West Midlands Commissioning Support Unit
Commissioning Policy for
Anti-VEGF Treatments in Eye Conditions

SET OF LEGAL OPINIONS

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Introduction

The following advice documents address the legal concerns with respect to developing a Commissioning Policy on the use of anti-VEGF treatments in eye conditions. In particular the funding of Lucentis and/or Avastin for the treatment of wet age-related macular degeneration (AMD), diabetic retinopathy, central vein occlusion, and rare disorders.

The first document (Advice 1) discusses the legal implications of drug marketing authorisation (licensing), statutory guidance from NICE, and the duties of Primary Care Trusts and individual clinicians within the broader context of EU and UK law. Opinions are given on the legality of the likely policy options.

The second document (Advice 2) reviews the original advice in light of the Human Medicines Regulations 2012, which came into force on 14 August 2012, and the decision of the Court of Justice of the European Union in Case C-185/10 Commission v Poland, concerning the supply of medicines within the EU.

The third document (Advice 3) expresses a further opinion on the lawfulness of the supply of repackaged Avastin for use in treating eye conditions by the three main sources.

The key points, opinions and implications are summarised below:

Key background points

- Lucentis is licensed for the treatment of: AMD, and macular oedema caused by diabetes or by central vein occlusion. NICE Technology Appraisal Guidance (TAG) has recommended Lucentis for the treatment of AMD but not for the other conditions.

- Avastin is licensed for the treatment of certain cancers but is widely prescribed ‘off-label’ for the treatment of the above eye conditions. It has not been appraised by NICE for eye conditions.

- The off-label use of Avastin to treat eye conditions requires it to be repackaged into smaller doses.

- Clinicians are legally allowed to prescribe unlicensed drugs and licensed drugs for both the licensed conditions and other off-label conditions.

Key opinions given in the documents

- The licensing of a treatment implies no legal obligation on NHS commissioners to provide funding for it. NHS commissioners are also free to fund off-label and unlicensed treatments (Advice 1 paras 10-13).

- The NHS commissioner does not owe a private law duty of care to a patient (Advice 1 paras 14-15).
The clinician owes a duty of care in law to their patient. A commissioning policy may permit a particular treatment but it is the responsibility of the clinician to make the decision of whether or not it is suitable (Advice 1 paras 16-18).

Where a choice exists between a licensed and an unlicensed/off-label treatment, the clinician has a professional duty to prescribe the licensed treatment unless the alternative would better serve the patient (Advice 1 paras 19-25).

Where there is no statutory guidance on the funding of treatments for particular conditions, the NHS commissioner is free to fund treatments irrespective of their license status (Advice 1 paras 19-25).

Commercial suppliers may only market a treatment for the conditions covered by its license. However, they are not legally responsible for the use to which the NHS puts the treatment (Advice 1 paras 26).

The repackaging of Avastin into smaller doses suitable for the treatment of eye conditions by a hospital pharmacy does not contravene the Human Medicines Regulations 2012 (Advice 2 paras 10-18).

The supply of repackage Avastin by Royal Liverpool Hospital Manufacturing Unit and Moorfields Pharmaceuticals to other NHS hospitals is likely to be lawful (Advice 3 paras 1-14; Note 1 para 2).

There may be significant legal difficulties for a commercial drugs company, such as ITH Pharma, supplying repackaged Avastin to NHS hospitals (Advice 3 paras 7, 8, 14), unless such repackaging takes place in a pharmacy (Note 1 para 2).

Where there is statutory guidance from NICE, the commissioner must fund the recommended treatment (Advice 1 paras 27-31).

It would be legal for a policy to encourage clinicians to consider the financial costs of the choice of treatment (Advice 1 paras 32-35) provided:

- If they are working to a fixed budget, that there is a possibility for the commissioner to extend the budget in exceptional and unforeseen circumstances.
- If additional funding is made available as a reward for savings being made, that the clinician still exercises clinical judgement in the best interest of the patient, and the patient retains access to any treatments recommended by NICE.

The Judgment of the Court in the case of C-185/10 Commission v Poland deals with the supply of medicines in the EU rather than the use to which licensed medicines are put within a national healthcare system. As such, there is nothing in the Poland case to suggest funding of Avastin for eye conditions is unlawful (Advice 2 paras 19-25).

**Key Implications**

For the treatment of AMD - the commissioning policy must include the funding of Lucentis. Avastin may also be funded. The clinician may consider the financial implications, given certain provisos, but remains under a professional duty to prescribe Lucentis unless Avastin better serves the patient.
• For the treatment of diabetic retinopathy, central vein occlusion, and other rare eye disorders - the commissioning policy may fund Lucentis and/or Avastin. If both are funded the clinician may consider the financial implications but should exercise clinical judgement in the best interest of the patient.

• Any NHS body that wishes to source repackaged Avastin for the treatment of off-licence conditions from a third-party supplier, such as the Royal Liverpool Hospital Manufacturing Unit, Moorfields Pharmaceuticals or ITH Pharma, should seek their own legal advice or assurance from the supplier that they are acting lawfully in supplying the vials.

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15 March 2013
1. I have been asked to advise the West Midlands Commissioning Support Unit, which is part of the University of Birmingham, concerning a policy document they are preparing to release to guide Primary Care Trusts (and the Clinical Commissioning Groups that will replace them) relating to the use of a class of drugs known as anti-VEGF Treatments in Eye Conditions.

2. The medical background to this issue is very well known and is set out in detail in the policy document. I shall therefore only summarise it to the extent needed to provide a factual context for this Advice. The research evidence shows that patients with certain eye-related conditions, in particular wet AMD, can be assisted with anti-vascular endothelial growth factor ("anti-VEGF") drugs. These drugs are generally not a cure for the underlying condition but have significantly beneficial effects in slowing the progress of chronic eye-related conditions. There are two relevant anti-VEGF drugs which are widely used for AMD patients, ranibizumab (known by its trade name of Lucentis) and bevacizumab (known by its trade name of Avastin). I shall refer to the 2 drugs as Avastin and Lucentis for the purposes of this Advice.

