Cancer Research UK – Written evidence (EEH0014)

Please indicate which of the following industries or policy areas are you responding in relation to: energy, environment, health, food trade, agriculture, fishing, climate change, chemicals.

1. Cancer Research UK (CRUK) welcomes the opportunity to respond to this timely and important inquiry. We are submitting evidence on the EU-UK Trade and Cooperation Agreement's (TCA's) implications for health (including health research).

What is your assessment of the relevant provisions in the UK-EU Trade and Cooperation Agreement, and their impact on your business or policy area?

2. Overall, we see the TCA as a first step in developing a fuller, long-term relationship between the UK and EU. We particularly welcome the TCA's commitment to UK-EU collaboration in the promotion of public health[1] and support efforts to develop this collaboration further.

3. We're encouraged that the TCA includes arrangements that reduce uncertainty and lay the foundation for continued collaboration with the EU in life-saving cancer research, including:

    a. Provisions for continued UK-EU data transfers until a data adequacy status decision is made;[2]

    b. Confirmation of the UK's participation in Horizon Europe;[3] and

    c. UK-EU regulatory cooperation via the Working Group on Medicinal Products.[4]

4. However, several key barriers to UK-EU collaborative research remain unaddressed because the TCA does not feature Mutual Recognition Agreements (MRAs) for clinical trial Sponsors or medicine batch testing and QP certification.[*] Although we welcome the UK Government's moves to minimise disruption in these areas, longer-term solutions must be negotiated with the EU.

What do those provisions achieve?

5. International collaboration is a critical part of CRUK's work to improve survival rates for people with cancer. Nearly 50% of all UK cancer research is global[5] and 28% of CRUK trials take place with at least one EU Member State.[6]

[*] Batch testing and QP certification are processes used to monitor the safety of medicines after they're manufactured. For further detail, please see paragraph 8 (overleaf).

6. Patients value this international collaboration. 99% of people affected by cancer we surveyed believe the UK and EU should negotiate a relationship that allows cross-border trials to operate as easily as they did during the Transition Period.[7] The new relationship partially delivers this:

    a. UK-EU personal data exchanges will continue for up to six months, in order to give the EU time to grant the UK data adequacy status.[8] These data transfers are essential for running UK-EU clinical trials, as they need to routinely send patient data and test results across international borders.
    b. The UK has agreed to participate in the EU's research programme, Horizon Europe.[9] This programme will be worth €95.5 billion (£84.1 billion) of research funding between 2021-2027[10] and includes a 'cancer mission' designed to fund research into cancer prevention, diagnosis and treatment.

    c. The UK has unilaterally agreed to recognise EU/EEA Sponsors of clinical trials,[11] meaning UK researchers will face minimal legal and administrative barriers when participating in EU-led clinical trials. This is especially valuable for UK-EU collaborative research into rare and childhood cancers, as individual countries often lack the patient numbers needed to run these trials on their own and must therefore recruit people across multiple countries.

7. These three provisions significantly reduce some of the uncertainty around UK-EU research. Continuity of UK-EU data transfers and UK recognition of EU/EEA Sponsors are particularly vital, as without these, UK-based researchers' and patients' participation in EU-led clinical trials would have been severely disrupted after the Transition Period ended.

8. Every month, 37 million packs of medicine move from the EU to the UK, and 45 million from the UK to the EU.[12] This trade is underpinned by batch testing of medicines when they're manufactured, which is then certified by a Qualified Person (QP) to confirm compliance with safety standards. In the EU, these standards are set by the European Medicines Agency (EMA) and enforced nationally by EU Member State regulators,

9. With the UK now outside the EU regulatory framework, the UK's Medicines and Healthcare products Regulatory Agency (MHRA) will no longer automatically share these standards with the EMA. Instead, the TCA's provisions replace some of this framework in order to facilitate access to medicines on both sides of the border:

    a. The UK will unilaterally recognise EU batch testing and QP certification for a 2-year period, meaning EU medicines imported into the UK will not need to be retested.[13] This minimises the risk of disruption to the UK's supply of medicines (including those used in clinical trials).

b. The UK and EU will recognise each other's inspections of manufacturing facilities, meaning the MHRA and EMA will not need to re-inspect manufacturers on the other side of the border.[14]

c. A Working Group on Medicinal Products will facilitate UK-EU regulatory cooperation and work to minimise the risk of regulatory divergence between the MHRA and EMA.[15] This Working Group can also act as a forum for discussing future MRAs.

