National Institute for Health and Clinical Excellence

Anaphylaxis
Guideline Consultation Comments Table
11 July – 08 August 2011

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	Airedale NHS Foundation Trust	25.00	Full	1.1.8	9	In our experience and in the below cited literature there is a small sub-group of patients who have suffered from serious side-effects of adrenaline during the treatment of anaphylaxis, mainly coronary artery spasm/thrombosis. O'Shea L, Oloko S, Miranda J.. Int J Clin Pract. 2009 Sep;63(9):1394. Ameratunga R, Webster M, Patel H. Postgrad Med J 2008;84:659-661.Johnston SL, Unsworth M, Gompels MM,. BMJ 2003; 326:589-590.Caballero JAR, Dominguez JFO et al.. Rev Esp Cardiol 1999;52:273-76. We have also mesenteric artery spasm/ ischaemia. There is also a small group of patients who in the context of an allergic reaction/anaphylaxis can experience significant supra-ventricular tachycardias even without the administration of adrenaline For both groups of patients it would be prudent to get immediate advice or arrange an urgent specialist appointment first before supplying an adrenaline injector	Thank you for your comment. The committee did consider the potential adverse events associated with the provision of adrenaline injectors. However, they concluded that the risk of harm was offset by the considerable benefits of preventing adverse outcomes from a recurrent anaphylactic episode.
SH	Airedale NHS Foundation	25.01	Full	1.1.9	9	We suggest the appointment of a clinical lead	Thank you for your comment. Unfortunately

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	Trust					for anaphylaxis in each hospital that receives acute admissions to co-ordinate the availability of expertise.	the specific makeup of the hospital staff is outside the remit of this guideline.
SH	Airedale NHS Foundation Trust	25.02	Full	3.1.2	16	Extraneous 'of' in the sentence below **False negative** People who have had an anaphylactic reaction but who have a diagnosis ~~of~~ not considered to be anaphylaxis will not be referred for specialist assessment or management.	Thank you for your comment. This is a typo which has been amended.
SH	Alder Hey Children's NHS Foundation Trust	26.00	Full	1.1.9	9	Anaphylaxis related deaths are associated with poorly controlled or unrecognised asthma. It is my opinion that all patients should be evaluated by clinical history for evidence of poorly controlled asthma and treatment initiated accordingly before discharge. Subsequent follow up can be determined by the allergist to whom the patient is referred and their GP.	Thank you for your comment. Unfortunately the management of associated co-morbidities was outside the scope of this guideline.
SH	Alder Hey Children's NHS Foundation Trust	26.01	Full	1.1.9	9	Epipen training as it stands is insufficient. Recent studies have shown that despite training people often do not use pens These guidelines should take the opportunity to provide guidance on more indepth epipen teaching – addressing the emotional component of an emergency situation, the importance of the patient being prone when a reaction occurs (often missed).	Thank you for your comment. The committee felt that as an interim measure pending an appointment with an allergy specialist that information and a demonstration on the use of an adrenaline injector would be sufficient.
SH	Alder Hey Children's NHS Foundation Trust	26.02	Full	General		The population of children who are not defined as having anaphylaxis but who have had severe allergic reactions may need to be included in future drafts.	Thank you for your comment. However, the final decision as to whether any reaction was anaphylaxis is taken following referral to a specialist allergy service, which is outside the remit of this guideline.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	Anaphylaxis Campaign, The	23.00	Full	General		The Anaphylaxis Campaign feels that a definition of a Specialist Allergy Service should be prominently included at the beginning of the document.	Thank you for your comment. The recommendations have been amended to define the type the areas of care that an individual requires following a referral. However, it is not possible to provide an exact definition of a specialist allergy service and its makeup as this is outside of the remit of this guideline.
SH	Anaphylaxis Campaign, The	23.01	Full	General		The term anaphylaxis is often misinterpreted and we feel the phrasing should be amended throughout to "anaphylaxis and severe allergic reaction". This is important as many patients will presenting with a severe reaction may not be treated as having anaphylaxis (due to mis-diagnosis) yet they would still benefit from following the guidelines. This is particularly important in the recommendations as they may be viewed without the full guideline.	Thank you for your comment. The definition of anaphylaxis has been clarified following consultation. The committee did consider the various terms currently used within the medical field and how anaphylactic reactions are sometimes termed severe allergic reactions. It was decided that to prevent any confusion as to the type of reaction that was covered by this guideline, that a definition for "suspected anaphylaxis" would be provided which listed the main clinical features of the reaction.