3. The key differences between the 2 drugs appear to me to be as follows:

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1 I have referred in this advice to NHS commissioners as being PCTs. The present legal commissioners are Primary Care Trusts though, in practice, many of the PCTs have delegated commissioning responsibility to committees which are shadow CCGs. The commissioning functions undertaken by PCTs and CCGs are, for all practical purposes, identical and therefore references in this Advice to PCTs can be taken as references to CCGs after the Health and Social Care Act 2012 comes into effect.
a. There is a different dosage regime for the 2 drugs for wet AMD patients. These drugs are injected into the eye and I understand that Avastin requires fewer injections. This can make Avastin clinically preferable for some patients. I am not aware of the clinical regimes for the use of the drugs for other eye-related conditions;

b. There is limited RCT² trial data to support the use of Avastin for wet AMD but it is commonly and successfully used throughout the world³. The reason that Avastin does not have a marketing authorisation for use for wet AMD appears to be as a result of a commercial decision taken by Hoffmann La Roche Ltd which owns the ultimate worldwide intellectual property rights in both drugs;

c. There are RCT trials for wet AMD sufferers for Lucentis and, building on that data, Novartis Europharm Ltd, has obtained an marketing authorisation for Lucentis for treating AMD from the European Medicines Agency⁴;

d. Lucentis has been the subject of a National Institute for Health and Clinical Excellence (“NICE”) Technology Assessment Guidance No 155. This has certain legal consequences for the PCT which I will explore below;

e. Avastin has a marketing authorisation for use in colorectal cancer. It is therefore not an “unlicensed drug” as such. However the marketing authorisation defines the vial size for the drug. I understand that vials of Avastin that are used for AMD patients are subdivided into smaller vials for ophthalmic use. Once this process has occurred the drug is in an unlicensed form;

f. Avastin is very considerably cheaper than Lucentis. Accordingly the West Midlands PCT could make substantial savings if wet AMD patients and/or other

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² Randomised Controlled Trials.
³ The evidence in the case of R (Ota Novatis) v SHIPP PCTs suggests that over 50% of the wet AMD patients in the USA are treated with Avastin because healthcare management organisations, including government organisations, refuse to fund Lucentis for such patients.
patients with eye-related conditions were prescribed Avastin rather than Lucentis or were switched from Lucentis to Avastin. Those resources would be then available for other NHS patients (not necessarily limited to other ophthalmic patients).

**Legal risks for usage where there is no licence for the proposed use for either drug.**

4. I have first been asked to advise on the legal risks of a PCT commissioning policy for an eye-related condition where neither Lucentis nor Avastin have been “licensed” for the proposed use. I have been asked to assume that there is no statutory guidance or a NICE Technology Assessment Guidance (“TAG”) relating to the proposed use, but that there is some non-statutory guidance which suggests that Avastin could be used successfully to treat relevant patients in addition to Lucentis.

**What is meant by a drug being “licensed”?**

5. In order to respond to this request it is necessary to say a little about the concept of a drug being “licensed”. The term “licensed” in this context refers to a medicinal product where a marketing authorisation has been granted to a commercial organisation by either the European Medicines Agency (“EMA”) or the Medicines and Regulatory Products Agency (“MHRA”). A marketing authorisation is required before a commercial organisation is able to market and/or sell any medicinal products within the EU. However whether a drug has a marketing authorisation or not has no direct effect on whether it is lawful for a clinician to prescribe that drug for a particular patient.

6. The origins of the "marketing authorisation" regime lie in EU Directive 2001/83/EEC which seeks to set standards of quality and safety relating to the marketing and sale of medicinal products for human use. The Directive primarily seeks to regulate the activities of pharmaceutical companies supplying and marketing medicinal products but does not seek to regulate the activities of doctors or other clinicians prescribing medicinal products. It is not a breach of the Directive for a doctor to prescribe a medicinal product for a patient which does not have a marketing authorisation under the Directive (prescribing an unlicensed product) or to prescribe a medicinal product
for a patient outside the terms of the licence (off-label prescribing). This is shown in recital 33 to the Directive which provides:

"The provisions dealing with the classification of medicinal products for the purpose of supply do not infringe the national social security arrangements for reimbursement or payment for medicinal product on prescription"

7. The limitations of the scope of the Directive were also set out in Article 4(3) which provides:

"The provisions of this Directive shall not affect the powers of Member States’ authorities either as regards the setting of prices for medicinal products or their inclusion in the scope of national health insurance schemes, on the basis of health, economic and social conditions"

8. Thus the Directive does not affect the power of the NHS to include a medicinal product in the scope of the UK nationalised healthcare system. That limitation appears to be consistent with article 168(7) of the Treaty for the Functioning of the European Union which provides that the EU does not have competence to interfere with the functioning of the health care systems of individual member states. It provides:

"Union action shall respect the responsibilities of the Member States for the definition of their health policy and for the organisation and delivery of health services and medical care. The responsibilities of the Member States shall include the management of health services and medical care and the allocation of the resources assigned to them. The measures referred to in paragraph 4(a) shall not affect national provisions on the donation or medical use of organs and blood"

9. Whilst it is clear that the freedom to provide services within a National Health Service comes within the terms of the EU treaty (see for example Watts (Freedom to provide services) [2006] EUECJ C-372/04 at §86), article 168(7) provides that the EU has no competence over the allocation of resources and resource based decisions within the health care systems of Member States.

10. It follows that attempting to use the argument that a drug should not be used within the NHS for particular NHS patients on the grounds that the drug has not got a
marketing authorisation for use for those patients appears to me to be attempting to use the marketing authorisation for an improper purpose. I draw some support for this view from the Opinion of the Advocate General in European Commission v Poland [2011] EUECJ C-185/10 who confirmed that §19 of his Opinion that the aim of Directive 2001/83 is to safeguard public health as well as to ensure that trade is not affected in the market for medicinal products. However at §29 the Advocate General express the view that the Directive:

“.. only applies to medicinal products either prepared industrially manufactured by a method involving an industrial process. Indeed, any medicinal product prepared in a pharmacy in accordance with a medical prescription for an individual patient (commonly known as the magistral formula) or in accordance with the prescriptions of a pharmacopoeia and intended to be supplied direct to the patients served by the pharmacy in question (commonly known as the officinal formula) is excluded from the scope of Directive 2001/03”

11. The European Court of Justice is also made it clear that 2001 Directive does not apply to internal arrangements within the NHS in its recent ruling in Case C-62/09 R (ABPI) v MHPRA, 22 April 2010. Having considered Article 168(7) TFEU, the Court held that an incentive scheme to persuade doctors in the NHS to prescribe drugs in a cost effective manner was not in breach of the financial inducement provisions contained in Article 94(1) of the 2001 Directive. The Court said:

“32. ..... although the prohibition in article 94(1) of Directive 2001/83 may admittedly apply to independent third parties who are not acting for commercial or industrial purposes or not for profit-making purposes, such a prohibition cannot apply to national public health authorities, which are responsible, inter alia, (i) for ensuring that the existing rules, of which that Directive forms part, are applied and (ii) for defining the priorities for action in relation to public health policy, in particular so far as concerns the rationalisation of the public expenditure allocated to that policy which is precisely what they are responsible for.

5 There are arguments against this as advanced by Novartis in the Judicial Review brought against the SHIPP PCTs. Permission was granted in respect of that challenge in a decision of Mrs Justice Thirlwell dated 19th April 2012. I have not sought to list the various arguments deployed by the Claimant in that case and to set out the response because that would make this Advice unduly lengthy.

