Written submission by the British Pharmacological Society to the *Leaving the EU* inquiry of the Science and Technology Committee, House of Commons.

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1. Background

1.1 The British Pharmacological Society (BPS) is a charity with a mission to promote and advance pharmacology. Founded in 1931, the Society now represents over 3,500 members working across academia, industry, regulatory agencies and the health services, many of whom are medically qualified. Clinical pharmacology is the only medical specialty in the NHS focusing on the safe, effective and cost-effective use of medicines. The Society supports good prescribing in the UK, most recently notably by developing the Prescribing Safety Assessment with the Medical Schools Council and key activities are:

- Promoting and advancing high quality science, especially pharmacology and clinical pharmacology
- Supporting students and academics in research, as well as the UK university system
- Supporting UK industrial pharmaceutical discovery and development, and underpinning the role pharmacology and clinical pharmacology has to play in that environment

1.2 Before and after the referendum, the Society has prioritised engaging our members about the UK's relationship with European Union (EU), particularly development of a summary of the areas in which exiting the EU could impact on pharmacology, with associated opportunities and risks for our members (www.bps.ac.uk/europe). The Society has also been active in representing and sharing its members' expertise in the development of new policy. For example, it co-funded the 2016 Parliamentary Links Day, an annual discussion in the House of Commons that connects parliamentarians with around 200 individuals from across the scientific community, which was entitled 'Science after the referendum: what next?'[1]. Furthermore, the Society was the largest sponsor (gold partner) of the European Congress of Pharmacology held at the end of June in Istanbul immediately after the referendum, in order to demonstrate our support for networking and scientific exchange between over 300 attendees from across Europe. The Society is also sending a lecturer and aiming to host a reception at the Slovakian Society of Clinical Pharmacology's annual meeting in October, which will coincide with the Slovakian Presidency of the EU.

1.3 This submission takes into consideration the Science and Technology Committee's original *Leaving the EU* inquiry as well as our understanding of risks and opportunities from the perspective of pharmacology and clinical pharmacology in response to the further call for evidence. We have followed the structure of the terms of reference, but have integrated

sections on the risks into the main body text. We have also addressed priorities for future Government negotiations with the EU.

1.4 The Society wholeheartedly supports the recent statement from the seven national academies[2], the Academy of Medical Sciences, the British Academy, the Royal Academy of Engineering, the Royal Society, the Learned Society of Wales, the Royal Society of Edinburgh and the Royal Irish Academy, urging the Government to make 'a bold public commitment' to retain the UK's world leading position in research and innovation, and in future negotiations we would like to see a Government focus on the following areas:

- Freedom of movement of researchers, scientists and students
- Access to collaborations and partnerships
- Access to funding and funding strategy
- The opportunity to improve connections with scientists on a global scale
- Legislation and regulation (see Table 1)

1.5 The Society also welcomes the reassurance from Chancellor Philip Hammond that the Government will "guarantee EU funding beyond the date the UK leaves the EU"[3].

What the effect of various models available for the UK's future relationships with the EU will be on UK science and research

People: collaboration and mobility

2.1 When examining the effects of the UK leaving the EU, the Society would recommend considering the value and impact of international collaboration in the current 'ecosystem' of scientific discovery.

2.2 The UK is undeniably an international leader in scientific research – punching well above its weight. The UK represents only 1% of the world's population, but produces 16% of the world's most highly-cited articles from only 4.1% of the world's researchers. These researchers are highly collaborative, and maintaining these international connections enhances the impact of their efforts. For example, scientific papers that are co-authored with international researchers have a greater citation impact than those articles that are not[4]. More than 60% of the UK's internationally co-authored papers are written alongside EU partners[5].

2.3 Countries displaying high levels of research collaboration characteristically have high levels of researcher mobility, both of which are associated with high research quality[4]. UK researchers are highly collaborative and mobile across the world[4]. In addition, EU funding mechanisms create opportunities for collaboration. By way of an example, the Marie Skłodowska-Curie Actions enable researchers, from PhD candidates to highly experienced

researchers, to work in various countries, sectors and disciplines across Europe[6]. The budget for this programme is €6.16 billion in the period up to 2020[6].

2.4 Elsewhere, it is currently possible to see other examples of pan-European collaboration and mobility in support of UK and EU scientific discovery:

- The UK Government provides student loans and maintenance funding for EU students as a statutory obligation[7]
- The university sector contributes over £73 billion annually to the UK economy[8]
- EU nationals make up 15% of the UK-based academic workforce and EU students make up 5% of students in the UK[5]
- At 21%, science disciplines have a higher proportion of EU staff in comparison with 13% across other subjects[7]
- In 2013/2014, EU government bodies funded 8.5% of UK academic staff on fixed-term contracts and other EU sources, 2.1%[8].

2.5 This close relationship with the EU can be seen in the British Pharmacological Society's own membership. Of the Society's 800+ members (which is around 20% of our total membership) based outside of the UK at the start of 2016, around 40% were based in EU countries, and of this group 5% were UK 'ex-pat' pharmacologists living and working in the EU. In addition, of the Society's members based in the UK, 10% are EU nationals.

