

NUFFIELD COUNCIL ON BIOETHICS

Response to the Health Committee Inquiry

Brexit: medicines, medical devices and substances of human origin

26 October 2017

Introduction

- 1 The Nuffield Council on Bioethics is an independent UK body that examines and reports on ethical issues arising from developments in biological and medical research that concern the public interest. The Council welcomes the opportunity to respond to this important inquiry by the Health Committee.
- 2 Our response will address a selection of questions raised by the inquiry, and will draw on conclusions from five of our recent projects:
 - [Cosmetic procedures: ethical issues](#);¹
 - [Non-invasive prenatal testing: ethical issues](#);²
 - [Children and clinical research: ethical issues](#);³
 - [The collection, linking and use of data in biomedical research and health care: ethical issues](#);⁴ and
 - [Human bodies: donation for medicine and research](#).⁵

¹ Nuffield Council on Bioethics (2017) *Cosmetic procedures: ethical issues*, available at: <http://nuffieldbioethics.org/project/cosmetic-procedures/>.

² Nuffield Council on Bioethics (2017) *Non-invasive prenatal testing: ethical issues*, available at: <http://nuffieldbioethics.org/project/non-invasive-prenatal-testing>.

³ Nuffield Council on Bioethics (2015) *Children and clinical research: ethical issues*, available at: <http://nuffieldbioethics.org/project/children-research>.

⁴ Nuffield Council on Bioethics (2015) *The collection, linking and use of data in biomedical research and health care: ethical issues*, available at: <http://nuffieldbioethics.org/project/biological-health-data>.

⁵ Nuffield Council on Bioethics (2011) *Human bodies: donation for medicine and research*, available at: <http://nuffieldbioethics.org/project/donation>.

Cosmetic procedures: ethical issues

Following the UK's withdrawal from the EU, what alternative arrangements for the regulation of medicines, medical devices, medical products and substances of human origin could be introduced? What are the respective opportunities, risks and trade-offs involved?

3 The use of medicines, medical devices, and medical products is integral to the practice of invasive cosmetic procedures, which include surgery, Botox, and dermal fillers.⁶ However, at present, the UK lacks a strong regulatory framework for products used for cosmetic procedures. We therefore take the view that the UK's withdrawal from the EU offers the Government an opportunity to strengthen regulation in this area, and to ensure that the UK is an exemplar of best practice for invasive cosmetic procedures. In particular, we highlight two options through which the UK's regulatory position on products used for cosmetic procedures might be strengthened.

a) Introducing regulations for dermal fillers

4 Dermal fillers are wholly unregulated in the UK and have historically been excluded from EU regulation: for example, fillers are not currently defined as either medical devices or medicines, unless they are marketed for medical purposes (e.g., to treat lipoatrophy in people with HIV), or are pre-mixed with other substances such as anaesthetic that do fall within medicines regulation.⁷

5 The lack of regulatory control over the manufacture, supply, and use of fillers was highlighted by Sir Bruce Keogh in his 2013 review of cosmetic procedures.

“Dermal fillers are a particular cause for concern as anyone can set themselves up as a practitioner, with no requirement for knowledge, training or previous experience. Nor are there sufficient checks in place with regard to product quality – most dermal fillers have no more controls than a bottle of floor cleaner. There has been explosive growth in this market, driven by a combination of high demand and high profits in an era when all other commercial income is stalling. It is our view that dermal fillers are a crisis waiting to happen.”⁸

⁶ 'Invasive cosmetic procedures' share a number of common features: their purpose is to change a person's appearance in accordance with perceptions of what is normal or desirable; their purpose is non-essential with respect to physical functioning; and they are carried out by third parties in a clinical or quasi-clinical environment. See: paragraph 1.23 of the Council's report.

⁷ See, for example, Merz (2016) *Merz receives CE mark for Radiesse (+) lidocaine*, available at: <https://www.merz.com/blog/news/merz-receives-ce-mark-radiesse-lidocaine/>.

⁸ Department of Health (2013) *Review of the regulation of cosmetic interventions*, available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/192028/Review_of_the_Regulation_of_Cosmetic_Interventions.pdf, at page 5.