SH	Anaphylaxis Campaign, The	23.02	Full	Introduction	6	In the section on "Patient-centred care" we feel that reference should be made to patient support groups such as The Anaphylaxis Campaign.	Thank you for your comment. We recommend information is given to the patient on relevant support groups. We do not however define these groups within the main guideline but we do refer to them in the Understanding NICE guidance booklet that is produced alongside the main guideline. .
SH	Anaphylaxis Campaign, The	23.03	Full	1.1.7	8	We feel that the comment about shorter observation periods for those whose reactions are controlled promptly and easily needs careful	Thank you for your comments. The committee were aware of other pieces of guidance. However they felt, that based on the

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						consideration, as the RCP's "Emergency treatment of anaphylaxis in adults" recommends that "patients with suspected anaphylaxis should be observed in hospital for at least 6 hours and reviewed by a senior clinician".	evidence presented to them and their experience that the recommendations should not be changed.
SH	Anaphylaxis Campaign, The	23.04	Full	1.1.8	9	There is no guidance here for children under 10kg for whom an AI would not usually be prescribed	Thank you for your comment. The guidance document has been clarified and refers readers to the BNF for dosing. However, the recommendations have been amended to acknowledge that an appropriate adrenaline injector is offered. In addition the evidence to recommendations section has been update to reflect this point.
SH	Anaphylaxis Campaign, The	23.05	Full	1.1.8	9	The phrase "all patients who have been referred" is confusing as the guideline states that all patients should be referred. Needs to be reworded.	Thank you for your comment. The recommendations have now been clarified.
SH	Anaphylaxis Campaign, The	23.06	Full	1.1.12	9	Add "where possible" after age appropriate. If a specialist paediatrician is not available it is preferable for the child to see an adult with a speciality rather than a general paediatrician.	Thank you for your comment. Following consultation this recommendation has been amended, however this aspect has been retained.
SH	Anaphylaxis Campaign, The	23.07	Full	2	11	In the "Observation" box of the care pathway, we would like to see clarification of the term "young people".	Thank you for your comment. Following consultation the care pathway has been updated to reflect the amended recommendations.
SH	Anaphylaxis Campaign, The	23.08	Full	2	11	In the "Admission" box of the care pathway, we would like clarification that the term "children" refers to under 16s.	Thank you for your comment. Following consultation the care pathway has been updated to reflect the amended recommendations.
SH	Anaphylaxis Campaign, The	23.09	Full	2	11	In the care pathway box "Offer an adrenaline injector as an interim measure..." we would wish to see clarification of the dose of injector. If BNF guidelines are used, these suggest that a 500mg dose should be used, which **could** mean 2 injectors (depending on the brand).	Thank you for your comment. It is standard practice within NICE clinical guidelines to refer to the BNF for dosing.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	Anaphylaxis Campaign, The	23.10	Full	3.3.4	43	Under "Model assumptions", we would question why latex is not included in the list of mutually exclusive triggers of anaphylaxis.	Thank you for your comment. Latex was excluded because it accounts for a negligible (<1%) proportion of anaphylaxis (González-Pérez A,2010)
SH	Anaphylaxis Campaign, The	23.11	Full	3.3.4	44	In the "Adrenaline injectors..." bullet point, we would question the statement that adrenaline would prevent ALL deaths.	Thank you for your comment. This is a simplifying assumption in the model made on the basis of GDG expertise that the important determinants of effective adrenaline injector use are that they are used in a correct and timely manner. These are the factors captured in the model calculation.
SH	Anaphylaxis Campaign, The	23.12	Full	3.3.4	45	Under "Model parameters" we would query the "implication...that timely...use of adrenaline injectors **would** prevent deaths that might occur ..."	Thank you for your comment. This is a simplifying assumption in the model made on the basis of GDG expertise that the important determinants of effective adrenaline injector use are that they are used in a correct and timely manner. These are the factors captured in the model calculation.
SH	Anaphylaxis Campaign, The	23.13	Full	Evidence review	53	We are uncomfortable both with the mention of brand names in general and specifically with the mention of Jext, which is not yet on the market.	Thank you. Brand names have been excluded from the report.
