UPL3

JIC has developed and patented a technology known as UPL3 which allows increased seed size and oil composition in OSR. This technology has been licensed to industry for assessment. The technology exploits the genetic variation in OSR to discover a new regulatory component that works by prolonging seed maturation when oil is deposited. Once crossed into commercial varieties, it has the potential to increase oil content by 5-10% and yield by 10%. It will take five years to be bred into commercial varieties with attribution to JIC being 50%. **Using similar assumptions as pod shatter will lead to a UK yield impact of £77m or £733m across the EU-28.** According to AHDB, UK oilseed rape buyers typically pay an oil premium of 1.5% for every 1% of oil content above 40%. Taking the 2017 average price of £350 per tonne and **assuming 5-10% oil content increase would suggest £26-52 per tonne or £56m-£112m at the UK level and £158-316m across the EU-28**. While increased supply may reduce prices for OSR, the improved productivity will also help encourage farmers to grow OSR in rotation which will improve soil quality.

3.4 Healthier Wheat and Peas

JIC and Quadram Institute Bioscience are working on nutritional trait development in wheat and pea seeds focused on improving the diet and health of consumers. A key objective is to reduce dietary risk factors for diseases such as obesity, type 2 diabetes, heart disease and colorectal cancer by increasing the resistant starch content of foods, an important component of dietary fibre. Western diets tend to be deficient in dietary fibres[15].

Most starch is digested rapidly in the small intestine and this can elevate blood glucose levels in the body. A small proportion of starch, known as resistant starch, is not digested so rapidly and proceeds into the large intestine. There is evidence that increased consumption of this resistant starch or fibre can deliver health benefits as well as reducing appetite which can help control obesity.

The research uses a crop genetics approach to understand the effect of mutations in starch synthesis genes and how the proportion of resistant starch

[13] Defra (2018) Agriculture in the UK 2017 p32 OSR output value of £764m.
[14] Based on average commodity price of £315 over the past 5 years and 6.69m tonnes (Eurostat).
[15] Gemen et al (2011) Relationship between molecular structure of cereal dietary fiber and health effects: focus on glucose/insulin response and gut health. *Nutrition reviews*, *69*(1), pp.22-33.

might be increased through different mutations. JIC is testing the effect of different levels of resistant starch on yield, quality and processability. Human intervention trials are proposed to assess the impact on human health.

The outputs of the work will be pre-breeding traits and germplasm that wheat and pea plant breeders can use in their breeding programmes. It will take 2-4 years for these outputs to be available to breeders and several further years to be available in new varieties. Food processors will then be able to use wheat and pea-based products with higher levels of resistant starch.

Eating plenty of fibre is associated with a lower risk of heart disease, stroke, type 2 diabetes and bowel cancer.[16]. According to the BMA, poor diet costs the NHS around £6bn per year. In addition, Type 2 diabetes alone cost the UK £11.7bn in 2012[17]. A recent Canadian study found that for each additional gram of fibre consumed per day there were savings of CAD$2.6 to $51.1m for type 2 diabetes and CAD$4.6m to $92m savings for cardiovascular disease[18]. The recommended fibre consumption is 30g per day but the average consumption is 18g per day. The challenge has always been to get consumers to change their diet. By bringing more fibre into every day dietary items such as white bread, or pizza bases, JIC's research will create new market opportunities for food producers improved health for consumers and reduced healthcare costs to society.

3.5 Industrial Biotechnology and Synthetic Biology

Natural products represent over 50% of all drugs in clinical use[19] There is considerable future potential to find new useful drugs that can, for example, counter antibiotic resistance. There is also potential to produce rare and valuable plant products in new ways. JIC is active in both these areas.

3.5.1 Antibiotics

Growing antimicrobial resistance and the lack of financial incentive for commercial development of new antibiotics necessitates an ongoing need for public sector investment in antibiotic discovery and development.

The UK Government-commissioned 'Review on Antimicrobial Resistance' (AMR)[20] published its findings in 2016, highlighting a global market value for

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[16] https://www.nhs.uk/live-well/eat-well/how-to-get-more-fibre-into-your-diet/
[17] Kanavos et al (2012) Diabetes expenditure, burden of disease and management in 5 EU countries LSE.
[18] Abdullah et al (2015) Cost-of-illness analysis reveals potential healthcare savings with reductions in type 2 diabetes and cardiovascular disease following recommended intakes of dietary fiber in Canada. Frontiers in Pharmacology, 6, 167.
[19] Alam & Sharaf-Eldin (2016) Limited Production Of Plant Derived Anticancer Drugs Vinblastine And Vincristine Planta Med 2016; 82 - PC4
[20] Tackling drug-resistant Infections globally: Final report and Recommendations published 2016 see https://amr-review.org/

antibiotics of around $40bn per year, c.12% of sales being under patent - equivalent to annual sales of one top cancer drug. The report had ten recommendations to counter antibiotic resistance including a global awareness campaign, improved surveillance, improved hygiene and a combined global response. Two key recommendations relate to JIC, these being:

- The need for new rapid diagnostics to cut antibiotic use – see Iceni Diagnostics case study which is exactly in this area
- The need for improved funding and incentives to promote investment in existing and new antibiotics.

The report highlights an ongoing need for research. Naturally occurring microbes remain the most promising source of novel antibiotics[21] and actinomycetes and other bacteria continue to be a key source of investigation.

JIC's historic work in antibiotics and *Streptomyces* in particular was extensively reviewed in 2010[22]. For this report, these impacts have been updated where possible highlighting:

- additional global sales revenue potential of £306m per year for actinomycete-derived antibiotics[23]
- £46m global sales potential for cephalosporins (a class of beta-lactam antibiotics)
- supporting development of new anti-cancer and immunosuppressant drugs likely to exceed £120m per annum in the long term
- Increasing antibiotic productivity of £44.7m per year, and
- Potential animal health drug discoveries, leading to additional annual sales of £60m[24].

JIC continues to work with the pharmaceutical industry to generate new strains of *Streptomyces*.

The focus in this report is on new developments that have emerged since the last report.

[21] Singh, L. S., Sharma, H., & Talukdar, N. C. (2014). Production of potent antimicrobial agent by actinomycete, *Streptomyces sannanensis* strain SU118. *BMC Microbiology*, *14*, 278.

[22] Economic Impact of *Streptomyces* Genetics Research, BBSRC, April 2010.
[23] Antibacterial Drugs: World Market Prospects 2013-2023
[24] Economic Impact of *Streptomyces* Genetics Research, BBSRC, April 2010.