2.6 Following the vote result, there has been an uncertainty over the implications of the referendum in a number of areas including the Society's own relationship with Europe. For example, immediately after the referendum, a Fellow of the British Pharmacological Society reported that members of the Federation of European Pharmacological Societies (EPHAR) expressed confusion about the future role and membership for the UK in EPHAR.

Risk 1	The UK's ability to recruit and retain its scientific workforce may be impaired.
Cause	• Uncertainty about migration policies following the referendum result • If newly negotiated policies do not support a mobile scientific workforce, the UK would be a less attractive place to work
Impact	• Shortage of skilled staff across all areas as well as in the university sector and pharmaceutical industry, reducing the UK's ability to be a world leader in science • Reduced mobility in the UK's scientific workforce, which would

	impact upon scientific collaborations
Evidence	There is a significant uncertainty about the future status of EU scientists in the UK due to the impact of potential restrictions, which could cause these skilled employees to leave the country. Consideration should be given to: • The impact of restrictions on mobility on all sectors, including non-academic staff in academia and pharmaceutical industry. • The power of uncertainty to affect people's decisions
Mitigation measures	The president of the Royal Society, Professor Sir Venkatraman Ramakrishnan has called on the Government to reassure all EU citizens that they will be able to stay and work in the country regardless of negotiation results[9]. Speaking at the Wellcome Trust, Jo Johnson MP has said that he cannot commit to a particular form of freedom of movement, but that it will be important that UK remains open to the brightest and best from the EU and around the world[9]. He had identified 'training and attracting world-class scientists and engineers' as a priority[10]. The Scottish Government and Universities Scotland has issued a statement making it clear that EU nationals are welcome at Scottish universities following the referendum and that the contribution of EU researchers to the country's excellent research as well as to its economy, society and culture is valued[11]. **Recommendation 1:** The Government must prioritise a review of its migration policy requirements in light of the scientific workforce requirements. Such a review should consider the potential advantages and disadvantages of different approaches ahead of negotiations with EU member states. **Recommendation 2:** The Government should specifically consider granting exemptions for students. **Recommendation 3:** The Government will need to review its migration policies, and should take this opportunity to develop policies that enhance global connectivity in science in addition to addressing the issue of EU migration.

Risk 2	A fall in the number of students coming to the UK, and a reduced student experience
Cause	• Perception that the UK is not welcoming, and is 'closed for business' • Potentially higher cost to EU students • Uncertainty over the future of the EU students' tuition fee loans and immigration status
Impact	• Diminished position of UK universities in the world and subsequent negative impact on the economy
Evidence	The university sector contributes over £73 billion annually to the UK economy[8]. There are concerns that the number of EU students enrolling in the UK universities could significantly drop given that the country is now 'rather insular and inward-looking'[12]. The UK could potentially be perceived as insular and inward-looking by the rest of the world affecting the numbers of students coming to the UK to study overall. In addition, categorising EU students as overseas students at higher fees may reduce the number of students coming to the UK and have a long-term negative impact on the university sector[7]. Lower numbers at a higher cost per student may or may not affect total revenue, but should be factored into calculations. The uncertainty over the EU students' access to tuition fee loans for 2017–18 as well as over their immigration status, both of which will depend on the outcome of negotiations with EU[13] may affect decisions about studying in the UK in the near future. There are also concerns that the UK may be excluded from the Erasmus Programme, which is an EU student exchange scheme. Switzerland was not allowed to participate in the programme after limiting freedom of movement[14]. This would impact on the student experience. Consideration should be given to: • Whether or not the UK will benefit from not having to provide

	students loans and maintenance funding for EU students. • Whether or not fewer EU students might register at UK universities, if categorised as overseas students at higher fees[7], and what the resultant impact might be on the university sector. • How leaving the EU will impact upon the university experience of UK students. For example, the potential loss of the Erasmus scheme, reduction in opportunities for joint degrees and placement opportunities for students.
Mitigation measures	According to the statement on higher education and research from Jo Johnson MP, Minister of State for Universities and Science, EU students who are studying in England and Wales and are eligible to receive loans and grants from Student Loans Company, will continue to do so for the duration of their courses or if they are about to start. The future funding arrangements will depend on the negotiations with the EU[15]. **Recommendation 4:** The Government should provide reassurances about the immigration status of EU students, clarification about EU students' access to tuition fee loans for 2017–18 and assurances that any changes to these will only apply to students who will come to the UK to study after it has left the EU[13]. **See Recommendation 2**

Risk 3	The potential loss of collaborations and partnerships. (See Risk 5 for the related potential loss of funding associated with collaborative research structures)
Cause	• Uncertainty about the terms under which the UK will be able to participate in collaborative research schemes, if at all • Potential restrictions on freedom of movement making flexible collaborative working more difficult
Impact	• Ideally, collaborations should be driven by alignments in research interests and expertise, not geography. Limitations on freedom of movement may reduce the scope of collaborations