SH	Anaphylaxis Campaign, The	23.14	Full	Evidence review	53	It is wrong to base the eveidence for AIs on a shelf life of 6 months. This was a situation for a very short period of time and we would now expect to see shelf lives of 12 months. This needs to be amended as this model will be used into the future and needs to show the accurate picture.	Thank you for your comment. The base-case shelf life for adrenaline injectors has been changed to 12 months, and it has been noted that this may represent a conservative estimate.
SH	Anaphylaxis Campaign, The	23.15	Full	Evidence review	53	Based on the comment above (23.14) , if the economic model is reworked using the longer shelf life the paragraph which refers to brand names can be removed.	Thank you for your comment. The base-case shelf life for adrenaline injectors has been changed to 12 months, and it has been noted that this may represent a conservative estimate.
SH	Association of Paediatric Emergency Medicine	31.00	Full	General		Although the guideline is specifically relating to confirmation of an anaphylactic episode the lack	Thank you for your comment. The guidance document has been amended to provide

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						of a simple diagram including key clinical features of anaphylaxis (especially in the care pathway on page 11) will force users to use two guidelines simultaneously in clinical practice. This is unhelpful and will detract from the guidelines use.	details on the typical presenting signs and symptoms.
SH	Association of Paediatric Emergency Medicine	31.01	Full	1.1.4	8	Unless mistaken in interpreting the guidance this appears to apply to under 16 year olds. With reference to the World Allergy Organisation guidelines on management of anaphylaxis - tryptase levels are not specific for anaphylaxis especially in food related allergy (predominate mode in children). Performing unnecessary blood tests in young children especially after having already received an im injection should be avoided at all costs. WAO Journal Feb 2011	Thank you for your comment. A separate recommendation has now been made regarding the use of mast cell tryptase tests in children.
SH	Association of Paediatric Emergency Medicine	31.02	Full	1.1.6	8	This must be made much more explicit as if to become a quality indicator would have potential repercussions on the designation of short stay units or other related observation wards.	Thank you for your comment. This guidance does not address issues regarding national quality indicators.
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.00	Full	General		Anaphylaxis presents as a spectrum in terms of clinical features and severity. It is not a single entity and overlaps with severe allergic reaction. In A&E the term severe allergic reaction is more often used; the term anaphylaxis is often not used, even when it is anaphylaxis. In addition the severity of reactions varies (and is hard to quantify depending on many variables including timing of treatment) from one reaction to the next. It would therefore be clinically valuable to include the phrase 'or severe allergic reaction' after anaphylaxis in several places in the	Thank you for your comment. The definition of anaphylaxis has been clarified following consultation. The committee did consider the various terms currently used within the medical field and how anaphylactic reactions are sometimes termed severe allergic reactions. It was decided that to prevent any confusion as to the type of reaction that was covered by this guideline, that a definition for "suspected anaphylaxis" would be provided which listed

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						guideline, particularly the recommendations, as these will stand alone.	the main clinical features of the reaction.
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.01	Full	Introduction	3	Definition anaphylaxis. There is not a precise definition for anaphylaxis and international definitions include many supplementary and explanatory statements. The definition given in the guideline is unhelpful and likely to be misleading, as it presents too severe a picture and is very concise. Fatal or near fatal anaphylaxis is important but rare. Suggest add further clinical detail after your existing statement, to provide a more typical and balanced picture: patients either have respiratory difficulty or hypotension, usually with cutaneous features.	Thank you for your comment. The definition has been amended following consultation.
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.02	Full	1.1.8	9	'all patients who have been referred…' This is confusing, as all patients are to be referred. Suggest reword to emphasis the 2 most important actions required after emergency treatment for suspected anaphylaxis 1. all people should be given information about the need for referral to a specialist allergy service and the referral process; 2. and (or, as appropriate, their parent and/or carer) offered an adrenaline injector as an interim measure pending the referral appointment. At present the referral is buried in a rather long list of actions (1.1.9). The referral (or lack of) is the major block in the care pathway and this needs to be highlighted	Thank you for your comment. The recommendations have now been clarified.
