**National Institute for Health and Clinical Excellence**

# Drug Allergy
## Scope Consultation Table
## 3rd – 31st October 2012

| | Type | Stakeholder | Order No | Section No | Comments<br>Please insert each new comment in a new row. | Developer's Response<br>Please respond to each comment |
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| 1. | SH | Action Against Allergy | 1 | General | We note that there is nothing in the guidelines to cover excipients in drugs despite the fact that many excipients include lactose, whey, casein, starches, sucrose or colourings which can cause significant health problems, even to the point of anaphylaxis, in the allergic/intolerant population.<br>Although it is theoretically possible to obtain 'specials' drugs made without these excipients, these are extremely expensive and doctors are very reluctant to prescribe as the cost comes from their budgets.<br>As a result allergic people may either go without drugs that they need or make themselves ill by taking drugs that they require but which still trigger an allergic (immediate or delayed) reaction.<br><br>We would like the guidelines to strongly encourage (require?) manufacturers to make versions of at least the more standard medications which did not include common allergens such as lactose, whey, casein, wheat starch and azo-dye-based colours which could be obtained at a reasonable cost from high street pharmacies either OTC or by prescription. | Thank you for your comment.<br><br>Whilst we agree that allergy or intolerance to excipients may be a problem for some patients, it will not be within the remit of the guideline to make specific recommendations to manufacturers to exclude certain excipients from the medications. The guideline's scope will focus on patients who present with signs and symptoms of drug allergy. |
| 2. | SH | Association of | 1 | 3.2.b | It would be appropriate to refer to | Thank you the scope has been |

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| | | Anaesthetists of Great Britain and Ireland | | | neuromuscular blocking agents as “drugs given during general anaesthesia” rather than “general anaesthetic agents”. The current wording implies that neuromuscular blocking agents cause patients to become anaesthetised (unconscious) whereas their effect is to cause temporary paralysis of the muscles. They have no effect on consciousness. | amended accordingly. |
| 3. | SH | Association of Anaesthetists of Great Britain and Ireland | 2 | 3.2.b | “aspirins” should be in the singular | Thank you for your comment this has been amended. |
| 4. | SH | Association of Anaesthetists of Great Britain and Ireland | 3 | 3.2.d | “ureas” should be in the singular | Thank you for your comment this has been amended. |
| 5. | SH | Association of Anaesthetists of Great Britain and Ireland | 4 | 3.2.d | Severe drug allergy may be associated with disorder of the ability of the blood to clot normally, and it is suggested that “blood coagulation tests” is added to the list of tests that may be undertaken during an acute reaction. | Thank you for your comment this has been amended. |
| 6. | SH | Association of Anaesthetists of Great Britain and Ireland | 5 | 3.2f | Many people who have experienced an adverse event during anaesthesia are very anxious about the possibility of needing surgery in the future and, unless the cause is investigated and diagnosed, they may actively avoid referral for future surgical treatment, with a consequent risk to their health. It would be valuable to include this information in the Scope. | Thank you for highlighting this, we aim to keep this section of the scope succinct and it is not meant to be exhaustive we acknowledge that other information could be included. |
| 7. | SH | Association of Anaesthetists of Great Britain and Ireland | 6 | 4.1.1 | It would be helpful to include a definition of “drug”. Patients are exposed to many agents during their care that may precipitate allergy symptoms, for example radiological contrast media, dyes injected into the tissues during breast surgery, and chlorhexidine given as an antiseptic mouthwash after dental treatment. These substances are important causes of severe hypersensitivity or allergy | Thank you for highlighting this, We have included a definition in section 3.1.a. |