6 This is the Opinion of the Advocate General and accordingly the judgement of the full Court is awaited.

7 For these purposes this word means a formula for the preparation of compound medicines, and published by the authority of a government or a medical or pharmaceutical society.
33. In general terms, the health policy defined by a member state and the public expenditure devoted to it do not pursue any profit-making or commercial aim. Since a financial incentive scheme such as the one at issue in the main proceedings forms part of such a policy, it cannot be regarded as falling within the commercial promotion of medicinal products

12. It follows that in my opinion, save for issues of clinical negligence which are considered below, questions as to whether a drug is "licensed" or "unlicensed" are generally only relevant to circumstances outside the NHS. This was summarised by the Court in ABPI at §36 where the Court said:

"In accordance with article 168(7) FEU, European Union law does not detract from the power of the member states to organise their social security systems and to adopt, in particular, measures intended to govern the consumption of pharmaceutical products in order to promote the financial stability of their health-care insurance schemes: A Menarini Industrie Farmaceutiche Riunite Srl v Ministero della Salute (Joined Cases C-352/07-C-356/07, C-365/07-C-367/07 and C-400/07) [2009] ECR I-2495, para 19 and the case law cited"

13. It follows that once a medicinal product has been delivered by a commercial manufacturer or distributor to an NHS organisation, EU rules on the distribution or use of that medicinal product internally within the NHS are no longer generally applicable. As I have indicated above, there are arguments that the implied scope of the regime of granting marketing authorisations for medicinal products extends beyond the activities of commercial organisations and can affect policies adopted by the NHS. Those arguments are advanced by Novartis in the case of R (ota Novartis) v SHIPP PCTs. However, for the reasons set out above, I consider that the arguments are likely to fail if the case proceeds to a trial.

The nature of the legal duty owed by an NHS Commissioner to a patient.

14. NHS commissioners are delegates of the duties owed by the Secretary of State under sections 1 to 3 of the NHS Act 2006. This is a "target duty" to provide services to meet the reasonable requirements of patients. However it is not a direct legal duty owed by an NHS Commissioner to individual patients. Accordingly it is difficult if not impossible
to envisage the circumstances in which a PCT, exercising its commissioning functions, would owe a private law duty of care to a patient.

15. It is well established law that breach of a public law obligation in the health and social care the does not give rise to a right to damages that the suit of a person who has suffered loss as a result of the breach of the public or obligation. See O'Rourke v Camden London Borough Council [1998] AC 188. Accordingly if an NHS commissioner unlawfully exercises its discretion in refusing to fund a particular drug for a particular NHS patient this unlawful action is extremely unlikely to result in a damages claim against the NHS Commissioner.

**The situation where there is no statutory Guidance.**

16. There is nothing in principle in law to prevent a PCT adopting a commissioning policy under which the PCT agrees to fund an unlicensed\(^8\) drug in the absence of either statutory guidance or a NICE TAG to support the use of this drug in the described clinical circumstances. There is a general absence of licensed drugs in some areas of medicine, in particular in paediatrics, because it is not ethically possible for manufacturers to run the types of randomised controlled trials which are necessary to get through the licensing process.

17. It is, of course, a matter for individual clinicians, who do owe a duty of care in law to their patients, to decide whether to prescribe any particular drug for any particular patient. Clinical responsibility for these decisions rests solely with the treating clinician. A PCT commissioning policy simply means that a clinician has the right to prescribe this drug as part of NHS funded treatment. The decision as to whether the drug is suitable for an individual patient is a matter for the individual clinician.

18. There is the additional (albeit largely in view theoretical) risk that a case could be brought against the doctor for prescribing an unlicensed drug under the Consumer Protection Act 1987 on the ground that the drug was a defective product. I am not aware of a successful claim against a doctor under that section and, in any event, it

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\(^8\) “Unlicensed” in this sense means the absence of a marketing authorisation under the Medicines for Human Use (Marketing Authorisations etc) Regulations 1994 which implement the 2001 Directive.
could not be used to found a claim against an NHS commissioner. I do not therefore consider that the possibility of a claim under the Consumer Protection Act 1987 is likely to lead to a legal challenge to an otherwise lawful commissioning policy.

Situations where Lucentis has been licensed for an indication but NICE has not supported its use.

19. I am instructed that Lucentis has a marketing authorisation for use for patients with retinal vein occlusion and diabetic macular oedema. I understand that NICE has considered whether to make a TAG to recommend Lucentis for patients suffering from both of these conditions but has declined to recommend that Lucentis be provided as part of NHS funded treatment for diabetic macular oedema on the grounds that Lucentis does not provide a cost effective treatment. I understand that it appears likely that NICE will reach a similar decision in respect of the use of Lucentis for retinal vein occlusion.

20. PCTs are under a statutory duty to break even under sections 229-231 of the NHS Act 2006. They therefore have a discretion to decide how to apply their resources in order to seek to commission the maximum health care within their budgets. For the reasons set out above, there is nothing in law to prevent a PCT adopting a commissioning policy which provides for an unlicensed medical treatment to be funded as part of NHS funded healthcare where there is evidence that this is likely to be a clinically effective and cost-effective treatment.

21. If clinicians are given a choice between a licensed and an unlicensed medical treatment for the same condition, the present GMC guidance provides a strong steer for the clinicians to use the licensed product.

22. The GMC Code of Conduct explains the following professional obligations concerning the duties of a doctor where there are licensed and unlicensed drugs:

“Prescribing medicines for use outside the terms of their licence (off-label)

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9 See http://www.nice.org.uk/newsroom/pressreleases/RanibizumabForDMOFinalDraftGuidance.jsp and
19. You may prescribe medicines for purposes for which they are not licensed. Although there are a number of circumstances in which this may arise, it is likely to occur most frequently in prescribing for children. Currently pharmaceutical companies do not usually test their medicines on children and as a consequence, cannot apply to license their medicines for use in the treatment of children. The use of medicines that have been licensed for adults, but not for children, is often necessary in paediatric practice.

20. When prescribing a medicine for use outside the terms of its licence you must:

a. Be satisfied that it would better serve the patient's needs than an appropriately licensed alternative

b. Be satisfied that there is a sufficient evidence base and/or experience of using the medicine to demonstrate its safety and efficacy. The manufacturer's information may be of limited help in which case the necessary information must be sought from other sources

c. Take responsibility for prescribing the medicine and for overseeing the patient's care, monitoring and any follow up treatment, or arrange for another doctor to do so (see also paragraphs 25-27 on prescribing for hospital outpatients)

d. Make a clear, accurate and legible record of all medicines prescribed and, where you are not following common practice, your reasons for prescribing the medicine"

23. Hence a doctor is not entitled, within the scope of his professional obligations, to make a general choice between two drugs which he considers are equally clinically effective when one is licensed and the other is unlicensed. He “must” (i.e. it is an overriding professional duty or principle imposed by the GMC) be satisfied that it would better serve the patient's needs than an appropriately licensed alternative before he can lawfully prescribe the unlicensed drug.

24. The remedy for acting in breach of the GMC Guidance is that a complaint may be made about the individual doctor to the GMC. If the complaint is proved, the GMC can impose sanctions and, at worst, strike the doctor off the medical roll. However acting in breach of GMC Guidance does not necessarily mean that the doctor has breached any common law legal duty to the patient (and thus does not, of itself, given
any right for a patient to sue the doctor in the civil courts) but if the patient has an adverse reaction to the unlicensed medicine a doctor may well be held to have breached his duty of care to the patient by failing to prescribe the licensed medicine.