3.5.1.1 Procarta Biosystems

Procarta Biosystems is a spin-out from JIC focused on developing a whole new generation of antibiotics through a new disruptive technology. Procarta's technology works differently to normal antibiotics. Its proprietary delivery mechanism inserts short pieces of DNA into the infectious bacteria causing and then blocking a stress response. This sequence of events actively kills the bacteria. Unlike many antibiotics it works on both Gram positive and Gram-negative bacteria. It is also much less likely to lead to resistant bacteria – attempts to induce resistance in the lab have failed. Given the concern about antibiotic resistance, the technology has potential to revolutionise antibacterial treatments.

The initial priority is to target Carbapenem-resistant enterobacteriaceae (CRE). Carbapenems are strong antibiotics normally reserved for the most serious infections. CREs are bacteria which are highly resistant to antibiotics and are an increasing problem in hospitals. The Centre for Disease Control in the USA (CDC) has referred to them as 'nightmare bacteria'. Some of these bacteria may live harmlessly in the gut. However, on entering the bloodstream or body tissues they cause serious infection. It is thought that CREs originated in developing countries through uncontrolled use of antibiotics.

Public Health England has developed a tool kit to fight infection noting that the number of recorded CRE cases (carriers and infected) has risen from 5 in 2006 to 600 in 2013. Unrecorded cases may take this figure much higher. A recent study showed mortality rates from CRE of up to 40% with the lowest mortality being in patients treated with Carbapenems (18%)[25] Assuming half of UK cases are infections (as opposed to carriers) there could be conservatively in excess of 50 deaths per year in the UK[26] Official government guidance suggests preventing a fatality is valued at £1.89m[27] **A successful new treatment for these patients could be valued conservatively at £94.5m per year in the UK alone**. In the USA, there are 9,500 CRE infections per year with a cost of treatment of $70-180k per case and an estimated $975m in total[28]. **Better treatment would significantly reduce these costs. Assuming hospital treatment was still required, simply reducing costs to the lower level of the current range could save $326m per year (£250m@$1.3/£1).** Procarta is 3 years away from commercialisation. Attribution to JIC is 33%.

Procarta is also investigating the connection between a person's gut microbiome and a range of diseases such as obesity, Alzheimers, depression

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[25] Tzouvelekis et al (2014) Treating infections caused by carbapenemase-producing Enterobacteriaceae Clinical Microbiology and Infection Volume 20, Issue 9, Pages 862-872

[26] Based on 50% of 600 cases in 2013, with 18% mortality gives 54 deaths.

[27] DfT WebTAG 2017 Value of preventing a fatality.

[28] Bartsch. et al.(2017) Potential Economic Burden of Carbapenem-Resistant Enterobacteriaceae (CRE) in the United States. Clinical microbiology and infection: 23.1 (2017): 48.e9–48.e16.

and Crohn's disease. It aims to develop tailored treatments that can selectively suppress harmful bacteria in the gut while leaving normal, healthy bacteria unharmed. For example, flare-ups of Crohn's disease have been associated with overgrowth of one species of bacteria. Procarta has developed a novel agent that specifically removes this bacterium from the normal gut flora. The company anticipates two years to get to proof of concept for a Crohn's treatment and a further £5-8m of funding to reach human trials.

3.5.1.2 Antibiotic discovery

JIC has considerable ongoing research and activity in antibiotics. For example, a member of JIC staff sits on the Scientific Advisory Board of the charity 'Antibiotic Action' and JIC co-ordinates the local AMR group on the NRP.

JIC is seeking to discover new antibiotics in unusual places such as the in the nest of leaf cutter ants. It is also seeking to discover new strains more quickly, or to make new versions through genetic engineering.

Given the problems with AMR, JIC is researching the mechanisms of current antibiotics as they are poorly understood. Quinolones are the second largest class of antibiotics worth some $7.5bn globally per year[29]. JIC is investigating how administration of quinolones can lead to unexpected resistance to other antibiotics. Understanding this mechanism could help prevent antibiotic resistance developing.

JIC is part of the EU ENABLE consortium which is a drug discovery project for new antibiotics to counter bacteria such as *E. Coli*. ENABLE has identified new potential antibiotics which are being taken forward by industry.

JIC is also researching Thiophenes as potentially promising antibiotics that have been dropped by the ENABLE consortium due to toxicity. Toxicity is a major problem for many antibiotics and has led to rejection of many potentially promising drugs. Working with the Wellcome Trust, JIC's aim is to engineer around the toxicity to deliver a new class of antibiotics to the market. It will be at least ten years to commercialisation, but if successful Thiophenes could become a new class of antibiotics in their own right.

Alongside ENABLE, JIC is discovering new antibiotics in its own right. A recent discovery is Disaclomycin. JIC has discovered the pathway for producing it and is researching its properties as a potential antibiotic and anti-cancer drug. This research is at an early stage.

[29] Transparency Market Research (2014) Antibacterial Drugs—Global Industry Analysis, Size, Share, Growth, Trends and Forecast, 2013-2019.

3.6 High Value Products from Plants

JIC is researching methods to identify and isolate entire metabolic pathways to produce high value products of various kinds. A selection of these is set out below.

3.6.1 Vinca Alkaloids

JIC is continuing its work on understanding the pathways used by plants to produce some of the most rare and valuable natural products. For example, the anti-cancer drugs vinblastine and vincristine, produced by Madagascar periwinkle (*Catharanthus roseus*) are among the most expensive drugs estimated at $2m/kg and $15m/kg respectively, largely due to limited supply and strong demand[30].

These vinca alkaloids are used to treat cancers including Hodgkin's lymphoma, lymphoblastic leukaemias and nephroblastomas. For example, vincristine is particularly effective in the treatment of childhood leukaemia, the most common form of cancer among children. In 2015, there were 9,900 new cases of leukaemia in the UK alone, highlighting the need for ongoing supplies of drugs[31].

JIC has now elucidated the pathway for vinblastine and is working on its reconstitution. JIC has been able to produce small quantities of vinblastine for purification. The next stage requires input from chemical engineers to improve process efficiency as well as patenting the technology.

JIC has received funding of around £2m for its research to date[32] and anticipates a further £4m and 5 years to get its process to market. The impact of JIC's work will be to reduce the cost of producing these compounds, potentially to a small fraction of current costs. This will reduce the burden of cost on healthcare providers and widen access to cancer care. Attribution to JIC would be a third given its international partners in chemical engineering (Denmark) and reconstitution (France).