	• Reduction in the number of partnerships and highly-cited research projects leading to the loss of UK's science and research excellence • Reduced access to collaborative research partnerships may also mean reduced UK influence on the direction of research • There is a positive opportunity to better define how the UK collaborates on a global scale. Negotiations regarding ensuring access to collaborations and partnerships should embed a review of how the UK may better manage its research relationships worldwide
Evidence	As early as 30 June, there have been concerns that British scientists are already at risk of exclusion from major European projects[16]. Recently, the UK academics report that EU partners pull out of partnerships whilst UK academics themselves are asked to leave EU-funded projects[17,18]. The Department for Business, Innovation and Skills invited researchers to send evidence of discrimination to the email address research@bis.gsi.gov.uk. On 13 July 2016, Jo Johnson MP, Minister of State for Universities, Science, Research and Innovation, said at the House of Commons that evidence on discrimination remains anecdotal and that he had invited universities to send 'concrete evidence'[19]. Consideration should be given to: • Whether or not there will be an impact on the number of partnerships and highly-cited research projects which are reliant on EU researcher mobility, especially where sustainable funding mechanisms have created opportunities for partnerships. • Whether or not researcher mobility and collaborations that might be built outside of the EU (for example with institutions and individuals in the US) would be enough to sustain and develop the UK research base, should there be a reduction in EU collaborations.
Mitigation measures	The Nobel Prize-winning Professor Sir Paul Nurse has said that reimbursing all the lost funds would not replace the international collaborations[20]. **Recommendation 5:** As mentioned earlier in this paper, more than 60% of the UK's internationally co-authored papers are written alongside EU

	partners[5]. The Government should prioritise retaining the UK's access to research collaborations and structures. R**ecommendation 6:** The Government should also prioritise reviewing the UK's access to collaborations and partnerships on a global scale. **Recommendation 7:** In placing collaborations and partnerships at the heart of its approach for science, the Government should take the opportunity to consider how the UK may lead and reward such collaborative ventures in the future.

Access to funding

3.1 In 2007–2013, the UK contributed €78 billion to the EU, of which €5.4 billion was indicated as being for the EU's Research and Development (R&D) budget. During the same period, the UK received €48 billion, of which €8.8 billion was for research, development and innovation[8]. In other words, the UK received €1 billion per year on average which approximated to 15% of the national science budget during the same period[21]. Overall, the UK won 16% of research funding from the recent European Framework Programme (FP7) with only 12.7% of the EU-28 population[22].

European Research Area and Horizon 2020

3.2 The European Commission launched the European Research Area (ERA) in 2000 to coordinate research and innovation activities in the EU. ERA initiatives are delivered through periodic framework programmes[7]. Meanwhile Horizon 2020 is the largest ever EU research programme, aiming to allocate €74.8 billion for research and innovation from 2014 to 2020[21]. The European Research Council allocates funding on behalf of Horizon 2020, and UK universities are expected to receive approximately £2 billion in the first two years of the programme[7].

Partnerships: Joint Programming Initiatives (JPIs)

3.3 JPIs are public-public research partnerships between ERA countries. Common research agendas are agreed by participating countries to implement jointly. There are currently ten JPIs and the UK participates in all of these joint programmes[23]. Two of these programmes have a pharmacological aspect:

- Alzheimer's and other Neurodegenerative Diseases
- Antimicrobial Resistance- The Microbial Challenge - An Emerging Threat to Human Health

3.4 In addition, one of the four programmes initially proposed under Horizon 2020 is linked to pharmacology:

- **European and Developing Countries Clinical Trials Partnership 2 (EDCTP2):** EDCTP is a partnership between 14 African and 14 European countries that aims to support "collaborative research that accelerates the clinical development of new or improved interventions to prevent or treat HIV/AIDS, tuberculosis, malaria and neglected infectious diseases in sub-Saharan Africa"[24]. The UK is one of the 14 European countries. The European Union will allocate up to €683 million for the 10-year programme (2014–2024), to be matched by contributions from the European Participating States.

Partnerships: Joint Technology Initiatives (JTIs)

3.5 JTIs are public-private research partnerships between industry and EU member states. The current JTIs are active in a number of areas of strategic importance for the EU[25]. The largest public-private initiative is linked to pharmacology:

- **Innovative Medicines Initiative 2 (IMI2):** IMI2 is a joint undertaking between the European Union and the European pharmaceutical industry represented by the European Federation of Pharmaceutical Industries and Associations (EFPIA). The partnership supports collaborative research projects and builds networks of industrial and academic experts in order to boost pharmaceutical innovation in Europe[26]. It has a €3.3 billion budget for the period of 2014–2024[27] (half of the budget comes from Horizon 2020, €1.425 billion committed by EFPIA companies and up to €213 million by other life science industries or organisations).

3.6 During the first phase of the programme (2008–2013), IMI1, there was a budget of €2 billion. Half of this came from the EU's Seventh Framework Programme for research (FP7), and half of which came from EFPIA companies. It currently has over 50 projects focusing on varying topics including broader challenges in drug development like drug and vaccine safety, knowledge management, the sustainability of chemical drug production, the use of stem cells for drug discovery, drug behaviour in the body, the creation of a European platform to discover novel medicines, and antimicrobial resistance[27]. For example, CHEM 21, a €26.4 million project, brings together six pharmaceutical companies, 13 universities and four small to medium enterprises (SMEs) from across Europe with the aim to develop sustainable biological and chemical alternatives to finite materials. The project is led by The University of Manchester and GlaxoSmithKline and includes Pfizer, the Universities of Durham, York and Leeds and UK-based small to medium enterprises among other European participants[28]. Another project K4DD (Kinetics for Drug Discovery) with a budget of about €21 million involves seven pharmaceutical companies, nine universities/research organisations/public bodies/non-profit groups and four SMEs, among which are

GlaxoSmithKline, the Universities of Dundee, Nottingham and Oxford, Imperial College Of Science, Technology & Medicine and Heptares Therapeutics of the UK[29].