10. We welcome the MHRA's decision to recognise EU batch testing and QP certification for 2 years. Without this, UK patients would have faced significant delays in their access to medicines due to the administrative burden of duplicate testing on import. We are also encouraged that the TCA's provisions outline a path to further cooperation between the MHRA and EMA, such as through negotiation of MRAs for batch testing and QP certification.

What, if any, challenges arise because of those provisions? How could these challenges be resolved?

11. Whilst the TCA and relevant UK Government decisions do establish some of the conditions needed for full UK-EU collaboration in cancer research, several obstacles remain unaddressed:

    a. Although the UK Government has unilaterally decided to recognise EU Sponsors of clinical trials, the EU has not reciprocated this measure, meaning UK Sponsors of clinical trials operating in the EU/EEA now need EU-based legal representation.[16]

        i. Evidence from our research community shows that EU-based legal representation for multi-state trials can cost between £20,000 to £300,000 per year.[17] This would be prohibitively expensive for many non-commercial Sponsors (e.g. universities). Cancer research is particularly vulnerable to these costs, as approximately 40% of all UK cancer trials have non-commercial Sponsors.[18]

        ii. In the long run, these legal costs like these could make it harder for UK-based researchers to lead pan-European clinical trials, which would undermine the UK's reputation as a world leader in cancer research[19] and risks reducing UK patients' access to research. This would be particularly damaging to disease areas reliant on joint UK-EU clinical trials, such as rare and childhood cancers.

        iii. An ideal way of overcoming this challenge would be for the UK and EU to negotiate an MRA for clinical trial Sponsors, meaning the UK and EU would recognise each other's Sponsors and not require additional legal representation. However, this could be legally

challenging to achieve, as the EU's non-recognition of UK Sponsors is a part of EU law and applies to all Third Countries.[20] Consequently, amendments to EU law may be a prerequisite to a UK-EU MRA for clinical trial Sponsors.

iv. One option to address this challenge, would be for the UK Government to consider how it can offset the costs of EU legal representation now faced by UK Sponsors working in the EU/EEA. Doing so would minimise any impact these new legal barriers have on the UK's attractiveness as a research environment and ensure UK researchers aren't disadvantaged when leading pan-European clinical trials.

b. The UK has not received EU data adequacy status and the UK Government still recommends UK-EU trials use alternative data transfer mechanisms as a precaution.[21]

i. This poses a challenge because these alternative mechanisms (e.g. Standard Contractual Clauses) add a legal and financial burden on UK-EU research which would become permanent if the UK didn't receive data adequacy status.

ii. This added burden could discourage EU-based researchers from working with the UK in favour of EU Member States or Third Countries with data adequacy status. if the EU viewed the UK n as a less attractive research partners, that would lead to a fall in the number of UK-EU clinical trials and reduce UK patients' access to research. This would be particularly damaging for cancer patients, as cancer research is highly reliant on international clinical trials.[22]

iii. To address this challenge, the UK Government should work with the European Commission to secure data adequacy status as soon as possible and provide regular updates about this process.

c. The scope of UK association to Horizon Europe has not been negotiated yet, and the TCA does not specify how much of the programme's €95.5 billion (£84.1 billion) of research funding[23] the UK will be able to apply for.

i. For example, it's unclear what level of access the UK will have to schemes that fall under Horizon Europe's cancer mission, a programme which presents a unique opportunity for the UK to solidify its reputation as a world leader in cancer research.[24] Because research projects can take several years to set-up and deliver, this uncertainty is highly disruptive for UK and EU researchers wanting to plan collaborative research.

ii. To remove this uncertainty and allow UK researchers to apply for and receive EU funding on a similar basis to EU researchers, the UK

Government should negotiate associate status with Horizon Europe as soon as possible.

iii. The funding for the UK's association to Horizon Europe is also unclear. The UK invests less in R&D, as a percentage of GDP, than international comparator countries. We therefore recommend the UK Government fund the UK's association to Horizon Europe with new money; rather than by drawing on existing R&D commitments. Funding Horizon Europe association through existing R&D commitments would deprive the UK of the R&D investment needed to meet the ambition to be a science superpower and risks decelerating our economic recovery from COVID-19.