SH	British Society for Allergy & Clinical Immunology	19.03	Full	1.1.9	9	Remove the referral to 1.1.8 (see 19.02). This list is very long – and although it appears to be	Thank you for your comment. The recommendations have been amended.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	(BSACI)					chronological – the vital point is the referral. This is where the care pathway stops. This does not get sufficient emphasis here.	
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.04	Full	1.1.10	9	Add 'or severe allergic reaction' The reasons for this are: a. this is how anaphylaxis is commonly labelled in the acute setting eg A&E; b. these reactions involve a spectrum of severity, there is no exact cut-off between anaphylaxis and severe allergic reaction; c. the patient with a severe allergic reaction can be much worst in the next reaction and warrants referral as diagnosis and prevention are important. Please also see comment 19.00.	Thank you for your comment. The definition of anaphylaxis has been clarified following consultation. The committee did consider the various terms currently used within the medical field and how anaphylactic reactions are sometimes termed severe allergic reactions. It was decided that to prevent any confusion as to the type of reaction that was covered by this guideline, that a definition for "suspected anaphylaxis" would be provided which listed the main clinical features of the reaction.
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.05	Full	1.1.12	9	Suggest change to 'Refer people to a specialist allergy service, age-appropriate where possible, with the…' The reason is that when there is a lack of paediatric allergy services, referral to an adult allergy service is preferable to referral to a general paediatrician (if these are the options), as it is the specialist skills in allergy which are vital. This wording allows for referral to a paediatric allergist when one is available. Under present circumstances of inadequate allergy services nationally, this will enable best care for all, whereas the wording is restrictive.	Thank you for your comment. Following consultation this recommendation has been amended, however this aspect has been retained.
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.06	Full	Care pathway	11	Last box. After….'Refer people who have an initial anaphylactic episode'… Suggest add 'or severe allergic reaction'.	Thank you for your comment. The definition of anaphylaxis has been clarified following consultation.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							The committee did consider the various terms currently used within the medical field and how anaphylactic reactions are sometimes termed severe allergic reactions. It was decided that to prevent any confusion as to the type of reaction that was covered by this guideline, that a definition for "suspected anaphylaxis" would be provided which listed the main clinical features of the reaction.
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.07	Full	2	11	Last box. Please also see comment 19.05 for 1.1.12 Re-order 'Refer people to an age-appropriate specialist allergy service that has….' To 'Refer people to a specialist allergy service, age-appropriate where possible, that has….'	Thank you for your comment. Following consultation this recommendation has been amended.
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.08	Full		16	Suggest re-word	Thank you for your comment. The beginning of this section has been amended.
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.09	Full	3	16	Not clear why these terms have been used. This page assumes the test should always be positive in anaphylaxis. Clinicians know from experience that this is not the case. It may depend on the clinical picture; for example the tryptase level is less likely to be raised if the severe feature is respiratory rather than hypotension.	Thank you for your comment. This section is intended to describe the impact of these outcomes (ie. true positives, false positives, etc) from any potential diagnostic test for anaphylaxis. This has now been clarified in the guideline. The purpose is to set the context for assessing evidence on diagnostic accuracy. The evidence to recommendations section describes the application of these terms in the context of mast cell tryptase tests.
SH	British Society for Allergy	19.10	Full	3.1.3.2	17	The studies in anaesthesia are suspected	Thank you for your comment. The evidence to

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	& Clinical Immunology (BSACI)					anaphylaxis thus all are not necessarily anaphylaxis. Such series may include non allergic events caused by anaesthetic or surgical problems. Evaluating the usefulness of a test in a mixed population creates errors. Suggest amend evidence statement to reflect this	recommendations section has been amended to comment on the diversity of causes of anaphylaxis in the studies and the potential problems in interpretation of the results.
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.11	Full		26	Scranton 2009 study – suggest this should be excluded for the following reasons. Anaphylaxis was a side effect of immunotherapy (initial reaction medically induced in hospital) and not naturally occurring anaphylaxis. In addition the biphasic reactions were mild, and included 'malaise' (ie not a severe allergic reaction), many required no treatment. These are not significant reactions; and not biphasic anaphylaxis. Inclusion has resulted in a misleadingly high incidence of biphasic reactions. What is clinically important is the incidence of severe biphasic reactions – this is not reported	The Scranton study met the inclusion criteria as the initial presentation of the reaction met the definition of suspected anaphylaxis. The GDG acknowledged (and it was highlighted in the evidence to recommendations section) that the varying criteria used to classify a biphasic reaction had likely contributed to the high rates of biphasic reactions. Furthermore, removing this study will not have a large impact on the range off biphasic rates currently reported and, given that these studies were included as indirect evidence, it was decided that this study would remain included.