In 2005, the market for vinblastine was estimated at between $150m - $300m suggesting 75-150kg produced annually[33]. If successful, **JIC's technology could reduce the cost of production suggesting global savings of £100m-£200m in drug costs per year.**

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[30] Alam & Sharaf-Eldin (2016) Limited Production Of Plant Derived Anticancer Drugs Vinblastine And Vincristine Planta Med 2016; 82 - PC4

[31] Cancer Research UK

[32] ERC grant - €1.5m over 5 years; BBSRC grant £400k over 3 years; EPSRC grant of £350k over 3 years

[33] Medicinal Plants 1, Prota, 2008

3.6.2 Hypertrans® Technology

JIC's Hypertrans® technology enables plants to express a wide variety of proteins of potential commercial value. The high speed technology means vaccines can be tailored rapidly and accurately to specific threats as they emerge. Production does not require costly high-containment facilities.

JIC's patented technology has been licensed to Canadian company Medicago for production of vaccines for the global market. In 2015, the global annual impact of the Medicago investment was estimated by Brookdale at £1.37bn. This was based on achieving 19% market share, with improved vaccine efficacy resulting in 20% fewer flu cases across the vaccinated population[34] with reduced costs of £1.1bn in the USA, £142m in the EU and £127m in Japan[35]. These figures are based on production capacity of the new Canadian facility; additional capacity from the existing facility at RTP and a potential facility in Europe could easily double the impact. Medicago was acquired by Mitsubishi Tanabe in 2013 for $357m. Attribution to JIC is 50%.

The technology has also been licensed to UK start-up Leaf Expression Systems (LES), a joint venture between JIC, BBSRC and PBL, for commercialisation in other human and animal vaccine, biotherapeutic and high-value proteins markets. Early LES projects have focused on developing vaccines for emerging human viral pathogens, such as Zika and Chikungunya, and on the ability of the Hypertrans technology to respond rapidly to emerging outbreaks. Substantial future opportunities are also being pursued in the production of individual high-value proteins and in the manufacture of key components for diagnostics companies, including internal standards and controls. This is expected to lead to substantial future impacts in the UK and inward investment onto the NRP.

Total funding for the work has included £4.42m from BBSRC, €1.5m from the EU and £7m in a new facility for Leaf Expression Systems.

3.6.3 QS-21

QS-21 is a plant saponin extracted from tree bark of *Quillaja saponaria*, the Chilean Soapbark Tree. QS-21 is a potent adjuvant; it can significantly improve the efficacy of prophylactic vaccines and is being investigated for use in therapeutic vaccines for diseases such as cancer. It works by stimulating the body's response to fighting infections and has been found to be more effective than many other adjuvants.

In 2017, GSK's vaccine for shingles was the first vaccine approved in the USA and Canada that utilises QS-21 as a key adjuvant. The vaccine has been found

[34] The vaccinated population is around half of the total population in these advanced countries.

[35] US costs of $87bn*50%*19% market share*20%=$1.65bn=£1.1bn@$1.5/£1. EU costs of €10bn (midpoint of €6-14bn)*50%*19% market share*20%=€190m=£142m@€1.34/£1. Japanese costs of $10bn*50%*19% market share*20%=$190m=£127m@$1.5/£1.

to be very effective and its first quarter sales were £110m, well ahead of analyst expectations of £35m[36]. QS-21 Stimulon is also currently being evaluated in numerous GSK vaccine development candidates for both therapeutic and prophylactic applications.

As use of QS-21 increases, an emerging challenge is that current extraction methods are of variable quality and not sustainable. JIC is working on an engineered, alternative plant-production system for triterpenes such as QS-21. JIC has already identified and reconstructed the first part of the production pathway. QS-21 provides an ideal proof of concept for JIC's technology as it has recently come off patent. Success with QS-21 is likely to open up the possibility of producing other valuable plant triterpene products such as Bardoxolone with promise for treating lung disease.

The vaccine adjuvants market alone is anticipated to be worth £592m by 2021[37]. It is anticipated it will be at least 5 years before commercialisation. In the meantime, JIC is developing a database of enzymes that can modify triterpene scaffolds. Once the capabilities of the enzymes, and the pathways they derive from are fully understood, JIC will be able to make a whole host of valuable plant products, including new to nature molecules, with the potential to be new drugs or modifications to known drug molecules that have greater potency or fewer side effects. **Gaining as little as 10% market share of the vaccine adjuvants market would be worth £60m per year and give the UK a leading position in this growing area.**

3.6.4 New Herbicides

JIC has ongoing research in enzymes known as DNA topoisomerases which are which are highly successful targets for antibiotics. JIC unexpectedly discovered two enzymes, normally found in archaea and bacteria, that are also important in regulating plant growth. The two enzymes, are known as DNA gyrase and DNA topo VI, are potential herbicide targets.

For many years glyphosphate has been the chemical of choice for weed control with a global market size of $9bn. Resistance to glyphosphate as well as wider concerns over chemical use mean there is a need to look for natural alternatives. Working with scientists in Australia, research into DNA gyrase is continuing to ascertain how it could be utilised safely and effectively as a herbicide target. Research into topo VI involves screening for new inhibitors to plant growth. This work is part of a £1.2m Wellcome Trust Innovator award and is partly supported by Syngenta. Both of these research areas are at an early stage but they highlight the potential for natural products to provide innovation new products to support economic growth.

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[36] Reuters.

[37] Markets and Markets 2018 $769.4m converted to £592m at $1.3/£1.

4. KEC Highlights

JIC has seen a major step change in its KEC outputs as projects feed through to impact and as the reputation of the Norwich Research Park grows. Highlights are covered in this section with inward investment, spin-outs and a start-up business, as well as other wider interactions. as follows:

- Tropic Biosciences – inward investment to NRP
- Iceni Diagnostics – JIC spin-out
- New Heritage Barley – JIC start-up
- Agri-tech East – JIC contributing to the agri-tech sector in the region
- Norfolk Broads algal blooms – JIC supporting the regional tourism sector

4.1 Tropic Biosciences

Tropic Biosciences is an innovative start-up company formed in 2016 to develop new high yielding coffee and banana varieties. The rationale is that the population of the Tropics will grow by over 500m people by 2030, accounting for half the world's population. This will create an unprecedented need for more productive and environmentally friendly agricultural production.

Originally based in Israel and the USA, its founders conducted a global search to find the best location for the company to grow and thrive. Now based at NRP, having just moved out of JIC, the reasons for choosing this location are as follows:

- Supply of highly trained researchers with the right skills and talents.
- Facilities and equipment available on the NRP have avoided the need for early capital expenditure of £1-2m.
- Eastern Agritech and the NRP have provided a very supportive environment for growth
- Norwich is a pleasant place to live.