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| | | | | | reactions and should be included in the definition of drugs. | |
| 8. | SH | Association of Anaesthetists of Great Britain and Ireland | 7 | 4.3.1 and 4.5 | It would be valuable to be able to make recommendations concerning the ways in which patients can inform healthcare professionals about drug allergies. Hazard-warning bracelets are life-saving. Currently, the only way in which a patient can obtain a hazard-warning bracelet is to pay private providers. There is often a requirement for continuing, annual payments for being included in the private provider's database. The requirement for payment may deter low-income patients from applying for a hazard-warning bracelet. It would be helpful for this issue to be considered by the guideline development group. The cost-effectiveness of providing this service under NHS provisions could be usefully included in the scope. | Thank you for your comment. Communication has been identified in the scope. Please see sections 4.3.1.a (patient information) and 4.3.1 c (documentation). The GDG will prioritise areas for cost effectiveness analysis. |
| 9. | SH | Association of Anaesthetists of Great Britain and Ireland | 8 | 4.4 | It would be informative to include published evidence relating to the numerical proportion of individuals with suspected drug allergy who are subsequently found not to be allergic. This is mentioned specifically in relation to antibiotics in 3.2f, but the proportion may vary considerably between different classes of drug. | Thank you for your comments. This section outlines the main outcomes that will be collected when reviewing the evidence. We will consider other relevant outcomes such as numerical proportion of individuals with suspected drug allergy where appropriate. |
| 10. | SH | British Association of Dermatologists | 1 | General | In general the scope looks satisfactory, although we feel it important not to exclude investigations of allergies to topical creams completely, not least because topical application of drugs can occasionally provoke systemic sensitivity. | Thank you for your comments. We have amended the scope and no longer list 'investigations of allergies to topic cream' as an excluded topic. |
| 11. | SH | British Association of Dermatologists | 2 | General | We feel that there should be adequate dermatological representation on the guideline development group. | Thank you for your comment. The, we agree and the final list of Guideline Development group members includes a Dermatologist. |
| 12. | SH | British Association of | 3 | General | We feel that the list of stakeholders is | Thank you for your comment. |

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| | | Dermatologists | | | appropriate. | |
| 13. | SH | British Society for Allergy and Clinical Immunology | 1 | 4.3.1d and 3.2b | Two other groups of drugs implicated in allergic reactions include radiocontrast media (RCM) and biological agents (monoclonal abs). It is conceivable that it would be difficult to produce a comprehensive list of drugs for which testing would be feasible. However, it would be useful to broadly categorise them as follows:<br>1. Antibiotics<br>2. Anaphylaxis during general anaesthesia<br>3. Local anaesthetic agents<br>4. Aspirin and NSAIDs<br>5. Radiocontrast media (RCM)<br>6. Biological agents<br>7. Others | Thank you for your comment. We were unfortunately unable to cover all areas and focused on those that stakeholders initially suggested as important areas to address. We have listed the drugs most commonly referred to by stakeholders. |
| 14. | SH | British Society for Allergy and Clinical Immunology | 2 | 4.1.1b | **Special groups:**<br>It would be helpful to produce guidance for the following groups:<br>1. Cystic Fibrosis<br>2. Severe and Brittle asthma | If these are appropriate, subgroups will be covered in individual clinical reviews and the GDG will make decisions related to the evidence presented. |
| 15. | SH | British Society for Allergy and Clinical Immunology | 3 | General | 1. If 'drug allergy' rather than 'hypersensitivity' (HS) is being used as standard nomenclature, it would be helpful to clarify that only immediate and nonimmediate (not type-2 and type-3 HS responses) reactions will be within the scope of this guideline.<br>2. Given the 'unmet need' for specialist allergy services in UK, in particular those able to offer drug allergy testing, it would be helpful to produce guidelines regarding 'who should be investigated' ? eg: Who should be investigated for penicillin allergy ? This will help rationalise and maximise the limited resources. | Thank you, definitions of drug allergy will be considered by the GDG and clarified in the guideline.<br><br>Thank you for your comment. Management in non-specialist settings and referral to specialist services has been identified in the scope. Please see sections 4.3.1.d and e. Specific areas to be addressed will be discussed and prioritised by the GDG. |

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| | | | | | 3. Given the specialised nature of testing involved, and to maintain quality assurance, criteria should be set on 'who should provide these services'.<br>4. One of the difficulties in clinical practice is obtaining accurate information about drug reactions, particularly those that have occurred some years ago. It would helpful to introduce a short 'mandatory' questionnaire (symptoms, temporal association etc.) to be completed by physicians when a patient reports an adverse reaction to a medication that is deemed to be allergic, so this information could utilised at a future date should investigations become warranted.<br>5. **Special categories**:<br><u>Drug desensitisation</u>:<br>(A) Indications: eg: for aspirin – in nasal polyps, asthma, coronary artery disease, antibiotics, cancer drugs, biological agents used for immunological disorders ?<br>(B) Who should offer this service | . |
| 16. | SH | British Society for Cutaneous Allergy | 1 | 4.3.2 d) | We note that it isn't intended to cover investigation of allergic reactions to topical drugs.<br>We believe that there may be value in including this for the following reasons:<br>Allergy to topical drugs is a common cause of morbidity<br>Many topical drugs that commonly cause contact allergy are also used systemically such as corticosteroids, NSAID, antibiotics, local anaesthetic and may be available in | Thank you for your comments.<br><br>Where there is overlap between systemic and topical drug allergy this will be considered for inclusion. Much of the scope for this guideline is generic and some topical drug allergies may fulfil the criteria for inclusion. However they will not be examined separately.<br><br>We have removed the bullet point which |