- 6 We agree with Sir Bruce's conclusions on dermal fillers and take the view that there is an ethical imperative to regulate fillers, particularly in the light of reports of recipients suffering harm following injections.⁹
- 7 The introduction of the Medical Devices Regulation 2017 (MDR) will mean that, from May 2020, fillers will be subject to some level of regulatory control in Europe.¹⁰ However, it is currently unclear how clinical assessment of the risks and benefits of these cosmetic devices will be carried out. Much will depend on the content of the EU's 'common specifications' to be developed for use by notified bodies in making these assessments; and on how consistently these specifications will then be applied.¹¹
- 8 The implementation of the MDR will take place after the UK leaves the EU, and will therefore not be subject to conversion under the Repeal Bill. The UK Government may therefore later opt to harmonise its regulatory requirements for dermal fillers with those of the EU as set out in this Regulation; or it may choose to take its own regulatory approach to dermal fillers. Whichever path that the Government takes – and we strongly argue that it is not ethically neutral to do nothing in this context – we recommend that it must ensure that fillers are afforded prescription-only status in the UK. This change to the regulatory landscape would guarantee the involvement of health professionals qualified to prescribe for all procedures involving dermal fillers, and thereby provide greater protection for the safety of people in the UK who use fillers for cosmetic purposes.

b) Ensuring cosmetic procedure devices are evidence-based

- 9 It is worryingly straightforward to market devices in the UK for cosmetic procedures without evidence of their safety and efficacy. This situation leads to circumstances whereby individuals undergo invasive cosmetic procedures on the advice of magazine articles or celebrity endorsements,¹² rather than in accordance with guidance based on objective evidence of the procedures' efficacy and risk profiles. We argue that, given the absence of physical health benefits, the ethical starting point for regulating invasive cosmetic products and procedures should be the requirement to demonstrate both safety and effectiveness with respect to their claimed outcomes *before* they can be made publicly available. Brexit offers an opportunity to address this problem head-on.
- 10 The introduction of the MDR (see above) will mean that European Member States will have to adhere to 'common specifications' for the clinical assessment of cosmetic devices. These are yet to be finalised, and hence their appropriateness cannot yet be judged. Any assessment criteria used in the UK post-Brexit (whether implemented through harmonisation with EU requirements, or through a distinctly UK approach) should, we suggest, be based on the need to demonstrate the safety and effectiveness of such devices, through clinical trial data and outcome

⁹ See paragraphs 6.12-3 of the Council's report. See also: Arie S (2017) Cosmetic industry regulation is only skin deep *British Medical Journal* **357** j:3047.

¹⁰ European Commission (2017) *The new Regulations on medical devices*, available at: https://ec.europa.eu/growth/sectors/medical-devices/regulatory-framework_en.

¹¹ See further: paragraph 4.37 of the Council's report.

¹² See, for example, the discussion of 'vampire' treatments in Box 3.4 of the Council's report.

measures, before marketing authorisation can be granted. Overall, the UK must take a stronger stance on ensuring that devices used for cosmetic procedures have been thoroughly tested. The Medicines and Healthcare products Regulatory Agency (MHRA), as the UK's regulator for medical devices, will play a key role in this endeavour.

Non-invasive prenatal testing

Following the UK's withdrawal from the EU, what alternative arrangements for the regulation of medicines, medical devices, medical products and substances of human origin could be introduced? What are the respective opportunities, risks and trade-offs involved?

- 11 Brexit presents a number of challenges and opportunities for the regulation of in vitro diagnostic devices (IVDs) in the UK.
- 12 IVDs are used to perform tests on blood, urine, and other bodily samples to help diagnose medical conditions or detect infection. In March 2017, the Council published a report on the ethics of non-invasive prenatal testing (NIPT), an IVD that can be used to test whether fetuses have a number of genetic conditions and impairments, such as Down's syndrome and cystic fibrosis.¹³ Pregnant women and couples in the UK have been able to access NIPT in the private sector since 2012. The global NIPT market is forecast to grow at an annual rate of 17 per cent between 2016 and 2020.¹⁴
- 13 The manufacture and sale of IVDs in the UK are regulated by the UK Medical Devices Regulations 2002,¹⁵ which implement the EU In-Vitro Diagnostic Medical Devices (IVD) Directive.¹⁶ Devices that adhere to the Directive can apply for a CE mark and then be sold anywhere in the EU. In the UK, the MHRA is the competent authority for the Directive and it designates notified bodies to carry out assessments of devices. Manufacturers must have evidence to support the claims they make, and devices must meet the claims made for them, but there are no minimum performance specifications set out in the Directive.
- 14 This has enabled some manufacturers to offer NIPT for genetic variations such as sex aneuploidy and microdeletions to women and couples in the UK. The use of NIPT for these variations has not been widely researched, meaning that there is little or unreliable information available on test accuracy for potential customers. Where information about test performance is available, often there is a high chance that the result will be false. Women who receive a high chance result are likely to

¹³ Nuffield Council on Bioethics (2017) *Non-invasive prenatal testing: ethical issues*, available at: www.nuffieldbioethics.org/NIPT.