The company will generate its first revenues in 2018/19 and anticipates growing from its current level of 17 staff to 25 in 2019 and 50 in 2020. It will take about five years for its varieties to come to market and it attributes 20% of its growth to JIC.

4.2 Iceni Diagnostics

Iceni Diagnostics is a spin out from JIC and UEA set up in 2014. It is based on the Norwich Research Park employing 6 staff, having received seed corn investment and funding from Innovate UK. Iceni is developing advanced in-field diagnostic tools developed from JIC science. It aims to speed up testing results for various high profile viral infections with substantial economic impact.

Now at proof of concept stage, beta testing of devices will take place over the next 12-18 months. If successful, Iceni will license its products to industry. The global market for infectious disease testing is expected to grow to $20bn by 2020, with rapid or 'point of care' testing being the strongest growth segment[38].

Target diseases include avian flu in both poultry and humans and norovirus. Currently, lab tests are required to confirm presence or absence of these infections. A precautionary approach cannot always be taken. The costs associated with outbreaks can be very high. Early detection and isolation through rapid in-field testing can have a substantial impact on reducing the spread and costs of outbreaks.

Iceni's first product is for on-farm detection of avian flu in poultry. Used by vets, and similar to a pregnancy test kit, the avian flu detection would confirm an outbreak more quickly allowing control measures to be implemented at an earlier stage thus potentially affecting fewer farms than if the disease was confirmed later. Industry estimates suggest the cost of dealing with an outbreak is around £1m per business[39] not including government control and compensation costs. Several strains are circulating in Europe, Asia and North America in both wild birds and poultry increasing the UK risk level. Iceni estimates the market for rapid testing in avian flu to be worth £50m per year and anticipates 10% market share within 5 years. It is not clear at this stage whether the costs of avian flu outbreaks could be reduced so that has not been included in the assessment.

Avian flu can also infect humans, and Iceni anticipates taking 10% share of the human flu testing market within 5 years which it estimates is worth £500m per year.

A third product area is in norovirus testing. Norovirus is responsible for many outbreaks of gastroenteritis and is a major cost to the NHS and to the leisure industry, for example cruise ships. Research[40] has found that 88,000-113,000 NHS beds are closed due to gastroenteritis each winter. On average, 80% of providers are affected with closed beds for a median of 15-21 days each. Hospital costs of closed beds including staff absence from illness are £6.9m-£10m per year. A simple test on admission, would ensure that patients carrying the infection are isolated thus preventing wider outbreaks and reducing the costs of closures. Again Iceni anticipates taking 10% market share of this £50m market within 5 years. This could also help to substantially reduce the costs of closure in the NHS.

[38] Statista 2018
[39] Poultry Health and Welfare Group Impact of Avian Influenza UK and Global.
[40] Sandmann et al (2017) Burden, duration and costs of hospital bed closures due to acute gastroenteritis in England per winter, 2010/11 2015/16 Journal of Hospital Infection 97 (2017) 79-85

4.3 New Heritage Barley

New Heritage Barley is a start-up company that aims to make use of old malting barley varieties found in JIC's Seedstor outlet of the Germplasm Resouces Unit to capitalise on the trend for craft beers.

One variety, Chevallier, was the most popular malting variety in Victorian times and is New Heritage Barley's first product line. As well as flavour, it has excellent resistance to Fusarium head blight, a common disease of barley around the world. Seeds from JIC were carefully multiplied to produce several tonnes, enough for commercial planting. Contract farms, chosen for their growing expertise, then grew the seed to produce the final barley which is licensed to New Heritage Barley.

An exclusive agreement with Crisp Malting Group has led to the first new Chevallier malt for nearly a century. Brewers including Greene King in the UK and Goose Island in the USA have produced craft beers using the new malt for its unique flavour. Sales of £5m have been generated (across seed, malt and beer) since early 2018 with around a quarter exported.

The turnover of New Heritage Barley is expected to double over the next year and increase to £200k within the next five years. Other products such as heritage bread wheat or organic products are being considered for development. As well as economic impact, New Heritage Barley is sponsoring two iCASE PhD students. One at JIC is studying beneficial microbe root interactions for disease resistance while the other at Liverpool is studying the genetics of flavour.

The company highlights the potential for entrepreneurs to utilise germplasm resources to develop business opportunities in the food and drink sector.

4.4 Agri-tech East

Agri-tech East is a private not for profit membership organisation fostering collaboration and new connections across the agri-food value chain in the UK and internationally. It does this through various initiatives, for example, 'Pollinator' networking meetings, Special Interest Groups, the annual flagship Agri-Tech Week event and REAP conference, in which JIC has participated. Another initiative is the Young Innovators Forum where JIC early career scientists meet early career staff from industry. This helps to build cultural and technical understanding and networks as well as helping JIC staff to frame and develop new research questions. Within the four years since its inception, Agri-

Tech East's membership has grown to over 160 including JIC, other institutes, major universities, muti-national companies, SMEs and micro companies. JIC is a key member of Agri-tech East and sees this as an important channel for getting its science out into the economy and for hearing about particular challenges that may require new research.

4.5 Youth STEMM award

The Youth STEMM[41] Award was set up in 2015 by a JIC research scientist with support from JIC. The aim of the award is to inspire the next generation of STEMM professionals through an achievement award which promotes diversity and raises the impact of standalone engagement activities. In particular it aims to promote STEMM careers to girls from ages 13-18. With a tiered structure similar to the Duke of Edinburgh Award, participants complete their bronze, silver and gold awards by undertaking additional research tasks and study in areas of interest to them. The Government has identified critical skills shortages and mismatches in STEM which this project is helping to address[42]. In particular, the NAO has found that females are underrepresented in most STEM subjects[43].

Youth STEMM is now working in 28 schools and 15 partners across the UK as well as two international schools in Beijing and Milan. Participant numbers have grown from 200 in the first year to 842 in the most recent year. 70% of participants are female.

Based on initial feedback, 80% of participants have said they gained new skills and are likely to pursue a career in STEMM. Going forward Youth STEMM will:

- Develop a long-term tracking tool to assess career development of participants
- Extend its geographical reach into more schools
- Improve efficiency of running the awards
- Establish links with other STEMM organisations

4.6 The Broads National Park Algal Blooms

The Broads National Park is the UK's largest wetland habitat, is a Designated Special Area of Conservation (SAC) and Ramsar Wetland of international importance, and includes 28 Sites of Special Scientific Interest (SSSIs). The

[41] STEMM stands for science, technology, engineering, mathematics and medicine.
[42] https://beisgovuk.citizenspace.com/strategy/industrial-strategy/supporting_documents/buildingourindustrialstrategygreenpaper.pdf
[43] NAO (2018) Delivering STEM (science, technology, engineering and mathematics) skills for the economy.