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.12	Full	Table 11	45	Footnote b. Specialist care should reduce further costs in idiopathic anaphylaxis as it provides acute treatment to stop or reduce progression of reactions so that many patients self –care at home. Hosp admission/attendance avoided. In addition, in a proportion of patients further reactions can be prevented by regular antihistamine therapy. This is known through clinical expertise of specialist allergists although unpublished.	Thank you. Although this rationale sounds reasonable, in the absence of evidence, it was not practical to account for this effect in the base-case economic analysis. However, we have added a note to the discussion that the analysis may be conservative with regard to the efficiency of SS.
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.13	Full	Table 12	46	The shelf life of adrenaline auto-injectors used is incorrect. This is longer. For devices currently available it is approx 18 months. A new device	Thank you**.** The base-case shelf life for adrenaline injectors has been changed to 12 months, and it has been noted that this may

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						(Jext) with 24 month shelf life will be available in Sept 2011. Even allowing for some devices having a shelf life <18months at point of prescription, a shelf life of 12months will still be an underestimate. Suggest this should be increased.	represent a conservative estimate.
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.14	Full		General	There are UK papers looking at the effect of specialist allergy v. general care in nut allergy (a major cause of severe allergic reactions/anaphylaxis) on the effectiveness of specialist treatment and incidence of recurrence of reactions. Ewan and Clark. These are prospective studies involving large numbers of patients over several years. Data is provided for different degrees of severity. These should be included as support for specialist care, providing evidence of decreased use of health care resources and cost saving	Thank you for your comment. Unfortunately the effectiveness of specialist care is outside of the scope of the main review and as such it is not possible to include these papers.
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.15	Full		60-61	Information to patients: production of a standard hand out would be helpful. This would help staff in A&E who will not likely have the appropriate expertise and allow more even care across the country	Thank you for your comment. NICE does not produce this type of material however we acknowledge the use of a standard hand out would be helpful. NICE does produce an understanding guidance booklet which provides further details to patients about allergy organisations.
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.16	Full	3.4.6	61	Recommendation 1.1.9 As above (comment 19.15)	Thank you for your comment. NICE does not produce this type of material however we acknowledge the use of a standard hand out would be helpful. NICE does produce an understanding guidance booklet which provides further details to patients about allergy organisations.
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.17	Full	3.5	61-62	Models of care Suggest include evidence (as suggested in comment 15) on effectiveness of specialist care.	Thank you for your comment. Unfortunately the effectiveness of specialist care is outside of the scope of the main review and as such it

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						In these studies, the allergen causing anaphylaxis was nut, a food known to be difficult to avoid because of the high rate of further reactions. Specialist care reduced severe reactions to close to zero.	is not possible to include these papers.
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.18	Full	3.5.3.1	65	This statement is incorrect (see 19.17)	Thank you for your comment. Unfortunately the effectiveness of specialist care is outside of the scope of the main review and as such it is not possible to include these papers.
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.19	Full	10	73	Suggest amplify the definition of anaphylaxis (see comments 19.00 and 19.01)	Thank you for your comment. The definition of anaphylaxis has been clarified following consultation.
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.20	Full	General	1	Primary Care comment. The title was confusing	Thank you for your comment. The title is derived from the referral received from the Department of Health.
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.21	Full	General & introduction	3	Primary Care comment. The definition of anaphylaxis was not helpful. GPs need a clear definition of what anaphylaxis is	Thank you for your comment. The definition of anaphylaxis has been clarified following consultation.