12. Similarly, the TCA falls short in several areas that underpin patients' access to existing and new medicines:

    a. Although the UK Government has unilaterally decided to recognise EU batch testing and QP certification, the EU has not fully reciprocated this measure, meaning many UK medicines exported to the EU will need to be retested and recertified.[25]

        i. Licenced medicines imported into to the EU from the UK will need to be retested and recertified by an EU-based QP.

        ii. Investigational Medicinal Products (IMPs) imported into the EU from UK will not need to be retested, but they will need to be recertified by an EU-based QP.[26]

        iii. Under the TCA, if a UK-led trial wants to test a UK-manufactured IMP in an EU/EEA country, that IMP will need to be recertified by an EU-based QP once it enters the EU. This could delay the IMP's shipment to EU-based trial sites, creating complications for EU researchers participating in the UK-led trial. Re-certification at the border also adds to the UK researchers' administrative burden, as they have to spend time and resources managing the additional QP certification for the exported IMP.

        iv. In response, EU-based researchers may choose to avoid working with UK-led clinical trials in order to avoid the complications and costs associated with them under the TCA's provisions for UK medicine exports. If this occurred, this would lead to a reduction in UK-EU clinical trials and fewer opportunities for UK patients to access potentially life-saving research.

        v. To address this, the UK and EU should negotiate an MRA that covers batch testing and QP certification for both licenced and unlicensed medicines. This MRA should also include a confidentiality agreement to facilitate MHRA-EMA cooperation in monitoring medicine safety

(pharmacovigilance). We'd encourage the UK Government to use the TCA's Working Group on Medicinal Products to begin exploratory discussions on this matter.

b. The UK's unilateral recognition of EU batch testing and QP certification is only temporary and is scheduled to end in 2023.[27]

   i. If a UK-EU MRA for batch testing and QP certification has not been negotiated before this 2-year period ends, then the 37 million packs of medicine that move from the EU to the UK every month[28] would need to be retested once they enter the UK. This would add significant customs delays to the UK's medicines supply chain and risks severely disrupting patients' access to treatments and health services.

   ii. To avoid this, we recommend the UK and EU agree an MRA that covers batch testing and QP certification for both licenced and unlicensed medicines before the 2-year period ends.

c. Under the TCA, companies wanting to market new medicines now have to submit separate marketing authorisation applications to the MHRA in the UK, and to the EMA in the EU.

   i. The EMA covers 25% of global pharmaceutical sales; the UK on its own makes up just 3%.[29] Companies are therefore likely to submit applications for new drugs to the EMA before the MHRA, meaning UK patients risk having slower access to the latest medicines.

   ii. This already happens in non-EU countries. In Australia, Switzerland and Canada, nations with standalone medicine regulators, companies submit new drugs to these regulators on average between 3 and 4 months after they do to the EMA.[30] Because the MHRA is now outside the EMA's licencing processes, UK patients are at risk of facing similar delays.

   iii. A short-term solution to this issue would be to have the MHRA automatically adopt EMA licencing decisions for a time-limited period – akin to the UK's time-limited recognition of the EU's batch testing and QP certification.

   iv. The MHRA already has a mechanism that could deliver this, called the EC Decision Reliance Procedure (ECDRP).[31] The ECDRP enables the MHRA to quickly licence a new medicine after it's received EMA approval, thereby removing the need for a separate, time-consuming MHRA evaluation and accelerating UK patients' access to the new medicine.

   v. However, the ECDRP doesn't automatically apply to all EMA licencing decisions, meaning the MHRA has to manually decide which new medicines benefit from accelerated UK licencing. We recommend the

MHRA use the ECDRP pragmatically to ensure UK patients don't lose out on the latest medicines, especially in disease areas where treatment options are limited (e.g. rare and childhood cancers).

vi. Additionally, this approach is dependent on timely marketing authorisation applications being made by pharmaceutical companies. If companies do not apply quickly after receiving EMA approval, then the MHRA cannot use the ECDRP to accelerate patient access to the latest medicines. It's therefore critical that the UK Government encourages companies to submit new medicines to the MHRA quickly.