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| | | | | | both topical and systemic forms.<br>Individual's sensitised following topical administration may develop reactions following systemic administration of the same or related drug.<br>Patch testing, the main investigation for reactions to topical drugs, is also a useful tool in the investigation of specific cutaneous drug reactions to systemically administered drugs. | excluded the investigations into allergies to topic cream from the scope to reflect this. |
| 17. | SH | British Society for Immunology | 1 | 3.2 | Additional specialist investigations such as use of Basophil activation testing is not mentioned and should be included for completeness | Thank you for highlighting this, we aim to keep supporting information in the scope succinct and it is not meant to be exhaustive we acknowledge that other information could be included. |
| 18. | SH | Co Durham and Darlington PCT | 1 | 4.1.1b | Given that there are reactions differ between population groups (women, ethnic differences), different contexts (the use of many unlicensed drugs in children, pregnancy), and the relative exclusion of some or all of these groups in research trials, I think it would be helpful to include relevant sub-sections. | Thank you for your comment.<br><br>If these are appropriate subgroups will be covered in individual clinical reviews and the GDG will make decisions related to the evidence presented. |
| 19. | SH | Neonatal and Paediatric Pharmacists Group | 1 | General | Just a brief message to let you know that the Neonatal and Paediatric Pharmacists Group (NPPG) is happy with the scope as circulated. | Thank you for your comment. |
| 20. | SH | Regional Department of Immunology<br>Royal Victoria Infirmary, | 1 | 3.1d &e | Does not mention direct histamine-releasing effects of drugs | Thank you for highlighting this, we aim to keep this section of the scope succinct and it is not meant to be exhaustive we acknowledge that other information could be included. |
| 21. | SH | Regional Department of Immunology, Royal Victoria Infirmary | 2 | 3.1k | Reactions to general anaesthetic agents may occur without prior exposure | Thank you for highlighting this, it is noted in the scope in section 3.1.c as a general comment on drug allergy. |

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| 22. | SH | Regional Department of Immunology**,** Royal Victoria Infirmary | 3 | 4.4 | This will not be possible without modification of data collected on admissions and events i.e. the establishment of a national register. The scope therefore needs to discuss methodologies for collection of robust data collection. | Thank you for your comment. This is outside the remit of the guideline. |
| 23. | SH | Royal College of Anaesthetists | 1 | 3.2.b | It would be appropriate to refer to neuromuscular blocking agents as “drugs given during general anaesthesia” rather than “general anaesthetic agents”. The current wording implies that neuromuscular blocking agents cause patients to become anaesthetised (unconscious) whereas their effect is to cause temporary paralysis of the muscles. They have no effect on consciousness. | Thank you the scope has been amended accordingly. |
| 24. | SH | Royal College of Anaesthetists | 2 | 3.2.b | “aspirins” should be in the singular | Thank you for your comment this has been amended. |
| 25. | SH | Royal College of Anaesthetists | 3 | 3.2.d | “ureas” should be in the singular | Thank you for your comment this has been amended. |
| 26. | SH | Royal College of Anaesthetists | 4 | 3.2.d | Severe drug allergy may be associated with disorder of the ability of the blood to clot normally, and it is suggested that “blood coagulation tests” is added to the list of tests that may be undertaken during an acute reaction. | Thank you for your comment this has been amended. |
| 27. | SH | Royal College of Anaesthetists | 5 | 3.2f | Many people who have experienced an adverse event during anaesthesia are very anxious about the possibility of needing surgery in the future and, unless the cause is investigated and diagnosed, they may actively avoid referral for future surgical treatment, with a consequent risk to their health. It would be valuable to include this information in the Scope. | Thank you for highlighting this, we aim to keep this section of the scope succinct and it is not meant to be exhaustive we acknowledge that other information could be included. |