Broads are also a popular tourist attraction, with 15.5 million visitors a year who bring £568 million to the regional economy[44].

Formed from 12 Century peat diggings, the shallow networks of canals have become more saline due to rising sea levels. In turn this has led to golden algal blooms which produce toxins that suffocate fish. A healthy fish community is essential to maintaining a healthy wetland ecosystem that supports a quarter of Britain's rarest species, and an environment that is attractive to visitors. The Environment Agency and local angling clubs have, in the past, rescued affected fish, moving them to unaffected areas. A 2015 outbreak in Hickling Broad and Somerton cost the Environment Agency an estimated £40,000, not including volunteer time, but saved the fishery.

JIC has researched the science behind the problem and found that a virus infects the algae causing a toxin to be released which kills fish. Hydrogen peroxide was already known to be helpful in restoring the oxygen balance of affected waters. JIC conducted field trials with different levels of hydrogen peroxide to find the optimum management solution that could be implemented by the Environment Agency without harm to other organisms. JIC has also developed a hand-held diagnostic tool to test when the algae are present allowing early treatment and more effective management.

Tourism in Norfolk is worth £3.1bn to the economy and 47,500 jobs[45]. Around 35% of this impact is in countryside or coastal areas, the remainder being urban. This suggests around £1bn of spending related to assets such as the Broads where boating, angling and sightseeing are the main activities. JIC's work is improving the sustainability of the angling industry, in turn supporting the local tourism economy and saving the Environment Agency money.

4.7 Education and Training

JIC runs an extensive programme of training and engagement across the entire school and university spectrum aimed at inspiring and developing the next generation of scientists. This continuum of training has impacts from raising awareness or changing the perception of science as a career through to attracting young people into bioscience or helping them take the next step in their career.

A summary of training is set out below:

Schools

- **Youth STEMM Award** – see case study
- **Year 10 Science camp** - 2 weeks in the lab for 10-12 students

[44] http://www.nationalparks.gov.uk/students/whatisanationalpark/factsandfigures http://www.broads-authority.gov.uk/learning/facts-and-figures

[45] Destination Research (2017) Economic Impact of Tourism in Norfolk 2016

- **Women of the Future –** A one day event for 240, 14-15 year old girls, with a focus on those from lower socio-economic backgrounds
- **Nuffield Placement –** A summer placement for several weeks for up to 10 A-level students.

Undergraduates

- **International summer school** – A two month programme for UK/EU/International students who are strong candidates for a PhD to help inform their future decisions
- **Year in Industry students** – An opportunity for 4 Undergraduates to have a year long research project placement as part of their degree

Postgraduates

- **MSc Plant Genetics and Crop Improvement** – A joint project with UEA for 10-15 students with lectures at JIC as well as the carrying out of a research project
- **PhD** – There are more than 100 PhD students at JIC at any one time

Post doctoral

- **Training Workshops –** Three 2-week workshops for 20 people in the scientific community
- **Post Doctoral Researchers** – Over 150 Post doctoral researchers at any one time

JIC undertakes a considerable amount of staff training in computing, health and safety, leadership and management, post graduate specific training and professional development and wellbeing. Table 4.1 shows the number of different courses run, the number of courses delivered and the number of attendees. Contained in these figures are 5 different courses specifically for PhD students with a total of 65 participants.

Table 4.1 Staff Training at JIC

	No of different courses	No of courses delivered	No of Participants
Computing	12	53	251
Health and Safety	15	178	506
Leadership and Management	8	37	74
Post Graduate Training	8	14	147
Professional Development and wellbeing	29	141	474

In addition, JIC runs specific training in two areas; scientific and technical training and scientific computing with over 550 attendees.

Table 4.2 Scientific Training at JIC

	No of different courses	No of courses delivered	No of Participants
Scientific and Technical Training	15	37	333
Scientific Computing	12	21	228

The impacts of this training on UK productivity are assessed as part of the impact modelling of JIC.

5. Future areas of JIC impact

JIC's research is expected to lead to further impacts beyond those identified within the current assessment. A sample of six further research areas is set out below where research outcomes could lead to major societal and economic benefits in the future.

5.1 Wheat Yield

JIC has identified opportunities for further yield improvements based on changes to seed size and floret architecture. New genetic variation has been found with the potential to increase grain weight by 13%.

Separate research has identified a gene, TB1, that controls the shape and size of spikelets providing the potential to increase grain number. Increasing grain weight and number could have a substantial impact on yield over and above the forecasts made in the report.

5.2 Speed Breeding and Speed Cloning

The reduction in availability of effective plant protection products due to regulatory changes and development of resistance threatens the sustainability of crop production. In crops with complex genomes such as wheat, the speed at which genetic based resistance can be identified and the length of the breeding cycle act as bottlenecks for the development of resistant varieties.

Speed breeding uses controlled environment growth chambers to accelerate the growth cycle. In wheat the technology has already reduced the time from seed to seed from 18 weeks to 8 weeks.

Speed cloning, a genomics-based technology, has underpinned exponential growth in the discovery and cloning of disease resistance genes. Between 2003 and 2016, 14 genes were cloned by forward genetics. Since the development of RenSeq technologies in 2016 an additional 10 genes have been cloned. Plant breeders are already integrating the new resistances into commercial wheat varieties. JIC's work may increase the speed of adoption.

5.3 Insect and Virus Resistance

Aphids and other sap-sucking hemipteran insects cause substantial global crop losses, primarily via the transmission of plant viruses. Current control methods rely on chemical pesticides (neonicotinoids) that are being phased out in many parts of the world. Breeding insect-resistance into crops would offer an economically and environmentally attractive alternative. Genetic variation within a protein involved in the plant's immune response has recently been shown to confer aphid resistance and reduce viral-transmission in sugar beet.

The protein is conserved across a wide range of crop species and the resistance mechanism is also found across sap-sucking hemipteran insects (including whitefly and leafhoppers, as well as aphids). JIC's technology has the potential to create future insect and virus-resistant varieties in a wide range of important crop species.