25. Accordingly, if a PCT is prepared to fund both Avastin and Lucentis for retinal vein occlusion and diabetic macular oedema it seems overwhelmingly likely that doctors will follow the GMC guidance by prescribing Lucentis. However, given the substantially higher cost of Lucentis, I consider that it would be lawful for a PCT to consider a commissioning policy which only permitted Avastin to be prescribed for these conditions as part of NHS funded healthcare. If such a policy were to be adopted, individual doctors would not in practice face the regulatory dilemma which arises where they have a choice of different drugs.

Can a licensed product be lawfully supplied by a commercial supplier for an off-label use?

26. There have been arguments raised that a pharmacy that orders Avastin for the purpose of using it off label is acting unlawfully unless it is able to bring itself within the “specials” regime under Schedule 1 of the Medicines for Human Use (Marketing Authorisations etc) Regulations 1994. I consider that this argument is misconceived. A holder of a marketing authorisation is not entitled to market the product for any use other than in accordance with the terms of the marketing authorisation. However, given that use by clinicians of drugs off-label is (a) lawful and (b) the legal responsibility of the individual clinicians, I do not consider that any responsibility lies on the holder of the marketing authorisation to police the use made by the hospital pharmacy of the licensed product which is being sold to the hospital.

A choice of Avastin or Lucentis for wet AMD patients.

27. Finally I have been asked to advise concerning the lawfulness of providing clinicians with a choice of Avastin and Lucentis for patients with wet AMD where NICE TAG 155 applies. In 2003 the Secretary of State made the “Directions to Primary Care Trusts and NHS trusts in England concerning Arrangements for the Funding of Technology Appraisal Guidance from the National Institute for Clinical Excellence (NICE)” issued by
the Secretary of State for Health on 1st July 2003. Paragraph 2 of the Directions provides:

“Application of sums paid to Primary Care Trusts

2. Subject to paragraph 3 a Primary Care Trust shall, unless directed otherwise by the Secretary of State, in exercising those functions that it has been directed to exercise by the Secretary of State, apply such amounts of the sums paid to it under section 97C(1)(b) of the Act as may be required to ensure that a health care intervention that is recommended by the Institute in a Technology Appraisal Guidance is, from a date not later than three months from the date of that Technology appraisal Guidance, normally available:

(a) to be prescribed for any patient on a prescription form for the purpose of his NHS treatment;

or

(b) to be supplied or administered to any patient for the purpose of his NHS treatment”

28. The duty under the 2003 Directions on each PCT is to apply sufficient sums of the NHS funds to “ensure” that a health care intervention in a NICE TAG is “normally available” to those patients within the class of patients in the TAG. Thus the duty looks primarily to the financial arrangements of the PCT and requires the PCT to make an explicit decision to ensure that sufficient sums are made available to comply with a NICE TAG where such a treatment is prescribed by a clinician. In practice that means that patients within the clinical categories identified in the TAG must be offered the opportunity to have the recommended treatment.

The NICE TAG for Lucentis.

29. In August 2008 NICE published TAG 155 related to Lucentis (ranibizumab). For present purposes it is sufficient to note that the TAG recommended Lucentis in the following terms:

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10 See http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsLegislation/DH_4083088
11 See http://guidance.nice.org.uk/TA155
“Ranibizumab is recommended as a possible treatment for people with wet AMD if all the following apply to their eye:

- The best possible visual acuity after correction with glasses or contact lenses is between 6/12 and 6/96.
- There is no permanent damage to the fovea (the part of the eye that helps people to see things in sharp detail).
- The area affected by AMD is no larger than 12 times the size of the area inside the eye where the optic nerve connects to the retina.
- There are signs that the condition has been getting worse.”

30. The combined effect of the TAG and the 2003 Directions was that, 90 days after publishing the TAG, all PCTs were obliged to make resources available to ensure that Lucentis was “normally available” to be prescribed as part of NHS treatment for those patients coming within the clinical indicators in the TAG.

31. If the PCT were only to commission an Avastin service then it would, in my opinion, act unlawfully because it would be acting in breach of the 2003 Directions. However the TAG does not mean that every relevant patient must be provided with treatment according to the TAG. It would be lawful (in public law terms) for the PCT to have a commissioning policy which offered patients a choice. This would mean that clinicians would have the opportunity to prescribe either Avastin or Lucentis to patients with wet AMD. There are a variety of model policies adopted by different PCTs to deal with this situation and, as far as I am aware, no successful Judicial Review has been brought against any such policy for breaching the Directions (and this is not part of the challenge in the *SHIP* case). Accordingly, provided the clinicians are given a genuine choice between the 2 drugs (and subject to the EU arguments raised in the *SHIP* case which I have considered above) I do not see a significant legal risk in such a policy.

32. Lastly I am asked to advise whether it is possible to link decisions by clinicians to fund the cheaper drug, Avastin, to the availability PCT resources to support treatment for other eye conditions. The corollary of this approach is that clinicians would know that, if they elected to prescribe Lucentis for wet-AMD patients, there would be less funding for their other patients who had eye related conditions. This appears to me to be a proposed “programme budgeting” approach under which ophthalmologists are
to be provided with a set amount of funds for prescribing eye treatments and were left to make the most cost effective choices within the budget in order to serve the maximum number of patients.

33. This scenario seems to me to be very similar to the facts of *R (ABPI) v MHPRA* [2011] P.T.S.R. 391 where, as part of an overall policy of reducing the costs of medicines, primary care trusts and local health boards in England and Wales introduced schemes which rewarded medical practitioners financially for favouring the prescription of certain named medicines which were different from medicines that were already prescribed to patients or would have been prescribed but for the scheme, and which belonged to the same therapeutic class as, but did not contain the same active substance as, the replaced medicines. The Claimants in that case suggested the scheme was unlawful because it sought to persuade the doctors to act in their own economic interests and thus, by implication, against the interests of patients, and in breach of the EU rules on providing incentives to prescribe specified medicines. In that case the Court said at §33:

“In general terms, the health policy defined by a member state and the public expenditure devoted to it do not pursue any profit-making or commercial aim. Since a financial incentive scheme such as the one at issue in the main proceedings forms part of such a policy, it cannot be regarded as falling within the commercial promotion of medicinal products”

34. The Court also noted at §40 that a prescribing doctor is required, from the point of view of professional conduct, not to prescribe a given medicinal product if it is not fitting for the therapeutic treatment of his patient, despite the existence of public financial inducements for its prescription. It therefore did not accept that a financial inducement to switch medicinal product A (branded) to medicinal product B (unbranded) engaged the marketing and anti-incentive rules imposed by EU law.