¹⁴ Research and Markets (2016) *Global non-invasive prenatal testing market 2016-2020*, available at: <http://www.researchandmarkets.com/research/vt4hv2/global>.

¹⁵ Part IV of The Medical Devices Regulations 2002, available at: <http://www.legislation.gov.uk/uksi/2002/618/part/IV/made>.

¹⁶ Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices, available at: https://ec.europa.eu/growth/single-market/european-standards/harmonised-standards/iv-diagnostic-medical-devices_en.

be very anxious about this. We heard anecdotal evidence that NHS staff are helping women interpret results of this kind and, more seriously, that they can lead to women seeking diagnostic procedures (which carry a small risk of miscarriage), either in the NHS or in the private sector.

- 15 To modernise the regulatory system, after considerable consultation and discussion, the EU In Vitro Diagnostic Device Regulation was adopted in April 2017. This would have come into force in the UK after a transition period of five years. Under the new Regulation, IVD manufacturers in the EU will be required to produce significantly more evidence on clinical performance, including diagnostic sensitivity, diagnostic specificity, positive predictive value, and negative predictive value. The Regulation states: “Devices shall be designed and manufactured in such a way that they are... suitable with regard to the performance they are intended to achieve, taking account of the generally acknowledged state of the art.”¹⁷ It has been suggested that this will be a step towards manufacturers becoming fully responsible for the clinical utility of their devices.¹⁸
- 16 The implementation of the EU In-Vitro Diagnostic Device Regulation will take place after the UK leaves the EU, and will therefore not be subject to conversion under the Repeal Bill. The UK Government may therefore choose to harmonise its regulatory requirements with those of the EU for IVDs or adopt its own regulatory approach. If the latter, the UK Government should take into consideration the improvements to the system set out under the new EU IVD Regulation.
- 17 Brexit also presents an opportunity to ensure women and couples accessing NIPT tests in the UK are receiving a high quality service. Currently, the UK Medical Devices Regulations and the EU Regulation do not regulate testing services, only the devices used in the testing services when they are placed on the market in the EU. Therefore, if a blood sample is taken in the UK but sent outside of the EU for analysis, this device is not covered by the UK or EU Regulations. Currently, many NIPT tests being carried out by UK hospitals are sent to the US or China for analysis, which have different systems of regulation.¹⁹ The impact on patients of sending samples to different jurisdictions for analysis should be considered when developing regulation for IVDs in the UK after Brexit.

Children and clinical research: ethical issues

- 18 Scientifically valid and ethically robust research that addresses questions of importance to the health of children and young people should be seen as intrinsically good, and as a natural and necessary part of a healthcare system. Without well-conducted research, there is no prospect of improving healthcare for

¹⁷ Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU, available at: <http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=OJ:L:2017:117:FULL&from=EN>.

¹⁸ BSI (2016) *How to prepare for and implement the upcoming IVDR – dos and don'ts.*, available at: [http://www.bsigroup.com/LocalFiles/EN-AU/ISO%2013485%20Medical%20Devices/WP12_How_to_prepare_for_and_implement_the_upcoming_IVDR_Dos_and_Don'ts%20\(1\).pdf](http://www.bsigroup.com/LocalFiles/EN-AU/ISO%2013485%20Medical%20Devices/WP12_How_to_prepare_for_and_implement_the_upcoming_IVDR_Dos_and_Don'ts%20(1).pdf).

¹⁹ Nuffield Council on Bioethics (2017) *Non-invasive prenatal testing: ethical issues*, available at: <http://nuffieldbioethics.org/project/non-invasive-prenatal-testing>, at paragraph 4.7.

children now, or in the future, and there is a real risk that children will be harmed by procedures and medicines that are ill-adapted for their needs, or lack an adequate evidence base.²⁰ For these reasons, we urge the Government to consider carefully the risks which may befall paediatric research, and the children who benefit from it, as part of a regulatory shift post-Brexit. We set out our concerns further in response to the two inquiry questions below.

What are the implications for medical research and development, including for the timely patient access to new medicines, technologies and other relevant medical innovations developed within or outside the UK? How can any adverse consequences be avoided or mitigated and any potential opportunities be enhanced?