5.4 Biofilm Disruption

More than 99% of bacteria live in biofilm communities where they are much more resistant to antibiotics/antimicrobials/biocides. This causes serious health concerns in several sectors (food, environmental & biomedical) with biofilms costing industry, cities and hospitals billions each year due to equipment damage, product contamination, energy losses and medical infections[46].

Advances in the understanding of genetic regulation in Pseudomonads bacteria is allowing the development of novel antibiotics that can disrupt and clear biofilms. These novel antibiotics have the potential to be highly transferable with applications for seed & crop pre-treatments, raw meat treatment, human and animal chronic bacterial infections, medical device coatings, wound care and industrial cleaning. JIC's research could lead to substantial benefits.

5.5 Carbohydrate Bioactives

Human milk oligosaccharides (HMOs) are known to protect breast-fed infants from a range of bacterial infections. HMOs act as decoys to infective bacteria with the first HMO recently being authorised as a novel food under EU law. Making HMOs available in sufficient volumes is a challenge. JIC is working on newly discovered enzymes to allow commercial scale production of HMOs and the development of non-natural variants. Recent studies suggest that a combination of HMO prebiotics with live microorganisms (probiotics) may confer health benefits with the potential of a new class of alternative antibiotics termed Synbiotics. These new Synbiotics could play a key role in reducing the neonatal deaths resulting from severe bacterial infections.

5.6 Hypertrans® Technology

JIC's Hypertrans® technology is cheaper and has lower infrastructure requirements than conventional pharmaceutical production systems making it ideal for vaccine production and therapeutic treatment for infectious diseases in developing countries for example, Sub-Saharan Africa.
The surface protein (known as glycoprotein) of many viruses is the main target of the immune system and an appropriate immune response directed against it can protect against infection. Whilst many proteins can be produced at high

[46] Romling et al (2014) Microbial biofilm formation: a need to act. The Association for the Publication of the Journal of Internal Medicine.

levels in plants, many glycoproteins are made inefficiently limiting vaccine production. The discovery of chaperones that circumvent this issue has created the opportunity to develop vaccines for Zika virus, Dengue virus, Chikungunya virus and Salmonid alphavirus. The technology is now being utilized to create vaccines for HIV and Rift Valley Fever. These vaccines and their production at low cost in Sub-Saharan Africa offers the potential for significant societal and economic impact.

6. Summary of Impacts

A summary of JIC's impact, based on the selected case studies, is set out below with assumptions set out in Appendix 1.

JIC is a major contributor to the **UK's Designing Future Wheat** programme as well as undertaking other extensive ongoing research in wheat. This work is estimated to contribute £100m GVA to the UK and £4.3bn to the rest of the world through improved wheat productivity over the next 25 years.

JIC's research in **high performance brassicas** could make a major contribution to UK production and help to reduce UK imports. Its work in reducing pod shatter and in improving oil content in **oilseed rape** is approaching the stage where the results can be adopted into commercial varieties. The combined impact of this research is an estimated £407m GVA to the UK and £1.3bn to the rest of the world over the next 25 years. Improving productivity of brassica crops will also encourage farmers to include such crops in rotations thus improving soil quality.

JIC's work in producing **healthier wheat and peas** comprising higher levels of dietary fibre has the potential to bring significant health benefits to consumers, estimated to result in health care costs savings equal to £9m GVA in the UK and £59m in the rest of the world over the next 25 years

Antibiotics is a long term research area for JIC generating many historic impacts. The latest developments include JIC spinout **Procarta Biosystems** which is developing a disruptive solution for antimicrobial resistance which represents a major global challenge. Procarta's treatment is 3 years from commercialisation and if adopted globally could reduce fatalities with an estimated health care cost saving equivalent to £129m GVA in the UK and £4bn in the rest of the world over the next 25 years.

JIC is developing systems for **novel plant production** of various chemicals. These include **Hypertrans® technology**, **QS-21 plant saponin and Vinca alkaloids**. These projects are at various stages of commercialisation but present a potential combined impact equivalent to £57m GVA for the UK and £4.4bn for the rest of the world over the next 25 years.

JIC's ongoing links with industry and the development of Norwich Research Park generate other economic benefits. Taking just one recent inward investment suggests an impact attributable to JIC of £12.6m GVA over the next 25 years.

Alongside the case studies an economic model has been developed to capture and estimate the impacts of JIC. This model assesses the actual and potential impacts of JIC using reasonable assumptions developed in consultation with JIC and industry.

All impacts are expressed as Gross Value Added (GVA) the Government's preferred method of economic activity.

A summary of the combined impacts is set out below over the next 10, 15 and 25 years at both UK and Global levels. The Return on Investment (RoI) of JIC's science is also estimated.

Two impact assessments have been undertaken, using different methods

- **Method 1**: An assessment of the impacts of a sample of research case studies, including a Return on Investment calculation (RoI) based on associated research grant and operating costs. This method is similar to that used in the previous report (2013) allowing comparison.
- **Method 2:** An assessment of the impacts of all research projects plus operational, training and visitor impacts, including a RoI based on all grant and operating costs[47]. This method will form the basis for a business case for JIC expansion.

Method 1 – Results

A total of eleven research/commercialisation case studies were reviewed - costing £21m (research grant plus 30% overheads).

These case studies are estimated to generate a total of £300m economic impact (GVA) in the UK economy over a 10-year period and £6.0bn GVA in the wider global economy. This represents a RoI of £14.22 for every £1 invested.

Table 6.1 Summary of JIC Impacts from the case studies

GVA impacts	NPV - 10 yrs
UK	£300,547,839
Rest of the world	£5,710,377,341
Total	£6,010,925,179

Attributable research costs	**NPV - 10 yrs**
Total	21,135,554

RoI (GVA leverage)	NPV - 10 yrs
UK research benefits divided by total research costs	14.22
Rest of the world research benefits divided by total research costs	270.18
Total research benefits divided by total research costs	284.40

The previous JIC impact report in 2013 identified £224m of GVA at the UK level over 10 years and a return on investment of £11.99 per £1 invested.

[47] Uses the latest figures and assumes JIC's income and expenditure remains stable over the period.

Method 2 - results

Appendix 2 shows the current BBSRC-funded research projects relevant to the case study areas. These account for £16.4m which is 22% of all current JIC research projects. This gives a scale up factor of 4.71 from the current project to the totality of JIC's current research.

JIC is estimated to generate a total of £1.8bn GVA at the UK level over the next 10 years, taking account of (a) operating impacts (b) education and training impacts (c) visitor spend and (d) the anticipated economic impact of the full portfolio of current research/commercialisation projects using the scale up factor above.