35. If a direct financial inducement to the doctors did not breach EU law, it seems highly likely that an indirect inducement arising from programme budgeting would also not be in breach of EU law. That raises the question whether such a scheme would be unlawful in domestic UK law. I consider that, in principle, programme budgeting
under which clinicians are given responsibility for making decisions about which drugs to prescribe for their patients within a fixed budget is lawful, provided there is the possibility of the PCT extending the budget if exceptional and unforeseen circumstances were to arise. A policy under which clinicians were allocated specific additional funds for other eye treatments if savings were made by prescribing Avastin rather than Lucentis carries greater risks but, under the ABPI case, would still appear to me to be a lawful approach provided:

a. The policy ensured that clinicians were still required to exercise their own clinical judgment in each individual case to determine the most appropriate treatment for any individual patient; and

b. Any patient who made the decision that they wished to have Lucentis rather than Avastin would be provided with this treatment.

36. I hope that this covers all matters upon which I have been asked to advise. If anything is unclear or there are further developments in this matter then please come back to me.

DAVID LOCK QC

20th April 2012.
1. I have been asked to review the written advice that I gave to the University of Birmingham on 20 April 2012 (which was relevant to the West Midlands Commissioning Support Unit which is part of the University) in the light of the decision of the full Court of Justice of the European Union (“the Court”/“CJEU”) in Case C-185/10 Commission v Poland which was handed down (in Polish) on 29 March 2012 and was subsequently published in English and in the light of the Human Medicines Regulations 2012.

2. The facts which gave rise to the need for legal advice are set out in my previous Advice. The question (for present purposes) is whether, on further consideration, the decision of the Court of Justice in Commission v Poland has changed the position on the lawfulness of an NHS body having a policy which promotes patients to have a choice between Avastin and Lucentis.

3. I noted in my previous advice that the term “licensed” in this context refers to a medicinal product where a “marketing authorisation” has been granted to a commercial organisation by either the European Medicines Agency (“EMA”) or the Medicines and Regulatory Products Agency (“MHRA”). A marketing authorisation is required before a commercial organisation is able to market and/or sell any medicinal products within the EU. However the overall policy position is that whether a drug has a marketing authorisation or not has no direct effect on whether it is lawful for a clinician to prescribe that drug for a particular patient.
4. The regulatory regime for marketing drugs in England arose under the Medicines for Human Use (Marketing Authorisations etc) Regulations 1994. These Regulations have now been repealed by the Human Medicines Regulations 2012 (“the 2012 Regulations”) which came into force on 14th August 2012.

5. The 2012 Regulations define a “medicinal product” as being “any substance or combination of substances presented as having properties of preventing or treating disease in human beings”. It is thus clear that both Avastin and Lucentis are medicinal products within the meaning of the 2012 Regulations.

6. I have not been provided with the manufacturer’s licence for Avastin but I understand that it provides that the drug is to be used for the purpose of treating patients with colorectal cancer. Accordingly I assume that sub-dividing the drug into multiple aliquots for use as an eye treatment drug is not in accordance with the manufacturer’s licence. It has been helpfully pointed out in my instructions that the MHRA website provides:

   "Examples of off-label use of medicines

   Off-label intravitreal use of bevacizumab (Avastin, licensed for treatment of various solid cancers) has been associated with reports of severe eye inflammation and sterile endophthalmitis. The production methods, formulation, and doses for bevacizumab were developed for use in oncology. Its use in the ophthalmology setting has not been authorised.

   Clarification (updated August 2011): The preparation of bevacizumab for intravitreal use involves manipulation of the authorised medicine to produce multiple aliquots, usually in plastic

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12 This is full quotation part of which is in my instructions. For the full text see http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON087990

13 This Note appears to me to be slightly misleading because it equates the use of a drug with its licence. The use of Avastin for treating wet AMD is very well recognised internationally. For example the evidence in the recent case involving Novartis showed that over 50% of wet AMD patients in the USA are treated with Avastin rather than Lucentis. It has also been the subject of large scale trials which have recently reported and have suggested that the side effects of both drugs are broadly similar. There is a legal difference in that the use of Avastin for wet AMD is outside the licence and hence no product liability could be brought in the case of Avastin used for wet AMD patients. However, to the best of my knowledge, no such claim has ever been brought and so that issue would appear to be of no practical benefit to patients.
syringes (so-called compounding). Therefore, it is important to note that this process also results in the creation of an unlicensed medicine.

7. As I have explained in my previous advice, the concept of “licensing” of medicines is a concept which is directed at the right to market and sell medicinal products, because the term “licence” is a shorthand for a “marketing authorisation”. It is not a concept that is intended to impact on the use of medicinal products by NHS bodies within their own hospitals. The MHRA “correction” therefore appears to me to be slightly misleading because it ought to say that the dividing of Avastin into aliquots creates a product which does not have a marketing authorisation, and that it would therefore be potentially unlawful for such a product to be commercially marketed once it has been created.

8. In contrast, the use of Avastin by clinicians for wet AMD patients in the NHS is, as the full quote from the MHRA website shows, an “off label use” of the drug. In the usual case there is no question (as I understand matters) of a hospital pharmacy being involved commercial marketing of the Avastin aliquots once created, and therefore the question as to whether the product would require a fresh marketing authorisation for commercial marketing is strictly irrelevant.

9. I can understand that doctors are concerned about the use of a drug “off licence” when there is a licensed alternative. The GMC are presently conducting a consultation on changing their advice to doctors in relation to off label prescribing to allow wider circumstances in which off label prescribing can be permitted. The relaxations are opposed by the ABPI and the MHRA, who appear to me to be pursuing understandable sectional interests in attempting to restrict off label prescribing, even if this is massively to the advantage of patients and the wider NHS. The GMC has yet to provide updated guidance but the consultation makes it clear that it recognises that doctors are routinely acting outside the present guidance.

14 I anticipate that the “Clarification” has appeared on the MHRA website following lobbying from Novartis which is conducting a vigorous campaign to attempt to dissuade NHS bodies from using any drug for wet AMD patients other than Lucentis. The MHRA, as the government body responsible for licensing, are also not entirely neutral in these issues.
10. In these circumstances it seems to me that the key question for the University of Birmingham is whether the guidance that it gives, which may result in NHS hospital pharmacies dividing Avastin into multiple aliquots to create a drug that can be used to treat AMD, is in breach of the 2012 Regulations. If NHS hospital pharmacies are not acting in breach of the 2012 Regulations then it becomes irrelevant whether the process anticipated in the guidance has created a drug which, if it were to be subject to commercial marketing, would require its own marketing authorisation (commonly known as a “licence”).

11. Regulation 17(1) of the 2012 Regulations provides:

   "(1) A person may not except in accordance with a licence (a “manufacturer’s licence”)—

   (a) manufacture, assemble or import from a state other than an EEA State any medicinal product; or

   (b) possess a medicinal product for the purpose of any activity in sub-paragraph (a)"

12. A hospital pharmacy that divides Avastin into multiple aliquots to create a drug that can be used to treat AMD is probably not manufacturing the drug. However the word “assemble” is defined as follows:

   "‘assemble’ in relation to a medicinal product includes the various processes of dividing up, packaging and presentation of the product"

13. A hospital pharmacy that sub-divides Avastin into multiple aliquots for use as an eye treatment drug is “assembling” the drug in a way that is not in accordance with the manufacturers licence. Accordingly, unless an exemption applies, the hospital would be acting in breach of Regulation 17.