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| 28. | SH | Royal College of Anaesthetists | 6 | 4.1.1 | It would be helpful to include a definition of "drug". Patients are exposed to many agents during their care that may precipitate allergy symptoms, for example radiological contrast media, dyes injected into the tissues during breast surgery, and chlorhexidine given as an antiseptic mouthwash after dental treatment. These substances are important causes of severe hypersensitivity or allergy reactions and should be included in the definition of drugs. | Thank you for highlighting this, We have included a definition in section 3.1.a. |
| 29. | SH | Royal College of Anaesthetists | 7 | 4.3.1 and 4.5 | It would be valuable to be able to make recommendations concerning the ways in which patients can inform healthcare professionals about drug allergies. Currently, the only way in which a patient can obtain a hazard-warning bracelet is to pay private companies. There is often a requirement for continuing, annual payments. The requirement for payment may deter low-income patients from applying for a hazard-warning bracelet. It would be helpful for this issue to be considered by the guideline development group. The cost-effectiveness of providing this service under NHS provisions could be included in the scope. | Thank you for your comment. Communication has been identified in the scope. Please see sections 4.3.1.a (patient information) and 4.3.1 c (documentation). The GDG will prioritise areas for cost effectiveness analysis. |
| 30. | SH | Royal College of Anaesthetists | 8 | 4.4 | It would be informative to include published evidence relating to the numerical proportion of individuals with suspected drug allergy who are subsequently found not to be allergic.<br><br>This is mentioned specifically in relation to antibiotics in 3.2f, but the proportion may vary considerably between different classes of drug. | Thank you for your comments.<br><br>This section outlines the main outcomes that will be collected when reviewing the evidence. We will consider other relevant outcomes such as numerical proportion of individuals with suspected drug allergy where appropriate. |
| 31. | SH | Royal College of Pathologists University Hospital Southampton | 1 | 3.1.d | There are also IgG mediated (type II and III hypersensitivity reactions to drugs) e.g. with penicillin. We will probably see more type III | Thank you for highlighting this. |

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| | | Drug Allergy Unit | | | with the increasing use of biologics. | |
| 32. | SH | Royal College of Pathologists University Hospital Southampton Drug Allergy Unit | 2 | 3.1.k | Risk factors would come under another heading not morbidity and mortality? | Thank you for your comment, This has been amended. |
| 33. | SH | Royal College of Pathologists University Hospital Southampton Drug Allergy Unit | 3 | 3.2.b | Rephrase “drugs that commonly cause” to drugs commonly investigated/referred. This fits better with the “Current practice heading” | Thank you for your comment, This has been amended. |
| 34. | SH | Royal College of Pathologists University Hospital Southampton Drug Allergy Unit | 4 | 3.2.c | May we worth a reference to specialist tests done. Basophil activation (our centre (University Hospital Southampton (UHS)) and others (Sheffield) do use this as part of our patient assessment of drug allergy. Delayed type hypersensitivity reactions may require skin biopsy and histology (any dermatology comment on this?) | Thank you for highlighting this, we aim to keep this section in the scope succinct and it is not meant to be exhaustive we acknowledge that other information could be included. |
| 35. | SH | Royal College of Pathologists University Hospital Southampton Drug Allergy Unit | 5 | 3.2.d | Other tests include haptoglobin if red cell haemolysis suspect. ANA, I expect this is specifically histone antibodies that are important (this may be missed on some ANA screens and should be specifically requested).<br><br>Typo comma placement antineutrophil cytoplasmic (,) antibodies | Thank you for highlighting this, we aim to keep supporting information in the scope succinct and it is not meant to be exhaustive we acknowledge that other information could be included. |
| 36. | SH | Royal College of Pathologists University Hospital Southampton Drug Allergy Unit | 6 | 3.2.f | This also applies to adults; most of the adults we test for penicillin are negative. | Thank you we agree with your comment. This reference used was specific to children. |
| 37. | SH | Royal College of Pathologists University Hospital Southampton Drug Allergy Unit | 7 | 4.3.1.e | For managing patients in non-specialist centres the most important aspects are appropriate management of the acute event (if out of the scope of this we should at least refer to appropriate document on this) and identifying that a drug reaction has occurred and which type. | Thank you for your comments. |
| 38. | SH | Royal College of Pathologists University | 8 | 4.4.e | Delayed procedure/surgery is particularly important for those who have had | Thank you we agree with your comment. We have only listed main |