This represents a RoI (impact divided by total operating costs) of £4.25 per £1 invested over a 10-year period, rising to £7.10 per £1 invested, over a 25-year period (allowing for the maturing of impacts of a number of the research projects).

GVA impacts	NPV - 10 yrs	NPV - 15 yrs	NPV - 25 yrs
UK	1,847,434,408	3,451,899,803	6,108,251,211
Rest of the world	26,933,888,548	121,146,239,004	249,964,390,361
Total	28,781,322,956	124,598,138,806	256,072,641,572

Operational cost	NPV - 10 yrs	NPV - 15 yrs	NPV - 25 yrs
Direct costs	434,409,232	601,599,983	860,894,777

RoI - total benefits divided by total costs	NPV - 10 yrs	NPV - 15 yrs	NPV - 25 yrs
UK	4.25	5.74	7.10
Rest of the world	62.00	201.37	290.35
Total	66.25	207.11	297.45

The study also identifies six areas of research that could deliver additional future impacts over the longer term. On-going investment in JIC research will see these new areas feed through.

7. Appendix 1 Methodology

In order to measure impact, each area of JIC science was reviewed and routes to impact assessed. Eleven areas were chosen as case studies in consultation with JIC. The areas were chosen to give the best representation of current research effort, taking into account the 2013 impact report and giving a mix of existing and new research areas.

In each case, the impacts were assessed by modelling socio-economic outcomes of the research such as improved health, improved productivity, and reduced costs. Where relevant, such outcomes are quantified at the UK level, though much of JIC research has global application. Softer impacts such as academic, collaboration and human capital are also highlighted along with international impacts.

The report contains a mixture of actual and potential impacts, as some research has not yet fed through to final impacts. In all cases, best estimates have been used of actual and potential impacts based on available evidence with conservative estimates. The impacts reported in the case studies are gross. They are then reduced to net impacts by taking account of implementation costs required to achieve impact (by researchers and industry), what would have happened in the absence of the work (deadweight) and any activity which may be displaced. Displacement at the UK level is important to note. Where JIC has assisted an individual company leading to increased sales, it may simply displace other economic activity at the UK level. The company will have benefited but the UK will only benefit if imports can be displaced or there is some other value added.

Attribution of the results to JIC is calculated based on either its share of total project costs or its share of the research undertaken. This varies for each area.

Estimates of the rate of adoption of the research/technologies are also included so that net impacts are measured over a 10, 15 and 25 year period (base year 2018) by way of a net present value (NPV) and a discount rate of 3.5% in line with HM Treasury Green book. The 10, 15 and 25 year NPVs presented can be considered the net contribution to the UK economy. The value for money or return on investment for JIC's research can then be measured by dividing the net economic impacts by the research costs plus any other inputs. We have presented two methods for the RoI. The first method includes research impacts identified divided by the direct BBSRC research costs associated plus 30% overheads. This can be considered as the RoI for BBSRC grant investment and is comparable with previous reports. The second method compares the case study impacts, plus operating and training impacts with the full annual costs of running JIC over the appraisal period, based on the 2017 figures. The case study impacts are multiplied by a scale up factor based on the case study research costs as a proportion of total BBSRC research funding. Within the limitations of this exercise, this methodology provides a reasonable basis for estimating the totality of JIC impact. The first method might be considered to underestimate the total costs, while the second method may underestimate the total impacts. The different figures given may, therefore, be considered as a range for the RoI of JIC research.

8. Appendix 2 Case Study Assumptions

The following assumptions have been used to generate impacts in the model. These assumptions are based on consultations with JIC, industry consultees, market data and official sources. Where no information has been available, reasonable assumptions have been made by Brookdale. The economic model has been designed in accordance with HM Treasury Green Book and uses a discount rate of 3% except for health benefits which use 1.5%.

8.1 Wheat

Based on official data for UK and global wheat production (Defra and FAO).
Assume 0.5% productivity increase per year from year 1 to reflect JIC historic research.
Adopted by 30% of UK wheat production and 20% of global.
Periodic disease outbreaks e.g. yellow rust have 5% less impact than otherwise in years 10 and 17.
Disruptive productivity improvement implemented from year 10 giving a 20% uplift to the improved crop at the adoption rates above.
Any price changes of wheat are ignored.
Attribution of 30% to JIC.

8.2 High Performance Brassicas

Based on official data for broccoli and cauliflower production (Defra) and industry estimates of savings per ha. For indoor production, assume extra yield of £561 per ha and reduced harvesting costs of £2,808 per ha and reduced retail waste of 2.5% of farm gate price from year 4 building up from 500 to 2,000 hectares over 4 years. For field varieties, building up over years 7-10. For broccoli the mid-point of savings is used and for cauliflower, £1,120 plus £160 harvesting saving per hectare. Any price changes of product are ignored.
Attribution to JIC 50%.

8.3 Oilseed Rape – Pod shatter and UPL3

Based on official data from Defra, JIC estimates of pod shatter yield benefit (15%) and industry estimate of oil content benefit (11.25%) applied to latest UK price (£350) and production (2.167m tonnes) and equivalent data for EU from Eurostat and FAO (£315 per tonne over the past 5 years and 6.69m tonnes).
Adopted 100% due to the concentrated nature of OSR varieties.
Benefits from Year 5 building up over 4 years.
Any price changes of product are ignored.
Attribution of 50% to JIC.

8.4 Healthier Wheat and Peas

Based on the Canadian study referenced in the text for healthcare system savings per gramme of fibre increase. Type-2 diabetes and cardiovascular disease only.
Assume 8g out of the 12g deficit of fibre per day achieved in the UK and 4g per day EU.

Applied to UK and EU populations only assuming adoption into normal staple foods similar to cereal fortification. Benefits from Year 8 building up over 4 years. We assume that the technology is able to deliver two thirds of the increase in fibre needed from year 8, with a gradual build up in penetration over 4 years. Attribution of 50% to JIC.

8.5 Antibiotics
Based on Procarta Biosystems new disruptive treatment for CRE.
Using official DFT guidance for the value of preventing a fatality of £1.89m.
At the UK level assume 54 lives saved per year through the new treatment based on half of the 600 recorded cases (300) and the best outcome of 18% mortality (54 cases). Treatment costs are assumed not to change so not included in the model. UK benefits building up over years 4-7.
For the rest of the world the US number of cases are used at 50% of 9,414 and the same assumptions as the UK. The US figures are also used as a proxy for EU impacts based on similar population. Attribution to JIC 33%.