14. It is also relevant to consider Regulations 46(1) and (2) which provides:

   "(1) A person may not sell or supply, or offer to sell or supply, an unauthorised medicinal product.

   (2) A person may not sell or supply, or offer to sell or supply, a medicinal product otherwise than in accordance with the terms of—"
(a) a marketing authorisation;

(b) a certificate of registration;

(c) a traditional herbal registration; or

(d) an Article 126a authorisation"

15. It follows that, unless an exemption applies, an NHS pharmacy which sub-divides Avastin to use for wet AMD patients (in breach of the terms of the Avastin licence) would be acting in breach of Regulation 46.

16. The exemptions for pharmacies are in Regulation 4. Regulation 4(1) of the 2012 Regulations provides:

"Regulations 17(1) (manufacturing of medicinal products: requirement for licence) and 46 (requirement for authorisation) do not apply where any provision of section 10 of the Medicines Act 1968(1) so provides"

Accordingly if an activity is within section 10 of the Medicines Act 1968, it is outside the scope of Regulation 17 of the 2012 Regulations. Section 10 of the 1968 Act provides:

"10 Exemptions for pharmacists

(1) . . . The restrictions imposed by regulations 17(1) (manufacturing of medicinal products) and 46 (requirement for authorisation) of the 2012 Regulations(15) do not apply to anything which is done in a registered pharmacy, a hospital, a care home service or a health centre and is done there by or under the supervision of a pharmacist and consists of—

(a) preparing or dispensing a medicinal product in accordance with a prescription given by an appropriate practitioner, or

(b) assembling a medicinal product provided that where the assembling takes place in a registered pharmacy—

(i) it shall be in a registered pharmacy at which the business in medicinal products carried on is restricted to retail sale or to supply in circumstances corresponding to retail sale and the assembling is done with a view to such sale or supply either at that registered pharmacy or at any

(15) These are the 2012 Regulations as I have defined them in this Advice.
other such registered pharmacy forming part of the same retail pharmacy business, and

(ii) the medicinal product has not been the subject of an advertisement;

and those restrictions do not apply to anything done by or under the supervision of a pharmacist which consists of procuring the preparation or dispensing of a medicinal product in accordance with a prescription given by a practitioner, or of procuring the assembly of a medicinal product.

(2) . . .

(3) Those restrictions do not apply to the preparation or dispensing in a registered pharmacy of a medicinal product by or under the supervision of a pharmacist in accordance with a specification furnished by the person to whom the product is or is to be sold or supplied, where—

(a) the product is prepared or dispensed for administration to that person or to a person under his care, . . .

(b) . . .

(4) Without prejudice to the preceding subsections, the restrictions imposed by regulations 17(1) (manufacturing of medicinal products) and 46 (requirement for authorisation) of the 2012 Regulations do not apply to anything which is done in a registered pharmacy by or under the supervision of a pharmacist and consists of—

(a) preparing or dispensing a medicinal product for administration to a person where the pharmacist is requested by or on behalf of that person to do so in accordance with the pharmacist’s own judgment as to the treatment required, and that person is present in the pharmacy at the time of the request in pursuance of which that product is prepared or dispensed, or

(b) preparing a stock of medicinal products with a view to dispensing them as mentioned in subsection (1)(a) or subsection (3) of this section or in paragraph (a) of this subsection provided that such stock is prepared with a view to retail sale or to supply in circumstances corresponding to retail sale and the preparation is done with a view to such sale or supply either at that registered pharmacy or at any other registered pharmacy forming part of the same retail pharmacy business;

and those restrictions do not apply to anything which is done in a hospital or a health centre by or under the supervision of a pharmacist and consists of preparing a stock of medicinal products with a view to dispensing them as mentioned in subsection (1)(a) of this section.
(5) Without prejudice to the preceding subsections, the restrictions imposed by regulation 46 of the 2012 Regulations do not apply to the preparation or dispensing in a registered pharmacy of a medicinal product by or under the supervision of a pharmacist where—

(a) the medicinal product is prepared or dispensed otherwise than in pursuance of an order from any other person, and

(b) the medicinal product is prepared with a view to retail sale or supply in circumstances corresponding to retail sale at the registered pharmacy at which it is prepared, and

(c) the medicinal product has not been the subject of an advertisement.

(6) Without prejudice to the preceding subsections, the restrictions imposed by regulation 17(1) of the 2012 Regulations do not apply to anything which is done in a registered pharmacy by or under the supervision of a pharmacist and consists of preparing a medicinal product with a view to retail sale or to supply in circumstances corresponding to retail sale at that registered pharmacy.

(6A) . . .

(7) . . .

(7A) The . . . Ministers may make regulations prescribing conditions which must be complied with if a thing is to be considered for the purposes of this section as done under the supervision of a pharmacist.

(7B) Conditions prescribed under subsection (7A) may relate to supervision in the case where the pharmacist is not at the place where the thing is being done, and in that case the thing is not to be so considered if no such conditions are prescribed.

(7C) In any case, compliance with any applicable conditions is sufficient for the thing to be so considered.

(8) For the purposes of this section “advertisement” shall have the meaning assigned to it by regulation 7 (advertisements relating to medicinal products) of the 2012 Regulations.

(9) In subsection (1) of this section, “care home service” has the meaning given by paragraph 2 of schedule 12 to the Public Services Reform (Scotland) Act 2010 (asp 8)”
18. I have set this out in full because it covers a variety of different circumstances and thus provides a variety of ways in which the actions of hospital pharmacies could be considered to be lawful, depending on the precise facts of an individual case. However in the usual NHS arrangement, the instructions to prepare the aliquots of Avastin are given to the pharmacy by the ophthalmologists. The ophthalmologists then use the preparation for their own patients. The process therefore appears to come within section 10(3) of the 1968 Act, and thus is exempted from the provisions of Regulations 17 and 46 of the 2012 Regulations. It follows that such a process is not unlawful even though the doctors are using the product in a way that does not accord with the terms of Avastin’s marketing authorisation.

19. Secondly I have been asked to advise concerning the Judgment C-185/10 Commission v Poland. This judgment does not cause me to alter my view, as summarised at paragraph 13 of the original Advice, that as a result of article 168(7) of the EU Treaty, the EU has no competence to specify which medicines are used by an EU state healthcare provider (including the NHS) for treating individual patients. The EU regulates the market in medicinal products but has no competence in determining which drugs a doctor can prescribe for his or her own patients.