- 19 A post-Brexit UK must accommodate the fact that paediatric research relies more heavily on international collaboration than other forms of research, because of the relative rarity of many childhood conditions, and consequently small cohorts of potential research participants. The UK, through its membership of the EU, has enjoyed successful collaborations in this context,²¹ and it is imperative that these alliances in paediatric research continue for the benefit of young people inside and outside the UK's borders.
- 20 An important part of continuing cross-border collaboration in paediatric research will involve ensuring that the provisions of the 2006 Paediatric Regulation are subsumed into UK law through the Repeal Bill. The importance of this Regulation was noted by a 2013 European Commission report which concluded that the Regulation has *started* to make a welcome difference to the amount of information available to prescribers on the effect of medicines on children.²² In addition, the Regulation has led to an increase in the proportion of clinical trials involving children, and a growth in the number of children who participate in clinical trials.²³ These positive steps in increasing knowledge of children's medicines must continue in the UK post-Brexit.
- 21 Another key legal instrument for paediatric research is the Clinical Trials Regulation 2014 (CTR). We are concerned at recent reports²⁴ which suggest that the delay to the implementation of the CTR will have implications for the Government's ability to convert its provisions into UK law through the Repeal Bill. In the context of paediatric research, the CTR makes several important requirements for the continuation of well-conceived paediatric research, including: setting out consent

²⁰ See paragraph 1.19 of our report.

²¹ For a range of examples of successful pan-European collaboration, see paragraph 3.25 of our report.

²² European Commission (2013) *Report from the Commission to the European Parliament and the Council: better medicines for children - from concept to reality*, available at: <http://www.ipex.eu/IPEXL-WEB/dossier/files/download/082dbcc53eea9c03013f75ffb4243058.do>.

²³ Ibid. See also: paragraph 3.17 of our report.

²⁴ Department for Exiting the European Union (21 September 2017) *Leaving the EU: implications and opportunities for science and research*, available at: <http://www.parliament.uk/documents/commons-committees/science-technology/170921-Robin-Walker-to-Norman-Lamb-DExEU%20letter.pdf>.

requirements for the involvement of children in research participation decisions; and ensuring that professionals with the necessary skills make available age-appropriate information for young people who consider taking part in research. We therefore highlight the importance of the Government taking a proactive approach to post-Brexit negotiations to ensure that the terms of the CTR continue to be part of the UK's regulatory framework.

What are the key considerations that arise for companies, healthcare services and regulatory bodies in the UK as a result of the UK's withdrawal from the EU? Focussing on patients and the public, what needs to be done to ensure that any adverse impact is minimised or eliminated, and that opportunities to enhance services are maximised?

- 22 Our response to this question focuses on the role of the European Medicines Agency (EMA) and its Paediatric Committee (PDCO), and the powers bestowed on it by the Paediatric Regulation (see above).
- 23 The Regulation confers several responsibilities on the EMA and PDCO, including primary responsibility for handling paediatric investigation plans (PIPs), deferrals, and waivers. However, the EMA does more than police the system established by the 2006 Paediatric Regulation: it also encourages and promotes effective research with children and young people through a variety of practical means, such as facilitating collaboration,²⁵ offering free advice (via PDCO) on paediatric trials to researchers, keeping a public database of paediatric studies, and maintaining and updating an inventory of paediatric research needs. The organisation thus acts as a hub for paediatric research and provides a very effective infrastructure for paediatric clinical trials for the UK, as part of our membership of the EU.²⁶ Post-Brexit, any future arrangements must at least equal the proactive work of the EMA: it is not ethically acceptable to allow paediatric research in the UK to stall in the wake of Brexit.

The collection, linking and use of data in biomedical research and health care: ethical issues

- 24 Developments in biotechnologies, healthcare systems, and computing have led to a dramatic growth in the volume and variety of data about people's health and biology. There are more ways to collect, link, and analyse health and biological data in order to generate information for research and other purposes. For these reasons, the Government should consider carefully the risks which may impact on data sharing in biomedical research and healthcare as part of a regulatory shift post-Brexit. We set out our concerns further in response to the relevant inquiry question below.

²⁵ For a range of examples of successful pan-European collaboration, see paragraph 3.25 of our report.

²⁶ For further discussion of the positive role of the EMA in the context of paediatric research, see paragraph 5.44 of our report.

What are the key considerations that arise for companies, healthcare services and regulatory bodies in the UK as a result of the UK's withdrawal from the EU? Focussing on patients and the public, what needs to be done to ensure that any adverse impact is minimised or eliminated, and that opportunities to enhance services are maximised?