vii. A long-term solution to this issue would be for the MHRA and EMA to formally cooperate in licencing decisions; minimising regulatory overlap and working together to accelerate UK and EU patient access to new medicines. We recognise the UK cannot fully participate in the EU's market structures and this precludes a level of MHRA-EMA integration similar to that of an EU Member State. However, our evidence shows that MHRA-EMA coordination in licencing decisions would best serve the needs of UK and EU patients, especially for those with limited treatment options (e.g. rare and childhood cancers).

viii. The Working Group on Medicinal Products is an ideal forum to begin these discussions, as its remit includes facilitating MHRA-EMA regulatory cooperation and dialogue. We recommend the UK Government use this Working Group to explore options for the MHRA's pragmatic participation in the EMA's licencing processes.

What should the UK seek to accomplish with the EU in relation to your industry or policy area within the parameters of the Agreement in the short- and mid-term?

13. Within the next six months, the UK and EU urgently need to negotiate:

    a. The UK's data adequacy status, in order to maintain UK-EU data transfers and provide much-needed certainty to UK-EU clinical trials; and

    b. The terms of the UK's association to Horizon Europe, including the fullest possible access to initiatives that fall under the cancer mission. The UK Government should finance the costs of association using new money and not by drawing on existing R&D commitments.

14. Within the next 12-18 months, the UK and EU should negotiate an MRA that covers batch testing and QP certification of licenced and investigational medicinal products. This MRA should also include a confidentiality agreement to facilitate MHRA-EMA cooperation in monitoring medicine safety (pharmacovigilance). We recommend the UK Government use the TCA's Working Group on Medicinal Products to begin exploratory discussions of a MHRA-EMA MRA as soon as possible.

15. In the medium term, the UK and EU should use the Working Group on Medicinal Products to discuss their ambitions for UK-EU collaboration in medical research. These talks should serve as prelude to future negotiations of the TCA, including the negotiation of a UK-EU MRA covering clinical trial Sponsors.

About Cancer Research UK

Cancer Research UK is the world's largest cancer charity dedicated to saving lives through research. We support research into over 200 types of cancer, and our vision is to bring forward the day when all cancers are cured. Our long-term investment in state-of-the-art facilities has helped to create a thriving network of research at 90 laboratories and institutions in more than 40 towns and cities across the UK supporting the work of over 4,000 scientists, doctors and nurses.

References

[1] Official Journal of the European Union. (2020). *Trade and Cooperation Agreement between the European Union and the European Atomic Energy Community, of the one part, and the United Kingdom of Great Britain and Northern Ireland, of the other part*. [Online]. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:22020A1231(01)&from=EN [Accessed 27 January 2021]., p. 517.

[2] Argar, E. (2020). *Letter to the health and care sector about the UK–EU Trade and Co-operation Agreement*. [Online]. Available at: https://www.gov.uk/government/publications/letter-to-the-health-and-care-sector-about-the-uk-eu-trade-and-co-operation-agreement [Accessed 27 January 2021].

[3] UK Research and Innovation (2021). Horizon Europe. [Online]. *Working on EU-funded projects*. Available at: https://www.ukri.org/our-work/collaborating-internationally/working-on-eu-funded-projects/ [Accessed 27 January 2021].

[4] Official Journal of the European Union. (2020). *Trade and Cooperation Agreement between the European Union and the European Atomic Energy Community, of the one part, and the United Kingdom of Great Britain and Northern Ireland, of the other part*., p. 520.

[5] Cancer Research UK. (2014). *Exploring the Interdependencies of Research Funders in the UK*. [Online]. Available at: https://www.cancerresearchuk.org/sites/default/files/interdependencies_of_funders_in_the_uk_march2014.pdf [Accessed 20 January 2021]., p. 26.

[6] Cancer Research UK. (2020a). *The UK and EU: What people affected by cancer need from the future relationship*. [Online]. Available at: https://www.cancerresearchuk.org/sites/default/files/whatpatientsneedfinal.pdf [Accessed 10 December 2020]., p. 4.

[7] Cancer Research UK. (2020a). *The UK and EU*., p. 4.

[8] Argar, E. (2020). *Letter to the health and care sector about the UK–EU Trade and Co-operation Agreement*.

[9] UK Research and Innovation (2021). Horizon Europe.