8.6 Vinca Alkaloids
Assume a successful plant production system can produce Vinblastine and Vincristine at a fraction of current costs. Production is limited by difficult extraction and is not environmentally sustainable. Typical extraction costs quoted per kg in the literature are assumed to reduce to 10% of current level. There are limited market data so assume Vincristine market is the same size as Vinblastine. Split the impacts pro rata UK/globally based on world population which gives 1% of impact to UK, 99% to the rest of the world. Estimated saving of £11.9m per year for the UK and £1.3bn globally if successful.
Applied from Year 6. Attribution to JIC 33%.

8.7 Hypertrans®
See case study for main assumptions. Attribution to UK on the basis of population size. Build up over years 3-6. Attribution to JIC 50%.

8.8 QS-21
Market size data of £592m from industry sources. Assume 10% market share achieved with build up from years 6-9. Benefits split pro rata between UK and rest of world on the basis of population size giving £2.96m per year UK and £56.2m per year rest of the world. Attribution to JIC 50%.

8.9 Tropic Biosciences
Taking anticipated jobs growth from Tropic and multiplying by GVA per head of £48k. After year 3 allowing a modest 5% growth in jobs. Attribution to JIC 20%.

8.10 ICENI Diagnostics
Market size data from industry estimates for 3 markets as set out in the case study. ICENI is targeting 10% of each. Benefits split pro rata between UK and rest of world on the basis of population size giving £266k per year UK and £5m per year rest of the world. Attribution to JIC 33%.

8.11 New Heritage Barley

Turnover data from NHB growing to £200k over 4 years converted to GVA. Attribution to JIC 100%.

8.12 Training

Modest salary uplifts are attached to the level of training in line with the UK literature on the impact of training on salaries. Salaries are then converted to GVA. Impacts tail off over 10 years.

9. Appendix 2 Research Costs

Relevant current BBSRC grants held by JIC give an indication of research costs per case study area and the basis for the scale up factor for Method 2. BBSRC accounts for around three quarters of JIC's total funding. BBSRC grant costs are therefore considered a reasonable proxy for direct research costs and the scale up factor. Note that JIC receives other grant funding. However, an overheads allowance of 30% has been added to the grant figure to allow for this.

Current wheat grants		
Understanding the genetics of abiotic stress tolerance in hexaploid wheat	Dr Simon Griffiths	73,932
Wheat Genomics for Sustainable Agriculture	Professor Michael Bevan	1,360,405
Production of wheat lacking B-type starch granules	Dr Cristobal Uauy	2,607
Engineering wheat for take-all resistance	Professor Anne Osbourn	806,167
13TSB_N4L2CRD: High Fibre Wheat for Healthier White Bread	Dr Simon Griffiths	60,048
A multi-R gene stack for durable resistance to wheat stem rust	Dr Brande Wulff	284,336
Eliminating Fusarium Head Blight susceptibility in wheat	Professor Paul Nicholson	95,042
Understanding the molecular control of senescence and nutrient remobilisation in wheat	Dr Philippa Borrill	298,912
Using field pathogenomics to study wheat yellow rust dispersal and population dynamics at a national and international scale	Dr Cristobal Uauy	168,321
Developing novel types of low protein wheat for breadmaking	Dr Simon Griffiths	161,811
Bilateral BBSRC-Embrapa: Exploiting natural and induced variation to increase Fusarium head blight and brusone resistance in wheat	Professor Paul Nicholson	712,330
15-IWYP: Molecular Dissection of Spike Yield Components in Wheat	Dr Cristobal Uauy	544,880
Exploiting novel sources of FHB and DON resistance for UK winter wheat	Professor Paul Nicholson	98,212

Using field pathogenomics to study wheat yellow rust dispersal and population dynamics at a national and international scale	Dr Diane Gail Owen Saunders	132,389
Utilising Illumina sequencing for high throughput genotyping of wheat	Professor Michael Bevan	198,877
Wheat Pan-genomics	Professor Michael Bevan	47,695
Characterisation of the low temperature tolerant locus (Ltp1) on wheat chromosome 5D	Professor Graham Moore	466,169
Current brassica grants		
Molecular analysis of the pleiotropic roles of the MADS-box gene FLC for development and yield in Brassica napus	Dr Judith Irwin	94,126
CIRC - Targeting subfunctions in Brassica ALCATRAZ genes to reduce seed loss in oilseed rape	Professor Lars Ostergaard	93,520
FACCE ERA-NET+: Securing yield stability of Brassica crops in changing climate conditions	Professor Lars Ostergaard	482,898
Exploiting seed coat properties to improve uniformity and resilience in Brassica seed vigour	Professor Steven Penfield	434,872
14 ERA-CAPS: Mechanistic Analysis of Quantitative Disease Resistance in Brassica by Associative Transcriptomics	Dr Christopher Ridout	466,516
Brassica Rapeseed And Vegetable Optimisation	Professor Lars Ostergaard	3,514,227
The ABC of fruit-shape formation in the Brassicaceae	Professor Lars Ostergaard	689,946
Australia: Promoting collaboration between JIC and EI (UK), SCU and CSIRO (Australia) in Brassica genomics and Brassica crop phenology	Dr Judith Irwin	23,732
Current starch grants		
14 ERA-CAPS. Designing starch - harnessing carbohydrate polymer synthesis in plants	Professor Rob Field	400,751
Elucidating the mechanism of starch granule initiation in developing wheat grains	Dr David Seung	304,886
Current antibiotic grants		

Biosynthetic Origins and Utility of the Natural Product Antibiotic Nybomycin			Professor Barrie Wilkinson	75,979
A Synthetic Biology Approach for the Total Biosynthesis of Semi-Synthetic Antibiotics			Professor Barrie Wilkinson	1,412,119
Identifying the biosynthetic origins of nybomycin, a reverse antibiotic			Professor Barrie Wilkinson	516,560
Plant production				
Engineering Quillaja saponin biosynthesis pathways for bio-production of QS-21			Professor Anne Osbourn	1,223,712
A pipeline for the discovery, sustainable production and commercial utilisation of known and novel highvalue triterpenes with new or superior biological activities			Professor Anne Osbourn	193,589
Synthetic Metabolism in Plants: Elucidating Vinblastine Biosynthesis and Implementing Strategies to Overproduce Complex Plant Metabolites			Professor Sarah O'Connor	191,670
Development of a commercially viable plant expression system for virus-like particle based vaccines			Professor George Lomonossoff	94,126
Total research costs				16,258,119
Add overheads			30%	4,877,436
Total costs				21,135,554