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| | | Hospital Southampton Drug Allergy Unit | | | perioperative anaphylaxis with the procedure aborted. | outcomes on the scope, specific outcomes relevant to each clinical question will be considered by the GDG. |
| 39. | 1. | Royal College of Physicians (RCP) | 1 | General | The RCP is grateful for the opportunity to respond to this draft scope. Overall, we believe that the scope requires modification to place drug allergy in the context of adverse drug reactions. To enable this going forward we would strongly recommend that the Guideline Development Group should include an appropriate clinical pharmacologist from the MHRA or one of the Yellow Card Centres.<br><br>We have also had sight of and would wish to endorse the response of the British Association of Dermatologists (BAD). | Thank you for your comment. The MHRA is a registered stakeholder and we look forward to their contribution to the guideline.<br><br>Your endorsement of the comments received from the British Association of Dermatologists is also noted. |
| 40. | 2. | Royal College of Physicians (RCP) | 2 | 3.1 | We agree that allergic reactions to drugs can be difficult to diagnose. They can also be difficult to differentiate from other adverse drug reactions. However, it is important to be clear what is meant. | Thank you for highlighting this, we aim to keep supporting information in the scope succinct and it is not meant to be exhaustive we acknowledge that other information could be included. |
| 41. | 3. | Royal College of Physicians (RCP) | 3 | 3.1b | This refers to 'other reactions are caused by drug intolerance, idiosyncratic reactions and pseudo-allergic reactions' The terms are undefined and do not fit with any standard nomenclature. This should be addressed. | Thank you for highlighting this, we aim to keep supporting information in the scope succinct and it is not meant to be exhaustive we acknowledge that other information could be included. |
| 42. | 4. | Royal College of Physicians (RCP) | 4 | 3.1 c | We believe that doctors experienced in adverse drug reactions (eg clinical Pharmacologists in the Regional Yellow Card centres) have a role to play in detection and diagnosis of drug allergy and other adverse | Thank you for your comment. |

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| | | | | | drug reactions. | |
| 43. | 5. | Royal College of Physicians (RCP) | 5 | 3.1 e | The description of adverse drug reactions as predictable or unpredictable, and the use of the term 'idiosyncratic' indicate an outdated view of the classification and pathogenesis of adverse drug reactions. [See for example Drug Safety: 2005 - Volume 28 - Issue 10 - pp 851-870] | Thank you for your comment. The scope has been amended. |
| 44. | 6. | Royal College of Physicians (RCP) | | 3.1 j | The figure here presumably refers only to immunological adverse drug reactions? | Thank you for your comment. These figures do refer to IGE mediated reactions. |
| 45. | 7. | Royal College of Physicians (RCP) | 6 | 3.1 k | 'the most important risk factor for drug allergy is a history of previous reaction to the same or related compound.'<br>This appears circular. | Thank you for your comment. We consider this to be an important point to be made and are happy with the wording. |
| 46. | 8. | Royal College of Physicians (RCP) | 7 | 3.2 c | Angiotensin-converting enzyme inhibitors do not 'commonly cause immunologically mediated adverse reactions'. Most cases of angioedema associated with ACE inhibitors are thought to be related to inhibition of the breakdown of bradykinin. | Thank you for your comment. This has been amended. |
| 47. | 9. | Royal College of Physicians (RCP) | 8 | 3.2 d | This omits a whole class of immunologically mediated dermatological adverse reactions (SJS/TEN); and other rarer reactions.<br><br>There is no discussion of the diagnostic accuracy of the tests | Thank you for highlighting this, we aim to keep supporting information in the scope succinct and it is not meant to be exhaustive we acknowledge that other information could be included. |
| 48. | 10. | Royal College of Physicians (RCP) | 9 | 3.2 e | What immunological causes other than allergy were to be considered? Drug-induced lupus? | Thank you for highlighting this, we aim to keep supporting information in the scope succinct and it is not meant to be exhaustive we acknowledge that other information could be included. |
| 49. | 11. | Royal College of Physicians (RCP) | 10 | 4.3.1 | Given the difficulties in establishing adverse drug reactions, and then in deciding whether an adverse reaction represents allergy or not, some guidance is absolutely required on | Thank you for your comment.<br><br>Thank you for your comment. The MHRA is a registered stakeholder and |

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| | | | | | when to suspect adverse drug reactions, and how to differentiate between immunological and non-immunological reactions. (See comments above regarding ACE inhibitors).<br><br>The scope (and the working group) really ought to include a clinical pharmacologist from MHRA or one of the Yellow Card Centres. | we look forward to their contribution to the guideline. |
| 50. | 12. | Royal College of Physicians (RCP) | 11 | 4.3.2 e | See comment above | Thank you for your comment. The MHRA is a registered stakeholder and we look forward to their contribution to the guideline. |
| 51. | 13. | Royal College of Physicians (RCP) | 12 | 4.4 | 30 day mortality and duration of hospital stay seem to be irrelevant outcomes, given that the guidance will not deal with the treatment of acute anaphylaxis, and no mention is made of SJS/TEN.<br><br>Given the outpatient nature of immunology and the emphasis on diagnosis, the correct outcome will relate to the diagnostic accuracy of the tests; the avoidance of further harm; and the non-avoidance of innocuous drugs (related to b, d, and f). | Thank you for your comment. The scope has been amended, and '30 day mortality' has been changed to 'mortality' and we believe that 'hospital length of stay' is relevant given the epidemiology of drug allergy.<br>We will not be looking at specific diagnostic tests and their accuracy and we believe that 'the avoidance of further harm; and the non-avoidance of innocuous drugs' have been covered in our current list of outcomes.<br><br>This is a list the main outcomes across all topics in the guidelines and the most appropriate outcomes will be considered for each specific review. |
| 52. | SH | Sheffield Teaching Hospitals NHS Foundation Trust | 1 | general | Maybe centres with expertise in adverse drug reactions should have a link included in the guideline. | Thank you for your comment. Specialist centres are not routinely listed in NICE guidelines. |
| 53. | SH | Sheffield Teaching | 2 | general | It may be worth mentioning that Tryptase | Thank you for highlighting this, we aim |