[10] European Commission. (2020a). *Commission welcomes political agreement on Horizon Europe, the next EU research and innovation programme*. [Online]. Available at: https://ec.europa.eu/commission/presscorner/detail/en/IP_20_2345 [Accessed 1 February 2021].

[11] Medicines and Healthcare products Regulatory Agency. (2020a). *List of approved countries for clinical trials and investigational medicinal products*. [Online]. Available at: https://www.gov.uk/government/publications/importing-investigational-medicinal-products-into-great-britain-from-approved-countries/list-of-approved-countries-for-clinical-trials-and-investigational-medicinal-products [Accessed 27 January 2021].

[12] Association of the British Pharmaceutical Industry. (2020a). *2020 Manifesto for Medicine*. [Online]. Available at: https://www.abpi.org.uk/media/7695/abpi-2020-manifesto-for-medicine.pdf [Accessed 21 January 2021]., p. 5.

[13] Medicines and Healthcare products Regulatory Agency. (2020b). *List of approved countries*. [Online]. Available at: https://www.gov.uk/government/publications/list-of-approved-countries-for-authorised-human-medicines/list-of-approved-countries [Accessed 27 January 2021].

[14] Official Journal of the European Union. (2020). *Trade and Cooperation Agreement between the European Union and the European Atomic Energy Community, of the one part, and the United Kingdom of Great Britain and Northern Ireland, of the other part*., pp. 517-520.

[15] Official Journal of the European Union. (2020). *Trade and Cooperation Agreement between the European Union and the European Atomic Energy Community, of the one part, and the United Kingdom of Great Britain and Northern Ireland, of the other part*., p. 520.

[16] Official Journal of the European Union. (2014). *Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC*. [Online]. Available at: https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf [Accessed 27

January 2021]., pp. 45-46.
[17] The dataset behind this statistic contains commercially sensitive data that cannot be shared publicly.
[18] World Health Organisation. (2020). Search Platform: Trials open to recruitment in May 2018. [Online]. *International Clinical Trials Registry Platform*. Available at: https://apps.who.int/trialsearch/ [Accessed 27 March 2020].
[19] Association of the British Pharmaceutical Industry. (2020b). *Clinical trials*., p. 5.
[20] Official Journal of the European Union. (2014). *Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC*., pp. 45-46.
[21] Argar, E. (2020). *Letter to the health and care sector about the UK–EU Trade and Co-operation Agreement*.
[22] Cancer Research UK. (2014). *Exploring the Interdependencies of Research Funders in the UK*., p. 26.
[23] European Commission. (2020a). *Commission welcomes political agreement on Horizon Europe, the next EU research and innovation programme*.
[24] Association of the British Pharmaceutical Industry. (2020b). *Clinical trials: How the UK can transform the clinical research environment*. [Online]. Available at: https://www.abpi.org.uk/media/8307/11275_abpi_clinical-trials-report-2020_aw-v1-high.pdf [Accessed 20 January 2021]., p. 5.
[25] Laura Williams. (2021). *We have a Deal: What does the new UK-EU relationship mean for cancer?* [Online]. Available at: https://scienceblog.cancerresearchuk.org/2021/01/04/we-have-a-deal-what-does-the-new-uk-eu-relationship-mean-for-cancer/ [Accessed 27 January 2021].
[26] European Commission. (2020b). *Notice to stakeholders: Withdrawal of the United Kingdom and EU rules in the field of clinical trials*. [Online]. Available at: https://ec.europa.eu/info/sites/info/files/brexit_files/info_site/clinical-trials_en.pdf [Accessed 4 February 2021]., pp. 2-3.
[27] Medicines and Healthcare products Regulatory Agency. (2020b). *List of approved countries*. [Online]. Available at: https://www.gov.uk/government/publications/list-of-approved-countries-for-authorised-human-medicines/list-of-approved-countries [Accessed 27 January 2021].
[28] Association of the British Pharmaceutical Industry. (2020a). *2020 Manifesto for Medicine*., p. 5.
[29] Cancer Research UK. (2020a). *The UK and EU*., p. 8.
[30] Cancer Research UK. (2020a). *The UK and EU*., p. 9.
[31] Medicines and Healthcare products Regulatory Agency. (2021). *European Commission (EC) Decision Reliance Procedure*. [Online]. Available at: https://www.gov.uk/guidance/european-commission-ec-decision-reliance-procedure [Accessed 28 January 2021].