Risk 4	Reduced financial security and stability of the Universities sector
Cause	• Uncertainty caused by the EU Referendum result.
Impact	• Diminished position of UK universities in the world and subsequent impact on the economy
Evidence	Reports suggest that the universities and other entities have been potentially losing income in various ways since the EU referendum: • **Loans and credits:** The European Investment Bank spokesman Richard Willis said that 'agreed loans are secure, but the fate of those that are just beginning to be considered is unclear'[30]. Eight British Universities, including universities of Leeds, Liverpool, Manchester, Cardiff, Keele and De Montfort, a number of which are Russell Group universities have had their credit status downgraded by ratings agency Moody's in the aftermath of EU referendum[31]. • **Pension fund:** There are concerns that the referendum results are likely to have worsened the £8.3 billion deficit in the university sector's main pension fund the Universities Superannuation Scheme[32]. • **Students:** If the concerns expressed earlier about the reduction in income from student fees becomes a reality, this will impact UK universities, but Scottish universities less so. Scotland provides free tuition to students from EU countries applying for undergraduate degrees at Scottish universities[13]. Audit Scotland released a report revealing that Scotland's higher education sector faces 'a number of significant challenges' being 'heavily reliant' on Scottish Government funding and increasingly reliant on income generated from fee-paying students from the rest of the UK and non-EU students[33]. Caroline Gardner, Auditor General for Scotland has said that the Scottish Government 'must be clear about its priorities for higher education'[34].
Mitigation measures	**Recommendation 8:** The Government should ensure clear messaging about negotiation priorities and successes to reduce uncertainty. A commitment by Government to engaging stakeholders to set negotiation

	priorities – and concerted communications with these groups through media and other channels – would offer reassurance and reduce uncertainty in preparation for and during negotiations. Openness and transparency about both wins and losses arising from these negotiations will also be important.

Risk 5	The potential loss of research income.
Cause	• Uncertainty about whether the UK is eligible to access EU funded projects to pre-referendum levels • Uncertainty about whether the UK Government will make up any shortfall in research funding • Uncertainty over the effect, of supporting a shortfall in research funding from the EU, on the level of response mode RCUK funding.
Impact	• Diminished position of UK universities in the world and subsequent impact on the economy • Reduced access to collaborative research funds and partnerships may also mean reduced UK influence on the direction of research
Evidence	In a negotiated model, it is uncertain whether the UK would be able to retain its contribution to the broad funding strategy that drives Horizon 2020. The German Chancellor Angela Merkel has said that a country wanting to leave the EU 'cannot expect to shed all its responsibilities but keep the privileges'[35]. The Russell Group has issued an EU referendum statement noting that leaving the EU will have a profound effect on the Russell Group universities and that they are already working closely with the Government for the 'best possible outcome' from negotiations over leaving the EU[36]. The 24 Russell Group universities, a number of which teach pharmacology, receive around £400 million of EU funding a year, which makes about 11% of their research income[7]. The chancellor of the University of Oxford, Lord Chris Patten has said that the research income of the university will fall significantly after leaving the EU unless the Government guarantees to cover the deficit[18]. The vice-chancellor of the University of Cambridge, Professor Sir Leszek Borysiewicz has said the

	17% of the University's research income comes from the EU[37]. In a confidential survey of the Russell Group universities, the Guardian revealed the cases of UK academics being asked to leave EU-funded projects or to step down from leadership roles immediately after the referendum as a financial liability in EU bids. It revealed that researchers across natural sciences as well as the engineering disciplines and social sciences are all affected[18]. Losing access to EU research funding may affect not only these but a number of other universities, organisations and bodies receiving EU research funding. It seems uncertain as to whether the UK will be able to stay in the ERA or retain its association with Horizon 2020 and influence the direction or focus of future programmes. Consideration should be given to: • Whether or not UK would be able to continue taking part in joint initiatives. The level of impact from leaving the EU would be different for various projects and programmes in which the UK currently participates or leads. Some projects, e.g. CHEM21 led by The University of Manchester and the GlaxoSmithKline, could be significantly affected. Since 2014, Swiss participants are no longer eligible for research funding from the EU and are funded by the Swiss Secretariat for Education, Research and Innovation (SERI). In addition, the Federal Council directly supports those who have been excluded from research cooperation[38].
Mitigation measures	In order to maintain access to the EU funding stream the UK will need to negotiate an agreement similar to those of other non-EU countries with access to Horizon 2020. In other words, it could become an 'associated country' which would mean paying GDP membership fee to join the stream. This would need to be negotiated carefully and the UK's terms would be different from those of other countries associated to Horizon 2020: Switzerland, for example, is only a partially associated country, with limited access to funding, let alone to setting strategic priorities, due to its restrictions on free movement[39]. The UK's situation is unique as no other country has ever left the EU[39]. The General Secretary of University College and Union Sally Hunt has urged the Government to provide assurances of support for the further and higher education sectors[40]. As seven UK academies urged the