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| | | Hospitals NHS Foundation Trust | | | should be taken at the time of the reaction, 4 hours and 24 hours later. | to keep this section of the scope succinct and it is not meant to be exhaustive we acknowledge that other information could be included. |
| 54. | SH | The Royal College of Paediatrics and Child Health | 1 | 4.1.1 a) | Please confirm that the term “children” means those between 0 and 18 years of age. | Thank you for your comment the guideline has been amended accordingly. |
| 55. | SH | The Royal College of Paediatrics and Child Health | 2 | 4.3.1 d)<br>4.3.2 c) | Please explain the reason for choosing only local and general anaesthetics, beta-lactam antibiotics and NSAIDs in asthma. | Thank you for your comments. These drug classes are most commonly presented to the allergy clinic and mentioned by stakeholders. |
| 56. | SH | The Royal College of Paediatrics and Child Health | 3 | 3 d) | Direct activation of complement independent of antibody generation is another mechanism which might be considered as non- or pseudo-allergic because it does not require prior sensitisation which is the essence of allergy. | Thank you for highlighting this, we aim to keep this section of the scope succinct and it is not meant to be exhaustive we acknowledge that other information could be included. |
| 57. | SH | The Royal College of Paediatrics and Child Health | 4 | 3.2 b) | Can radio-contrast media be included? | The guideline will cover general recommendations for any drug allergy and the ones highlighted have been chose for their frequency in presenting at allergy clinics and those highlighted by stakeholders. |
| 58. | SH | The Royal College of Paediatrics and Child Health | 5 | 3.2 c) and 3.2 d) | Serum for tryptase must be taken both at the time of an acute reaction and when the patient has recovered to establish that there has been a change and to exclude mastocytosis. | Thank you for highlighting this, we aim to keep this section of the scope succinct and it is not meant to be exhaustive we acknowledge that other information could be included. |
| 59. | SH | The Royal College of Paediatrics and Child Health | 6 | 3.2 f) | 94% is higher than most published studies for tolerance of drugs previously assumed to cause allergy. 85% is a more appropriate figure. | Thank you for your comment. The reference for this figure is Mirakian R, Ewan PW, Durham SR et al. BSACI guidelines for the management of drug allergy. Clin Exp Allergy. 2009;39(1):43-61. |

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| 60. | SH | The Royal College of Paediatrics and Child Health | 7 | 4.1.1b) | Patients presenting with life threatening sepsis may require emergency assessment if presumed to have allergy to antibiotics required for the illness. In this situation rapid desensitisation is possible if allergy is confirmed. | Thank you for your comment. Appropriate subgroups will be identified according to clinical reviews during development. |
| 61. | SH | The Royal College of Paediatrics and Child Health | 8 | 4.3.2 | Topical creams may actually initiate sensitisation to drugs which will later cause problems by exposure through other routes. | Thank you for your comments. We have removed topical drugs from the exclusion list. |
| 62. | SH | The Royal College of Paediatrics and Child Health | 9 | 4.3.1 d) | It would be useful to have a list of which drugs can be tested by skin prick testing/specific IgE. For some drugs this is very useful, for others this is not. Apart from the drugs mentioned in 4.3.1 d) it would be useful to have a list for other drugs as well. | Thank you for highlighting this, we aim to keep supporting information in the scope succinct and it is not meant to be exhaustive we acknowledge that other information could be included. |
| 63. | SH | The Royal College of Paediatrics and Child Health | 10 | 4.3.1 d) | It would also be useful to specify the safety of intradermal testing and whether DGH can do this in children. | Thank you for your comment. Management in non-specialist settings has been identified in the scope. Please see sections 4.3.1.d and e. Specific areas to be addressed will be discussed and prioritised by the GDG |
| 64. | SH | The Royal College of Paediatrics and Child Health | 11 | 4.3.1 a) | A major problem is over diagnosis by some General Practitioners of drug allergy in children, particularly for antibiotics. It would be useful to have guidance for them on when to label children allergic to specific drugs. | Thank you for your comment. Management in non-specialist settings has been identified in the scope. Please see sections 4.3.1.d and e. Specific areas to be addressed will be discussed and prioritised by the GDG |
| 65. | SH | The Royal College of Radiologists (RCR) | 1 | Section 3 Clinical Need | The RCR notes that accurate diagnosis of an allergic reaction to contrast agents is difficult and frequently confounded by adverse drug reactions rather than an allergic response. Absolute proof of allergy is exceptional and will, as stated in the draft scope document, usually be a supposition based on history and clinical findings. | Thank you for your comment. |
| 66. | SH | The Royal College of Radiologists (RCR) | 2 | 3.1.i | It would be useful to define anaphylaxis in this section. | Thank you for highlighting this, we aim to keep this section of the scope succinct and it is not meant to be |