20. The NHS does not generally manufacture its own drugs and accordingly it is required to purchase drugs and other products in the open market. It follows that the EU legal regime is relevant because the NHS must be able lawfully to purchase drugs from suppliers who are lawfully able to supply them to the NHS. Avastin is a medicinal product with a marketing authorisation for the treatment of colorectal cancer. It is thus a medicinal product which the NHS is entitled to purchase. There is nothing that breaches EU law, in my view, for an NHS body to purchase a licensed product with a view to using it for an off-label purpose. The use that an NHS makes of Avastin, once purchased, is not something over which EU law has any jurisdiction.

21. The Judgment of the Court in the case of C-185/10 Commission v Poland deals with the supply of medicines in the EU rather than the use to which licensed medicines are put within a national healthcare system. The court broadly concurs with the Opinion of Advocate-General Jääskinen on this topic (which was referred to at paragraph 10 of
my original Advice) but there are areas where the court has differences of approach and emphasis. However the following points are worthy of note:

a. At §49, specific reference is made to Article 4(3) of the Directive, emphasising Member State competence in relation to the setting of prices of medicinal products and the level of reimbursement by the national health insurance scheme (a provision not directly relied on by the Advocate-General). This confirms my own interpretation of this provision (and the related recital 33) at paragraphs 6 and 7 of the original Advice.

b. At §27, the Court appears to indicate that the “safeguarding public health” objective should continue to be approached at an appropriate level of generality. The Court appears not have applied the Advocate-General’s gloss (at §19 of his Opinion) that this objective is to be “achieved through the meticulous and uniform scrutiny of the pharmaceutical and medicinal properties of the product in question”, which could have conferred greater significance on this objective.

22. The Court did not directly refer to the observation raised in §29 of the Advocate-General’s Opinion, on which I relied at paragraph 10 of my original Advice, where reference was made to the exclusion from the scope of the Directive 2001/83/EC of medicinal products prepared in a pharmacy, as in the instant case. This view has therefore not been repeated by the Court but equally there is no suggestion in the judgment that the observation is not correct.

23. The University may also care to note that the IP rights holder for Lucentis, Novartis, commenced Judicial Review proceedings in December 2011 against a cluster of PCTs in Hampshire to complain about the unlawfulness of a policy to provide clinicians with a choice as to whether to prescribe Avastin or Lucentis. Novartis did not seek to rely on the Advocate General’s Opinion in the Poland case (or the subsequent decision of the Court) to suggest that the NHS bodies were acting unlawfully in having a policy which provided clinicians with a choice as to whether to prescribe Avastin or Lucentis. The Defence noted that Novartis did not allege that the policy under challenge and adopted by the PCTs breaches the 2001 Directive.
Novartis sought to advance their case by, amongst other matters, making an allegation that the Defendants’ decision somehow “undermines the objectives” of the 2001 Directive and that this in turn amounted to a breach of the duty of “sincere cooperation” contained in Article 4(3) of the Treaty on European Union (“TEU”). I was of the opinion that the case had little if any merit at the time the claim was made and remain of that view. I was surprised that Novartis were granted permission but the case never case to trial because a compromise was achieved and thus the point was never decided. However, of perhaps more significance, Novartis has (as far as I am aware) not attempted to run the same case with any of the many other NHS commissioning organisations which have a similar Avastin/Lucentis policy.

I therefore do not consider that the Poland case can successfully be relied upon to support a suggestion that the advice given by the University through the WMCSU to NHS bodies concerning possible approaches concerning the use of Avastin and Lucentis is unlawful. In my view the advice is lawful and there is nothing in the Poland case to suggest otherwise.

However I would observe however that the judgment in the Poland case has the potential to cause considerable difficulties for NHS bodies in other areas where a medical condition is treated using a medicinal product which does not carry a marketing authorisation and which is therefore ordered using the “specials” regime under article 5(1) of the Directive 2001/83/EEC and in accordance with Schedule 1 to the Medicines for Human Use (Marketing Authorisations etc) Regulations 1994 (as amended). A significant problem may arise if a pharmacologically similar medicinal product is brought onto the market (no doubt at very high cost as for a drug called Firdapse) which does have a marketing authorisation. In such circumstances the Poland case suggests that the NHS would not be able lawfully to continue to purchase the cheaper unlicensed medicine under the specials regime. Thus the NHS would appear to be obliged to purchase the more expensive medicine or will have to refuse to provide the required treatment to the patient. I can advise further on this point should it be relevant.
27. I hope that this covers all matters upon I have been asked to advise. Please come back to me if there is anything which is unclear.

DAVID LOCK QC

24th January 2013.
In the matter of the University of Birmingham

And in the matter of a proposed commissioning policy for Anti-VEGF Treatments in Eye Conditions

ADVICE (3)

1. I have been asked to provide some further advice about the lawfulness of advice given by the University of Birmingham concerning practices within the NHS relating to the purchase by NHS bodies of the drug Avastin for use for wet Age Related Macular Degeneration ("AMD") patients. In particular I have been asked to advise on the lawfulness of the practice of both NHS hospitals and a commercial company, ITH Pharma ("ITH"), in sub-dividing vials of Avastin and then selling the Avastin vials to NHS hospitals to use for treatment for AMD patients.

2. In summary I consider that the NHS hospitals, Royal Liverpool Hospital Manufacturing Unit and Moorfields Pharmaceuticals are likely to be acting lawfully in supplying sub-divided Avastin vials to NHS hospitals. However I consider that it is difficult to see how ITH can lawfully supply sub-divided vials of Avastin to NHS hospitals without breaches the relevant Regulations.

3. The background to this problem, as I explained in my last Advice, is that the use of Avastin for treating wet AMD is very well recognised internationally albeit this use is not in accordance with the drug’s marketing authorisation. The wide scale use of the drug for AMD patients is shown by the fact that (as I understand from a previous case in which I was instructed) over 50% of wet AMD patients in the USA are treated with Avastin rather than Lucentis. Avastin has also been the subject of large scale trials for wet AMD patients which have recently reported and have suggested that the side effects of both drugs are broadly similar. There is however a key legal difference in
that the use of Avastin for wet AMD is outside the terms of the drug’s marketing authorisation because the drug is only licensed for use for colorectal cancer patients.

4. Regulation 17 of the Human Medicines Regulations 2012 (“the 2012 Regulations”) provides that a person may not lawfully “assemble” a medicinal product. The definition of “assemble” under the 2012 Regulations includes dividing up a medicinal product into vials so that it is distributed otherwise than in accordance with the marketing authorisation. I understand that this is what the hospital pharmacies and ITH do in order to prepare Avastin in vials which can be used for AMD patients. It therefore seems to me that sub-dividing the vials of Avastin into smaller vials so that they can be sold on to provide treatment for AMD comes within the activities which are prohibited under Regulation 17. It follows that such an action would be unlawful unless the 2012 Regulations provide that an exemption applies to permit this activity to be carried out.

5. Regulation 46 of the 2012 Regulations provides that a person may not sell an unauthorised medicinal product. Once the vials of Avastin are sub-divided into smaller vials for use for AMD patients, the vials become an unauthorised medicinal product because the product is a medicinal product and it is not being prepared in accordance with the terms of the marketing authorisation. Accordingly Regulation 46 will be breached when the vials are sold to another NHS hospital unless an exemption applies.