	Government in a joint statement mentioned earlier, it is important to seek 'the closest achievable association with the EU research programmes'[2]. The Society welcomes the reassurance from Chancellor Philip Hammond that the Government will "guarantee EU funding beyond the date the UK leaves the EU"[3]. **Recommendation 9:** If unable to retain access to Horizon 2020, the Government would need to consider continuing to match lost research income (which approximated to 15% of the national science budget during the period of 2007-2013) in order to sustain science funding at current levels, and to remain competitive with the European counterparts[21]. Similar to Switzerland, it will be important to support those who have been excluded from research cooperation. **Recommendation 10:** The Government should commit to long-term and stable backing for the sciences, in order to ensure continued benefits to the UK economy and its global leadership. **Recommendation 11:** The Government could consider how it may work with UKRI to identify and implement new funding streams and partnerships. **Also see recommendations 5, 6 and 7.**

Access to infrastructure

European Medicines Agency (EMA)

4.1 Located in London, the EMA is responsible for the scientific evaluation, supervision and safety monitoring of medicines developed by pharmaceutical companies for use in the EU (since 1995)[41]. It is the largest EU body in the United Kingdom with a full-time staff of more than 600 people. British experts were leaders or co-leaders in examining 27 new drug applications in 2014[42]. The EMA ensures a 'centralised authorisation procedure' allowing a single marketing authorisation application to make a medicine available to all EU member states and the European Economic Area (EEA) countries Iceland, Liechtenstein and Norway[43]. The UK's Medicines and Healthcare Products Regulatory Agency (MHRA) works closely to support the EMA, for example it[44]:

- led a third of all EU-wide safety reviews since legislation was introduced in 2012
- was a rapporteur or co-rapporteur in 20 centralised procedures that led to granting of a Marketing Authorisation
- was appointed Reference Member States (RMS) in 43% of procedures where a UK licence was sought
- held 319 regulatory or advisory meetings to help applicants
- helped shape regulation and approvals through 96 European Scientific Advice meetings

The level of work undertaken on behalf of the EMA is considerable, representing 6.4% of total gross income in 2015/6[44]. This indicates that loss of MHRA expertise would put a considerable burden on EMA processes. This influence is expanded upon in the House of Commons Science and Technology Committee report "EU regulation of the life sciences"[45], where evidence from the Bioindustry Association stated that "the MHRA has been able to exploit its reputation, leadership and expertise to positively influence the EU medicines regulatory regime."[46] The report also discusses several instances of how MHRA has influenced EU regulation, for example Clinical Trials Regulation and Pharmacovigilance legislation.

The Unified Patent Court (UPC)

4.2 The agreement to create a unified patent court was signed by 25 EU Member States on 19 February 2013[47]. According to the agreement, the UPC will comprise of Court of First Instance, a Court of Appeal and a Registry. The Court of First Instance will be composed of a central division in Paris with two sections in London and Munich and local and regional divisions. The London section will be responsible for "Human necessities" and "Chemistry, metallurgy"[48]. There is a concern that the section of the Unified Patent Court will have to relocate from London before it even opens[42].

The European Strategy Forum on Research Infrastructures (ESFRI)

4.3 The ESFRI is a multi-disciplinary forum to support a coherent and strategy-led approach to policy-making on Research Infrastructure (RIs) in Europe and to facilitate initiatives leading to the better use and development of RIs[49]. All EU Member States are represented by two delegates on ESFRI including a number of Associated Nations. The current Chair of ESFRI is Professor John Womersley, the Chief Executive of the UK's Science and Technology Facilities Council[50]. The following landmarks that are pharmacology-relevant (health and food section) were identified in ESFRI Strategy Report on RIs (2016):

- **BBMRI ERIC** - Biobanking and BioMolecular resources Research Infrastructure
- **EATRIS ERIC** - European Advanced Translational Research Infrastructure in Medicine
- **ECRIN ERIC** - European Clinical Research Infrastructure Network

- **ELIXIR** - A distributed infrastructure for life-science information
- **INFRAFRONTIER** - European Research Infrastructure for the generation, phenotyping, archiving and distribution of mouse disease models
- **INSTRUCT** - Integrated Structural Biology Infrastructure

4.4 The UK takes part in BBMRI ERIC and INFRAFRONTIER and hosts the headquarters of ELIXIR (Hinxton) and INSTRUCT (Oxford). In addition, the UK hosts the headquarters of the Infrastructure for Systems Biology Europe (ISBE), the ESFRI Project in London (Imperial College London)[51]. As for ESFRI itself, which was setup as an informal forum in 2002[51], Norway and Switzerland participate in the forum and host the headquarters of projects. Given that, the UK is also likely to be able to continue its participation.