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| | | | | | | exhaustive we acknowledge that other information could be included. |
| 67. | SH | The Royal College of Radiologists (RCR) | 3 | 3.1.h (or elsewhere) | It would be useful to have a summary of how allergies are clinically manifest, in order of decreasing frequency, as a short section in the background. This is to be covered in section 4.3.1.a in the Guideline but an introductory paragraph would be useful. | Thank you for highlighting this, we aim to keep this section of the scope succinct and it is not meant to be exhaustive we acknowledge that other information could be included. |
| 68. | SH | The Royal College of Radiologists (RCR) | 4 | Section 3.2 Current Practice | The RCR understands that It is common practice in France for alleged contrast media allergy to be tested by patch skin testing to guide future exposure risk. Recommendations with regard to the scientific validity of this approach would be welcome. | Thank you for your comment this is outside the remit of the guideline. |
| 69. | SH | The Royal College of Radiologists (RCR) | 5 | 3.2.a | It would be better to say Cancer Centres may manage drug allergies related to their own treatment regimens. | Thank you for your comments. We have amended the scope. |
| 70. | SH | The Royal College of Radiologists (RCR) | 6 | 3.2.b / 4.3.1 | Contrast agents in Clinical Radiology include iodinated agents and gadolinium, but we note that other agents such as non-gadolinium agents used in MRI, ultrasound contrast agents and barium products all need including. | Thank you for your comment. This is beyond the remit of the guideline. |
| 71. | SH | The Royal College of Radiologists (RCR) | 7 | Section 4.3 Clinical Management | The RCR suggests that any recommendations arising from this guideline need to recognise the large numbers of individual doses of imaging agents administered in busy radiology departments. We advise that a practical and realistic approach is necessary to ensure acceptance. | Thank you for your comment. This is beyond the remit of the guideline. |
| 72. | SH | The Royal College of Radiologists (RCR) | 8 | 4.3.1 | The issue of documenting allergy, proven or supposed, in such a form that it is both accurate, available and highlighted in the radiology setting is very important. | Thank you we agree with your comment. |
| 73. | SH | The Royal College of Radiologists (RCR) | 9 | 4.3.2.b | It seems an omission to leave out treatment of an acute phase, including anaphylaxis, in guidelines on the management of drug | Thank you for your suggestion. This is beyond the remit of the guideline. |

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| | | | | | allergy. Anaphylaxis is specifically addressed in another NICE guidance but the acute management would be helpful for inclusion here. It is a key component of safe practice within Radiology. | |
| 74. | SH | The Royal College of Radiologists (RCR) | 10 | 4.3.f | The RCR suggests that there needs to be clarity on the criteria, to assist in patient care. This section is particularly relevant to Radiology as many patients are labelled as being 'Allergic to Contrast' or 'Allergic to Iodine', with many of these being inappropriate. | Thank you we agree with your comment and patient information and communication will be addressed in sections 4.3.1a and c. |
| 78 | SH | UK Clinical Pharmacy Association | 1 | General | The UKCPA fully endorses this much needed clinical guideline. The scoping document captures the many issues around this complex area. | Thank you for your comment. |
| 79 | SH | UK Clinical Pharmacy Association | 2 | 4.3.1.b | Documenting drug allergy. Could this be expanded to include communication of drug allergy between sectors (GPs, community pharmacies and hospitals). This should include documentation on prescriptions as well as sharing of or accessing information more easily. | Thank you for your comment. This is amended please see 4.3.1.c. |
| 80 | SH | UK Clinical Pharmacy Association | 3 | 4.5 | Economic analysis will hopefully cover the cost of declaring the patient does not have an allergy against the downstream savings of cheaper drugs, length of stay, mortality etc. There is growing evidence | Thank you for your comment. The GDG will decide upon areas in the scope which are prioritised for economic analysis. |