25 There are three considerations we would like to draw attention to in response to this question: using data to contribute to improvements in healthcare systems and patient health; ensuring access to health data is governed robustly; and maintaining public trust.

Using data to contribute to improvements in healthcare systems and patient health

26 There is a public interest in making use of data in order to contribute to a more efficient health service, and to the development of better treatments. Striving for continual improvements in productivity and improving health through developing better patient information, and treatment through research, have historically been the subject of separate information and governance systems. However, these are now being increasingly integrated. Therefore the Government needs to ensure it takes a proactive approach to managing this integration.

27 There is broad public support for some further uses of care data, such as in biomedical research. In leaving the EU, the UK Government must avoid a situation whereby the UK loses access to vital health and / or biomedical data from across Europe; and indeed the converse situation where European Member States would lose access to the UK's health and / or biomedical data. The health of UK citizens requires us to work with Member States to share knowledge gleaned from data analysis. Brexit should not undermine progress in healthcare, and the Government must make provision for sharing to continue after we leave the EU.

Ensuring access to health data is governed robustly

28 The use of data in biomedical research and healthcare should be in accordance with morally reasonable expectations and subject to appropriate governance.²⁷ Ensuring governance structures around the collection, use, and linking of this type of data must therefore be a priority for the Government ahead of Brexit. Considerations might include ensuring that all data sharing agreements are published and should include a requirement to maintain an auditable record of all individuals or other legal entities who have been given access to the data and of the purpose to which it has been put.²⁸ This should be available to all data subjects or relevant authorities in a timely fashion on request, and the Government must ensure that the relevant provisions are in place after the UK leaves the European

²⁷ For further discussion, see Chapter 5 of the Council's report.

²⁸ See paragraph 5 of the Council's report.

Union. This will include the terms of the General Data Protection Regulation (GDPR), which will be subsumed into UK law through the Repeal Bill.

Maintaining public trust

- 29 Trust in government and NGOs has broadly declined in recent times; this, in combination with the failures of previous initiatives, demonstrates the importance of public involvement and transparency to secure public trust during the process of creating any new initiative or legislation on data sharing. The use of data requires an approach that considers both public and private interests and that focuses on public values and the public good.
- 30 If, in the longer-term, the UK decides to determine its own legislation for the protection and sharing of data, this process requires transparency, openness, and honesty. If data were shared with the EU or any other organisations, we would recommend including a public statement about how data held by the relevant health or medical bodies should be used.
- 31 Lessons from previous data initiatives strongly suggest that there are serious consequences for public trust and for the viability of data initiatives if they do not first take steps to identify the applicable moral norms they must negotiate and put in place, in relation to these, well-supported measures to respect the interests engaged, supported by credible justification.²⁹
- 32 Unless there are trustworthy governance systems in place that can engage with and reflect reasonable expectations in continuously evolving circumstances, initiatives that could have wide public benefits may continue to be challenged and fail to secure public confidence. In the case of the UK's withdrawal from the EU, this could have detrimental effects on our access to public health and biomedical data.

Human bodies: donation for medicine and research

- 33 Our response in relation to our work on donation for medicine and research will focus on the following inquiry question:

What are the key considerations that arise for companies, healthcare services and regulatory bodies in the UK as a result of the UK's withdrawal from the EU? Focussing on patients and the public, what needs to be done to ensure that any adverse impact is minimised or eliminated, and that opportunities to enhance services are maximised?

- 34 Regulatory frameworks for the donation and use of various forms of bodily material in the UK are currently heavily influenced by EU Directives on organs, tissues and

²⁹ See paragraph 6.68 of the Council's report.

cells,³⁰ and blood.³¹ UK regulatory bodies in each of these areas currently act as 'competent authorities' in the UK under these Directives.³²

- 35 The harmonisation of requirements with respect to donation practice has meant that UK residents are currently able to benefit from inter-country arrangements, including allocation of organs via Eurotransplant, and access to sperm banks in other EU countries (in particular Denmark). Any future regulation of the donation and use of bodily materials should take into account these questions of interoperability of donation systems across Europe, and the important consequences for quality and access. In addition, future regulation must ensure that the same quality and safety requirements as currently set out in the Directives continue to be upheld in the UK.

³⁰ Directive 2004/23/EC.

³¹ Directive 2002/98/EC and Directive 2004/33/EC, with further technical requirements found in Directive 2005/61/EC and Directive 2005/62/EC.

³² The Human Fertilisation and Embryology Authority, the Human Tissue Authority, and the Medicines and Healthcare products Regulatory Agency.