Risk 6	Disruption and uncertainty from the risk of relocation for the European Medicines Agency (EMA)
Cause	• The jurisdiction of the EMA covers EU member states and the EEA. The UK's vote to leave the EU, and doubt over its membership of the EEA, has led to relocation offers from countries served by the EMA that are looking to be its new home.
Impact	• Disruption to the pharmaceutical industry • Loss of employment or relocation for the UK staff of EMA • Diminished reputation for the UK as a leader in medicines evaluation and assessment
Evidence	The risk of the EMA office relocating to another country is based on expressions of interest from Sweden, Italy, Denmark, Ireland, Spain and Germany in housing the EMA as a major boost for each country's entire life sciences field [52,53,54,55]. EMA released a statement noting that 'the implications for the seat and operations of EMA depend on the future relationship between the UK and the EU' and that the decision on the seat of the agency will be decided by common agreement among member state representatives[56]. The European Federation of Pharmaceutical Industries and Associations (EFPIA) released a statement warning that 'ensuring that Brexit does not negatively impact the regulatory capacity, processes and time-frames for the introduction of new medicines must be a priority'.[57] Richard

	Bergström, head of EFPIA, has said that relocating the EMA might be risky because a large number of UK employees with institutional knowledge might opt to leave the organisation if it relocated[53]. Eduardo Sanchiz, the chief executive of Spanish pharmaceutical company Almirall has said that a scenario in which the EMA relocated is associated with 'a very large disruption' and its impact on the approval process of new pharmaceuticals is worrying[58]. GlaxoSmithKline's chief executive Sir Andrew Witty also warned of the 'physical disruption' if the EMA relocates from the UK and doubled regulatory burden if the country creates its own regulatory body[59].
Mitigation measures	**Recommendation 12:** Serious consideration should be given to negotiating the retention of EMA headquarters in London.

Risk 7	The UK does not stay part of the EMA, and is required to significantly develop its own regulatory system
Cause	• Marketing authorisations approved by the EMA apply to EU member states and members of the EEA. The UK will no longer be an EU member state, and may not remain a member of the EEA.
Impact	• Loss of UK input in EMA evaluation processes, leading to reduced regulatory capacity of EMA and loss of UK expertise. • Reduced or slower access to medicines while alternative arrangements are established • Increased costs and regulatory burden for pharmaceutical companies wishing to access the UK market if separate authorisation procedures are required
Evidence	The UK could have a lesser priority in launch sequences of pharmaceutical companies if they were required to seek separate approvals in the UK[60]. The UK could continue its relationship with EMA to benefit from centralised marketing authorisations if the country stays part of the EEA, as is true for Iceland, Lichtenstein and Norway. Also, Switzerland, whilst not part of the

	EEA, is part of the European Free Trade Association (EFTA) and has a separate drug approval process[61] and mutual recognition agreements with the EMA[62]. In the absence of creative solutions to cooperating with the EMA, pharmaceutical companies will need to apply for marketing authorisations separately to the MHRA for every medicine they would like to supply in the UK[7]. This would add considerable regulatory and cost burdens to pharmaceutical companies wishing to access the UK market. MHRA released a statement noting that it continues to play an active role in European regulatory procedures 'contributing significantly in both the centralised and decentralised regulatory procedures'[63].
Mitigation measures	A ministerial working/steering group bringing together the chief executive officers of pharmaceutical companies and Government officials was launched on 6 July 2016 to advise the Government on the main priorities for the life sciences sector. The group was going to be co-chaired by Sir Andrew Witty, chief executive of GlaxoSmithKline, Pascal Soriot, chief executive of AstraZeneca and life sciences minister George Freeman MP[64] and was set to provide recommendations on forming a new relationship with the EU to the Ministerial Industry Strategy Group in September 2016. George Freeman MP was later appointed to another role[65]. Lord Prior now has this brief[66]. **Recommendation 13:** It is essential that the UK prioritises the harmonisation of regulatory processes with the EMA. Should the UK not remain part of the EEA, the Government should seek creative solutions to cooperation. It is both a priority for the UK's industrial strategy and a matter of public health that the interests and concerns of the pharmaceutical industry and patients are taken into consideration.

What the science and research priorities for the UK government should be in negotiating a new relationship with EU

5.1 The UK plays a leading role in the decision-making processes on science and research and has often played a key role in the development of EU policies. If the UK becomes an Associated Country its influence and position in defining **strategic priorities for science, research and funding** would be diminished[67]. Although it would be highly unlikely to retain

such an influential position under the circumstances, the UK would benefit from keeping at least some of its influence in the new relationship with EU.

5.2 Evidence suggests that the provision of **networks and opportunities of collaborations** is one of the most significant benefits and elements of the UK's EU membership. The extent of this provision is rather difficult to measure but can be roughly identified in three main ways:

- Collaborative funding programmes
- Researcher mobility
- Participation in shared research infrastructures[67]

5.3 The continuation of this provision should be a science and research priority for the UK Government. The importance of this matter had been outlined by a number of organisations and individuals including the seven UK academies, the Academy of Medical Sciences, the British Academy, the Royal Academy of Engineering, the Royal Society, the Learned Society of Wales, the Royal Society of Edinburgh and the Royal Irish Academy, that have issued a joint statement warning that the result of the EU referendum presents a challenge to maintaining the UK's research and innovation excellence. The academies urged the Government to 'safeguard the UK's assets in research, scholarship and innovation by

- seeking the closest achievable association with the EU research programmes;
- ensuring that talented researchers from other EU countries have certainty about the opportunities to work in the UK and likewise for UK researchers to work in other EU countries; and
- providing funding that will continue to promote international collaboration'[2].