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| | | | | | for “non-specialists” to use diagnostic allergy tests. Could this be included as a cost comparison to specialist services. | |

**These organisations were approached but did not respond:**

ADDEPT
Aintree University Hospital NHS Foundation Trust
Allergy Alliance
Allergy UK
Allocate Software PLC
Association of Clinical Pathologists
Barnsley Hospital NHS Foundation Trust
British Dental Association
British Infection Association
British Medical Association
British Medical Journal
British National Formulary
British Psychological Society
British Society for Medical Dermatology
Cambridge University Hospitals NHS Foundation Trust
Capsulation PPS
Care Quality Commission (CQC)
Clarity Informatics Ltd
Croydon Health Services NHS Trust
Cygnet Hospital Harrow
Department of Health

Department of Health, Social Services and Public Safety - Northern Ireland
East and North Hertfordshire NHS Trust
Epilepsy Action
Faculty of Intensive Care Medicine
Faculty of Pharmaceutical Medicine
Faculty of Sport and Exercise Medicine
Greater Manchester West Mental Health NHS Foundation Trust
Guy's and St Thomas' NHS Foundation Trust
Hammersmith and Fulham Primary Care Trust
Health Quality Improvement Partnership
Healthcare Improvement Scotland
Hindu Council UK
Hockley Medical Practice
Humber NHS Foundation Trust
Imutest Limited
Independent Healthcare Advisory Services
Institute of Biomedical Science
Integrity Care Services Ltd.
Lancashire Care NHS Foundation Trust
Leeds Community Healthcare NHS Trust
Meda Pharmaceuticals Limited
Medicines and Healthcare products Regulatory Agency
Mind
Ministry of Defence
National Institute for Health Research  Health Technology Assessment Programme
National Institute for Health Research
National Patient Safety Agency

National Treatment Agency for Substance Misuse
Newcastle upon Tyne Hospitals NHS Foundation Trust
NHS Connecting for Health
NHS Direct
NHS Plus
NHS Sheffield
NHS South of England
North Essex Partnership Foundation Trust
North West London Perinatal Network
Northumberland, Tyne & Wear NHS Trust
Nottinghamshire Healthcare NHS Trust
Oxford Health NHS Foundation Trust
Public Health Agency
Public Health Wales NHS Trust
Public Health Wales NHS Trust
Roche Diagnostics
Royal College of General Practitioners
Royal College of General Practitioners in Wales
Royal College of Midwives
Royal College of Midwives
Royal College of Nursing
Royal College of Obstetricians and Gynaecologists
Royal College of Physicians
Royal College of Psychiatrists
Royal College of Surgeons of England
Royal Pharmaceutical Society
Royal Society of Medicine

Scottish Intercollegiate Guidelines Network
Social Care Institute for Excellence
South East Coast Ambulance Service NHS foundation Trust
South West Yorkshire Partnership NHS Foundation Trust
Southampton University Hospitals Trust
Spectranetics Corporation
St Andrews Healthcare
St Mary's Hospital
The Anaphylaxis Campaign
UK Liver Alliance
Walsall Local Involvement Network
Welsh Government
Welsh Scientific Advisory Committee
Western Cheshire Primary Care Trust
Westminster Local Involvement Network
Wirral University Teaching Hospital NHS Foundation Trust
York Hospitals NHS Foundation Trust

a) WHO defines an ADRs as “harmful, unintended reactions to medicines that occur at doses normally used for treatment”. ADRs can be classified into reactions which may affect anyone (type A) and reactions which affect only susceptible individuals (type B). We have used the term drug allergy for an ADR either with an established immunological mechanism. Within the definition of drug allergy we have also included any reaction presenting with symptoms commonly associated with immune-mediated reactions such as urticaria, angioedmea or asthma because the mechanism at presentation may not be apparent from clinical history True hypersensitivity reactions are immune-mediated and classified into Gell and Coombs categories. Drug allergy requires prior exposure to the same or a cross-reacting compound (sensitization) at a dose tolerated by the majority of individuals, although patients do not always give a history of prior drug exposure. A variety of mechanisms underpin the allergic symptoms experienced with subsequent courses of drug.