6. There is, as I explained in my last advice, an exemption to the requirements under Regulations 17 and 46 of the 2012 Regulations for activities that come within section 10 of the Medicines Act 1968 (as amended). The text of section 10 is set out in my last advice and I will therefore not repeat it here. However in order to come within section 10 an activity needs:

a) To be “done in a registered pharmacy, a hospital, a care home service or a health centre”; 

b) To be “done there by or under the supervision of a pharmacist; and
c) To be an activity which comes within one of the specific sub-sections of section 10.

7. It seems to me that there may be a significant problem for ITM in fulfilling the first requirement. As a commercial company, it appears likely that ITM are not “a registered pharmacy, a hospital, a care home service or a health centre”. It is therefore difficult to see how they are able to bring themselves within the terms of section 10 (and it is not clear that they could rely on any other exemption because these products are not within the “specials” regime for the reasons set out in previous advices). I am conscious that the medicinal products in question here are not being purchased by the University of Birmingham. The medicinal products are being purchased by NHS bodies, but those bodies are being advised by the University of Birmingham.

8. In order to protect the position of the University, I recommend that the University of Birmingham includes in its advice to NHS bodies that there may be significant legal difficulties in purchasing sub-divided vials of Avastin for use for AMD patients from a commercial drugs company, and that NHS bodies who wish to do so should seek assurance from ITM that ITM is acting lawfully in supplying the vials to NHS bodies. Alternatively, it may be sensible for the University of Birmingham to ask my instructing solicitors to write to ITM to set out the problem, and to ask ITM to explain how they assert that they are acting lawfully. One paradox in this situation is that Avastin is marketed by Roche Products, which is a subsidiary of Hoffman La Roche. This company must be aware that ITM are sub-dividing Avastin vials for onwards sale for wet AMD patients but they are continuing to supply Avastin to ITM for such a purpose. Lucentis is marketed in Europe by a different company, Novartis. However Novartis are not the ultimate holder of the intellectual property rights in this drug. Those rights are held by another subsidiary of Hoffman La Roche. Thus Hoffman La Roche gains an income from both the sale of Avastin and the sale of Lucentis. The IP rights issue cannot affect the strict legality of the sales by Roche to ITM and their onward sale to the NHS, but it may explain why no action has been taken by Novartis to challenge the sales by ITM (because that would affect the commercial position of Roche).
9. In contrast, it seems likely that the Royal Liverpool Hospital Manufacturing Unit and Moorfields Pharmaceuticals are both part of the NHS Trusts in which they are located and are thus within the definition of a “hospital” in section 10(1) of the Medicines Act 1968. It also seems likely that Royal Liverpool Hospital Manufacturing Unit and Moorfields Pharmaceuticals can show that the sub-division of the vials takes place by or under the supervision of a pharmacist. Accordingly an exemption to the provisions of Regulations 17 and 46 of the 2012 Regulations will apply if one or more of the factual conditions in section 10 applies to the functions undertaken by Royal Liverpool Hospital Manufacturing Unit and Moorfield Pharmaceuticals.

10. Section 10(3) of the 1968 Act provides:

“Those restrictions do not apply to the preparation or dispensing in a registered pharmacy of a medicinal product by or under the supervision of a pharmacist in accordance with a specification furnished by the person to whom the product is or is to be sold or supplied, where—

(a) the product is prepared or dispensed for administration to that person or to a person under his care ..”

11. Thus if an NHS hospital were to commission the Royal Liverpool Hospital Manufacturing Unit or Moorfields Pharmaceuticals to “assemble” vials of Avastin for that hospital for use for AMD patients who are to be treated at the hospital, and then to sell the vials to the NHS hospital, it seems likely that these activities will come within section 10(3). The Regulations require that the specification for the medicinal product must be “furnished” by the NHS Hospital to Royal Liverpool Hospital Manufacturing Unit or Moorfields Pharmaceuticals. However I do not see any particular difficulty with this requirement in practice because the orders for the drug will be placed by pharmacists at the NHS hospitals with Royal Liverpool Hospital Manufacturing Unit or Moorfields Pharmaceuticals and thus the precise form of the vials can be set out by the acquiring hospital (even if this is in accordance with the standard product created by Royal Liverpool Hospital Manufacturing Unit or Moorfields Pharmaceuticals).
12. I therefore consider that this exemption is likely to apply and accordingly that the sale by Royal Liverpool Hospital Manufacturing Unit or Moorfields Pharmaceuticals to an NHS hospital is lawful because it is exempt from the provisions of Regulations 17 and 46 of the 2012 Regulations.

13. It is also possible that Royal Liverpool Hospital Manufacturing Unit and Moorfields Pharmaceuticals will be able to bring themselves within section 10(5) of the 1968 Act which provides that a medicinal product can be prepared with a view to “retail sale” or supply in circumstances corresponding to retail sale at the registered pharmacy at which it is prepared. The Royal Liverpool Hospital Manufacturing Unit and Moorfields Pharmaceuticals are not allowed to advertise the fact that they have this product on sale. However, provided they do not advertise, they are entitled to supply the product as part of a retail sale. There may be questions as to whether the supply of significant quantities of Avastin from one hospital to another amounts to “retail sales”. It could be argued that these were, properly analysed, wholesale transactions and not retail sales. However it is more likely that this will be classified as a retail sale because non-retail sales only cover cases where the product is supplied under circumstances where it is anticipated that there will be a further retail sale before the product reaches the customer.

14. I therefore consider that NHS bodies do not need to be overly concerned about acting unlawfully in purchasing sub-divided vials of Avastin from Royal Liverpool Hospital Manufacturing Unit or Moorfields Pharmaceuticals for use for wet AMD patients. There are however greater potential difficulties in purchasing the same product from a commercial organisation such as ITH and I would recommend that the advice given by the University should explain that this route to market may carry some legal risks.

15. I hope that this advice covers the additional questions raised in my instructions. Please come back to me if there is anything in the above advice which is unclear.
5th February 2013.
In the matter of the University of Birmingham

And in the matter of a proposed commissioning policy for
Anti-VEGF Treatments in Eye Conditions

NOTE

1. I have advised in detail concerning the legal position of NHS bodies that purchase vials of Avastin from NHS bodies for use for wet AMD patients. I have been asked to summarise my advice in this Note.

2. Although the law in this area is not straightforward, I consider that the NHS bodies are likely to be acting lawfully if their clinicians directed the NHS body to purchase Avastin from other NHS bodies such as Royal Liverpool Hospital Manufacturing Unit and Moorfield Pharmaceuticals who, in their own hospital pharmacies, have sub-divided the original vials of Avastin in smaller quantities that are suitable for AMD patients. I understand that there are some commercial drug companies who also offer this service. Unless those drug companies undertake the division work in a pharmacy, I consider that such companies are not likely to be acting lawfully in supplying sub-divided Avastin vials to NHS hospitals.

DAVID LOCK QC

19th February 2013.