5.4 It is crucial that new policies that govern the **movement of scientists** coming to the UK and UK nationals working overseas does not impact upon the quality of UK science[67]. At the moment, the uncertainty over the future status of not only researchers but other skilled employees could cause them to leave the country. The joint statement mentioned earlier also urged the Government to reassure the EU researchers and staff based in the UK about their future immigration status.

5.5 It is vital that the Government minimises the impact of Brexit on important contributors to the economy, namely the **university sector and pharmaceutical industry**. This will need to involve a number of measures before and after the negotiations for a new relationship with EU. The risk tables presented throughout this submission identifies the risks associated with each science and research priority.

5.6 The Government should also prioritise working closely with scientific institutions and organisations in order to support the communication of **clear messaging** to the community.

What science and technology-related legislation, regulations and projects will need to be reviewed in the run up to the UK leaving the EU

6.1 The UK is subject to EU legislation that has an impact on a range of pharmacology-relevant areas, e.g. pharmaceuticals, the working hours of doctors, clinical trials directive, directive 2010/63/EU on the protection of animals used for scientific purposes, and others. In return, the UK contributes to wider EU law in a variety of ways. For example, the Academy of Medical Sciences contributed to and led pan-European statements on research regulation and EU Research and Innovation strategy, and recently the Clinical Trials and Data Protection Regulations[68]. MHRA is a leading contributor to EU law and is respected internationally as one of the leading regulatory authorities for medicines and medical devices[69].

Table 1: Some regulations related to pharmacology and clinical pharmacology

No	Directive
1.	Clinical trials directive 2001/20/EC
2.	Working time directive 2003/88/EC
3.	Protection of animals used for scientific purposes 2010/63/EU
4.	Protection of personal data directive 95/46/EC
5.	Pharmaceuticals, e.g. 65/65/EEC1 75/318/EEC 75/319/EEC 93/41/EEC 2001/20/EC 2001/83/EC

	2005/28/EC

Clinical Trials Regulation

6.2 All clinical trials implemented in the EU are required to be conducted in accordance with the Clinical Trials Directive 2001/20/EC until the new Clinical Trials Regulation (CTR) EU No 536/2014 becomes applicable some time after 28 May 2016. The UK had played a significant role in influencing the improvements to the clinical trials regulation[67]. The EMA was commissioned to establish an EU portal and database as a single entry point for submission of data and information relating to clinical trials required by the Regulation[70]. The House of Lords' Science and Technology Select Committee's report "EU membership and UK Science"[67] notes that clinical trials regulations were "highlighted as causing UK business and research to be disadvantaged compared to competitors outside the EU" by the UK science community. However, the development of the new clinical trials regulation is seen as a considerable improvement.

Directive 2010/63/EU on the Protection of Animals Used for Scientific Purposes

6.3 Directive 2010/63/EU governs animal research in the EU. Revising the earlier Directive 86/609/EEC, it was adopted on 22 September 2010 and is based on the principle of the three Rs, to replace, reduce and refine the use of animals used for research[71]. Article 2 of the Directive outlines that member states can maintain stricter provisions aimed at ensuring more extensive protection of animals which were in force on 9 November 2010[72]. Recently, the European Commission had started an infringement process against Italy concerning the overly stringent transposition of the Directive, as stricter provisions were not in force in the country before this date[73]. In the UK, revised legislation transposing the new Directive came into force on 1 January 2013[74]. The House of Lords' Science and Technology Select Committee's report "EU membership and UK Science" highlights the UK's involvement in the development of the framework.

Risk 8	The burden of untangling UK legislation and regulation from that of the EU
Cause	• There is deep integration between UK and EU legislation and regulation
Impact	• Decline of UK science through changes to working regulations or

	retaining various controversial regulations • Resources may need to be diverted from other important work • Loss of UK expertise in shaping EU regulation
Evidence	Concerns have been expressed among unnamed senior civil servants about 'untangling 40 years of EU legislation' and 'deciding on what to keep, amend and reject'[75]. It was reported that the process could create 'constitutional mayhem' given that EU laws were incorporated into the devolution statutes in Scotland, Wales and Northern Ireland[76]. The process may lead to an oversight or neglect of legislation crucial for science to thrive but could equally present an opportunity to move away from some controversial EU directives. Before the referendum, concerns had been expressed about the 'apparent trend towards the development of over-arching EU regulations'. The detrimental effect of some regulations on UK and EU science had also been reported[67]. Consideration should be given to: • Priority legislation that requires immediate review and is crucial to the future of science in the UK
Mitigation measures	It would be helpful to develop a timeline for reviewing all the EU legislation before starting the process providing as much time as the process requires even if it would mean decades. It would also be useful to approach certain controversial legislation, such as clinical trials regulation, separately. **Recommendation 14:** The Government should work closely with the relevant sectors to identify the regulation that will be affected, and to understand its intricacies. It will be important to be clear about where synergy and mutual recognition is necessary, and where there are opportunities to create better UK frameworks.

The status of researchers, scientists and students working and studying in the UK when the UK leaves the EU, and what protections should be put in place for them

7.1 Please see 'People: collaboration and mobility' (2.1-2.6), and Risk 1 and 2.

The opportunities that the UK's exit presents for research collaboration and market access with non-EU countries, and how these might compare with existing EU arrangements

8.1 As noted earlier, it is important to retain collaborations and partnerships stemming from the EU membership which also extended to non-EU and non-European countries[67]. The collaborative relationship with the rest of the world can be seen in the Society's reciprocal membership arrangements with countries like United States of America and Australia. There is an opportunity to revise migration policy and systems in a way that enhances global relationships.

What other measures the Government should undertake to keep UK science and research on a sound footing, with sufficient funding, after an EU exit.

9.1 The Government should **prioritise UK leadership and influence** through strong domestic policies that invest in science. Evidence indicates that public investment in science contributes to the economic growth through leveraging private sector investment and productivity, as well as encouraging quality science through opportunities for collaboration[77].

Risk 9	Pharmaceutical companies reduce their level of investment in the UK
Cause	• The UK is a major draw for the pharmaceutical industry. This is due to expertise in the MHRA, the strength of the research base, skilled workforce and universities sector, and because it offers a supportive environment for spin-outs and the biotech industry including incentives such as the Patent Box. Any change in this reality, or perception of it, may trigger reduced investment in the UK.
Impact	• Loss of contribution to the UK economy by pharmaceutical companies • Reduced capacity for innovative cross-sector research and development
Evidence	The pharmaceutical industry accounts for 20% of total expenditure on R&D implemented in UK businesses[78]. The sector brings a trade surplus of £3 billion per year[79] but it is safe to say there is some risk to the maintenance of that surplus. As previously discussed, the pharmaceutical

	labour force might be affected by restrictions on mobility, and participation of pharmaceutical companies, particularly small to medium enterprises in EU programmes, e.g. IMI2 would be restricted. In addition, the UK's access to the Small and Medium-sized Enterprises (SME) Instrument – a mechanism that allows EU to support growing businesses – is under question. The budget for the SME Instrument for 2014–2020 is €3 billion (4% of Horizon 2020)[50]. It should, however, be also noted that concerns had been expressed about the participation of large UK businesses in recent European Framework Programme 7 which lagged behind of key competitor nations such as Germany and France and was below the EU average[67]. HM Treasury has flagged that the benefits of the single market including access to wider market for pharmaceutical companies and their products would be at risk in the event of Brexit[80]. However, early signs are that companies are not committing to relocation, given what is seen as a strong UK offering. For example, GlaxoSmithKline recently invested £275 million in three British manufacturing sites[59], indicating that there is an opportunity for the UK to maintain and strengthen its assets. GlaxoSmithKline representative has said that they do not 'currently anticipate a material adverse impact on the business, the group's results or financial position'[81]. Sir Andrew Witty also said that about 14% of the company's staff in the UK are from other European countries and that "they are super welcome at GSK and in the UK"[59]. However, some top EU executives working in the UK are already looking for opportunities elsewhere whilst rumours of EU pharma executives declining offers of employment in the UK are circulating[82].
Mitigation measures	A ministerial working/steering group bringing together the chief executive officers of pharmaceutical companies and Government officials was launched on 6 July 2016 to advise the Government on the main priorities for the life sciences sector. The group was going to be co-chaired by Sir Andrew Witty, chief executive of GlaxoSmithKline, Pascal Soriot, chief executive of AstraZeneca and life sciences minister George Freeman MP and was set to provide recommendations on forming a new relationship with the EU to the Ministerial Industry Strategy Group in September 2016[64]. George Freeman MP was later appointed to another role which raised questions on if and how the Government will address the concerns of the UK's life-sciences industry[65]. Lord Prior now has this brief[66].

	Recommendation 15: The UK must prioritise maintaining its leadership in science and innovation. It is important to ensure that the UK remains attractive to not only the pharmaceutical industry but to other science-related industries. This could potentially involve legislation or tax incentives as part of a broad UK industrial strategy and commitment to domestic funding measures.

Mutually reinforcing or mutually exclusive risks and opportunities

10.1 The preceding sections identified nine risks presented throughout the document from the pharmacology and clinical pharmacology perspective. Many of these stem from the uncertainty that followed the referendum result. The Society believes the following risks are mutually reinforcing or mutually exclusive:

- The continuing uncertainty over the immigration status of scientists, researchers and students will reinforce the departure of skilled employees from the UK (Risk 1), the decline in the number of students coming to the UK to study (Risk 2), the loss of collaborations and partnerships (Risk 3) and potentially the loss of research income (Risk 5).
- In Risk 2, the decline in the number of students coming to the UK to study could potentially turn into an opportunity for universities and non-EU students because of the higher overseas fees.
- If the UK does not continue its relationship with the EMA (Risk 7), this may reinforce other risks such as the potential loss of contributions to the economy by the life-sciences industry (Risk 9).
- The regulatory burden (Risk 8) could also be an opportunity to improve upon the current provision offered by EU directives.

10.2 Science is a collaborative venture. Overall, the sum of many of these risks is to hinder the formation of such collaborations and access to the funding, infrastructure and workforce required to support them. The Society believes that by focusing on achieving a post-EU environment that is conducive to building global collaborations there is an opportunity for the Government to ensure the UK continues to be a world leader.

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