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.22	Full	2	11	Primary Care comment. The care pathway was liked but a request for more links to acute treatment suggests it may not be sufficiently clear that this guideline is what happens *after* acute treatment	Thank you for your comment. The first point of the care pathway is the provision of emergency treatment
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.23	Full	General		Primary Care comment. Auto-injectors. GPs require guidance on numbers of pens, dose of adrenaline to give, and some guidance on age and weight for prescribing different pens. There is inadequate knowledge in this area.	Thank you for your comment. As stated within the guidance document the guideline does not make recommendations on drug dosage; instead prescribers should refer to the 'British national formulary' for this information. The guideline also assumes that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.24	Full	General 3.4 3.4.5 3.4.6 Recs 1.1.9 and 1.1.11	57 - 60	Primary Care comment. It was felt the guideline could be more directive, and provide examples of what information to give to patients; and where to refer. It may be helpful to include that BSACI provide a list of NHS allergy clinics with their areas of expertise. www.bsaci.org (clinics). See comment 19.15	Thank you for your comment. The recommendations state the different areas of information that should be given. In addition the recommendations do state that patients should be referred to a specialist allergy service. While, it is not possible to provide a list of NHS allergy clinics within the guideline, recommendation 1.1.13 does state that referral pathways should be in place.
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.25	Full	General	24	Primary Care comment. GPs questioned whether tryptase could realistically be taken in a community setting. After treatment of severe allergic reactions patients are likely to be sent to A&E.	Thank you for your comment. The GDG considered the practicalities of this recommendation but felt that blood should be taken regardless of setting.
SH	British Society for Allergy & Clinical Immunology (BSACI)	19.26	Full	General		Primary Care comment. The guideline was felt to be rather long and cumbersome.	Thank you for your comment. The guideline is published with a quick reference guide which consists of the recommendations and the pathway to allow for a more concise read,
SH	British Society of Paediatric Gastroenterology, Hepatology & Nutrition (BSPGHAN)	9.00	Full	Care pathway		Patient information and support Information should be provided for families and carers of infants about a suitable replacement diet if cow's milk elimination is advised,	Thank you for your comment however this is outside of the scope of the guideline.
SH	British Society of Paediatric Gastroenterology, Hepatology & Nutrition (BSPGHAN)	9.01	Full	3.4.6 & 3.5.6		families and carers of infants on an exclusion diet should receive follow up from a specialist paediatric dietician to ensure that the replacement diet is adequate and to monitor growth	Thank you for your comment. Unfortunately the care that an individual should receive following referral is outside the scope of this guideline.
SH	Cambridge University Hospitals NHS Foundation Trust	17.00	Full	General		Anaphylaxis is not tightly defined and presents as a spectrum in terms of both clinical features and severity. It therefore is not a single entity	Thank you for your comment. The definition of anaphylaxis has been clarified following consultation.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	(Addenbrookes)					and overlaps with severe allergic reaction. In common medical usage, the term severe allergic reaction is more often used. Staff may be unsure – was this anaphylaxis, so tend not to use this term. It would therefore be important and clinically valuable to include the phrase 'or severe allergic reaction' after anaphylaxis in many places, especially the recommendations, each of which needs to stand alone.	The committee did consider the various terms currently used within the medical field and how anaphylactic reactions are sometimes termed severe allergic reactions. It was decided that to prevent any confusion as to the type of reaction that was covered by this guideline, that a definition for "suspected anaphylaxis" would be provided which listed the main clinical features of the reaction.
SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes)	17.01	Full	Introduction	3	Definition anaphylaxis. This is unhelpful for the target audience and rather misleading, as it presents too severe a picture, because fatal or near fatal anaphylaxis is rare. In international definitions, there are always several qualifying statements after the core definition. Suggest add further clinical detail giving a more typical picture, line 3, new sentence. 'Patients either have respiratory difficulty or hypotension, usually with cutaneous features.'	Thank you for your comment. The definition has been amended following consultation.
SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes)	17.02	Full	1.1.8	9	'all patients who have been referred…' This is confusing, as all patients are to be referred. Suggest reword Following emergency treatment for suspected anaphylaxis, all people should be given information about the need for referral to a specialist allergy service and the referral process; and (or, as appropriate, their parent and/or carer) offered an adrenaline injector as an interim measure pending the referral	Thank you for your comment. The recommendations have now been clarified.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						appointment.' These are the 2 most important actions required after emergency treatment and should be in a bullet point. At present the referral is buried in too long a list of actions (1.1.9)	
SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes)	17.03	Full	1.1.9	9	Remove the referral to 1.1.8 (see above). This list is very long – and although it seems to be chronological – the most vital point is the referral. This is where the care pathway stops currently. This does not get enough emphasis here.	Thank you for your comment. The recommendations have been amended.
SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes)	17.04	Full	1.1.10	9	Add 'or severe allergic reaction' The reasons for this are: a. this is how anaphylaxis is commonly labelled in the acute setting eg A&E; b. these reactions involve a spectrum of severity, there is no exact cut-off between anaphylaxis and severe allergic reaction; c. the patient with a severe allergic reaction can be much worst in the next reaction and warrants referral as diagnosis and prevention are important.	Thank you for your comment. The definition of anaphylaxis has been clarified following consultation. The committee did consider the various terms currently used within the medical field and how anaphylactic reactions are sometimes termed severe allergic reactions. It was decided that to prevent any confusion as to the type of reaction that was covered by this guideline, that a definition for "suspected anaphylaxis" would be provided which listed the main clinical features of the reaction.
SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes)	17.05	Full	1.1.12	9	Change to 'Refer people to a specialist allergy service, age-appropriate where possible, with the…' The reason is that when there is a lack of paediatric allergy services, referral to an adult allergy service is preferable to referral to a general paediatrician (if these are the options), as the specialist skills in allergy are vital for	Thank you for your comment. Following consultation this recommendation has been amended, however this aspect has been retained.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						these patients. This wording allows for referral to a paediatric allergist when one is available. It should also widen access to specialist care.	
SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes)	17.06	Full	Care pathway	11	Last box. After….'Refer people who have an initial anaphylactic episode'… Add 'or severe allergic reaction'.	Thank you for your comment. The definition of anaphylaxis has been clarified following consultation. The committee did consider the various terms currently used within the medical field and how anaphylactic reactions are sometimes termed severe allergic reactions. It was decided that to prevent any confusion as to the type of reaction that was covered by this guideline, that a definition for "suspected anaphylaxis" would be provided which listed the main clinical features of the reaction.
SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes)	17.07	Full	2	11	Last box. Re-order 'Refer people to an age-appropriate specialist allergy service that has….' To 'Refer people to a specialist allergy service, age-appropriate where possible, that has….' Explanation as 1.1.12 above	Thank you for your comment. Following consultation this recommendation has been amended.
SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes)	17.08	Full		16	Suggest re-word	Thank you for your comment. The beginning of this section has been amended.
SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes)	17.09	Full	3	16	This page assumes the test should always be positive in anaphylaxis. Clinicians know from experience that this is not the case. It may depend on the precise clinical feature eg tryptase is less likely to be raised if the severe	Thank you for your comment. This section is intended to describe the impact of these outcomes (ie. true positives, false positives, etc) from any potential diagnostic test for anaphylaxis. This has now been clarified in

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						feature is respiratory rather than hypotension.	the guideline. The purpose is to set the context for assessing evidence on diagnostic accuracy. The evidence to recommendations section describes the application of these terms in the context of mast cell tryptase tests.
SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes)	17.10	Full	3.1.3.2	17	The studies in anaesthesia are '**suspected** anaphylaxis' ie all are not necessarily anaphylaxis. Such series may include non allergic events caused by technical anaesthetic or surgical problems. Evaluating the usefulness of a test in a mixed population creates errors. Suggest amend evidence statement to reflect this	Thank you for your comment. The evidence to recommendations section has been amended to comment on the diversity of causes of anaphylaxis in the studies and the potential problems in interpretation of the results.
SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes)	17.11			24	Research recommendation. To study mast cell tryptase in anaphylaxis of different causes.	Thank you for your comment. Following consultation the committee drafted additional research recommendations and agreed on the top 5 to include in the guideline. Research into MCT in anaphylaxis of different causes was not felt to be a priority. Instead research into other potential mediators was of a greater importance than further research into MCT.
SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes)	17.12	Full		26	Scranton 2009 study – suggest this should be excluded as this is immunotherapy (initial anaphylactic reaction was medically induced in hospital) and not naturally occurring anaphylaxis. In addition the biphasic reactions were mild, and included 'malaise' and 'itching', many required no intervention. These are not significant reactions; and they are not biphasic anaphylaxis. Inclusion has resulted in a misleadingly high incidence of biphasic reactions. Clinically important is the incidence of severe biphasic reactions – this is not reported	The Scranton study met the inclusion criteria as the initial presentation of the reaction met the definition of suspected anaphylaxis. The GDG acknowledged (and it was highlighted in the evidence to recommendations section) that the varying criteria used to classify a biphasic reaction had likely contributed to the high rates of biphasic reactions. Furthermore, removing this study will not have a large impact on the range off biphasic rates currently reported and, given that these studies were included as indirect evidence, it was decided that this study would remain

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							included.
SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes)	17.13	Full	Table 11	45	Footnote b. Specialist care should reduce further costs in idiopathic anaphylaxis as it a. provides acute treatment to stop or reduce progression of reactions so that many patients self –care at home. Hosp admission/attendance avoided. b. in a proportion of cases further reactions can be prevented by regular antihistamine therapy. This is unpublished but well known through clinical experience of specialist allergists	Thank you for your comment. Although this rationale sounds reasonable, in the absence of evidence, it was not practical to account for this effect in the base-case economic analysis. However, we have added a note to the discussion that the analysis may be conservative with regard to the efficiency of SS.
SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes)	17.14	Full	Table 12	46	Shelf life of adrenaline auto-injectors used is incorrect. It is longer than stated. For devices available now ~18 months. A new device (Jext) with 24 month shelf life will be available in Sept 2011. Even allowing for some devices having a shelf life <18months at point of prescription, a shelf life of 12months will still be an underestimate.	Thank you. The base-case shelf life for adrenaline injectors has been changed to 12 months, and it has been noted that this may represent a conservative estimate.
SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes)	17.15	Full	General		On the question of effectiveness of specialist treatment and incidence of recurrence of reactions, there are UK papers looking at the effect of specialist allergy v. general care in nut allergy, a major cause of severe allergic reactions/anaphylaxis. These are prospective studies on large numbers of patients over several years and data is provided for different degrees of severity. These should be included as support for specialist care, providing evidence of decreased use of health care resources hence cost saving eg see 3 papers from the Cambridge group Ewan, Clark 2001, 2005, 2008	Thank you for your comment. Unfortunately the effectiveness of specialist care is outside of the scope of the main review and as such it is not possible to include these papers.
SH	Cambridge University Hospitals NHS	17.16	Full		60	re information to patients; production of a standard hand out would be helpful. BSACI	Thank you for your comment. NICE does not produce this type of material however we

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	Foundation Trust (Addenbrookes)					Standards of Care Committee could assist with this.	acknowledge the use of a standard hand out would be helpful
SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes)	17.17	Full	3.4.6	61	Rec 1.1.9 re information to patients; production of a standard hand out would be helpful. BSACI Standards of Care Committee could assist with this.	Thank you for your comment. NICE does not produce this type of material however we acknowledge the use of a standard hand out would be helpful
SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes)	17.18	Full	3.5	61-62	Models of care Suggest include evidence as suggested 3 boxes above (comment 16), on effectiveness of specialist care. In this study the allergen causing anaphylaxis is nut, a food known to be difficult to avoid because of the high rate of further reactions. Specialist care reduced severe reactions to close to zero.	Thank you for your comment. Unfortunately the effectiveness of specialist care is outside of the scope of the main review and as such it is not possible to include these papers.
SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes)	17.19	Full	3.5.3.1	65	Statement incorrect for reasons given above	Thank you for your comment. Unfortunately the effectiveness of specialist care is outside of the scope of the main review and as such it is not possible to include these papers.
SH	Cambridge University Hospitals NHS Foundation Trust (Addenbrookes)	17.20	Full	10	73	Suggest amplify the definition of anaphylaxis (as comment 2)	Thank you for your comment. The definition of anaphylaxis has been clarified following consultation.
SH	College of Emergency Medicine	15.00	Full	1.1.8	8	Suggest that 'all' is overly didactic, we suggest that a better form of words would be 'Children and young people who have suffered an anaphylactic episode should be usually admitted to hospital'	Thank you for your comment. The GDG considered the wording of this recommendation but felt that all children should be admitted under the care of a paediatric medical team.
SH	College of Emergency Medicine	15.01	Full	1.1.9	8	Again this is overly didactic. I am not sure it is necessary to teach patients or provide an epipen how to use an epipen before discharge,	Thank you for your comment. The committee felt that it was necessary for these actions to be carried out prior to discharge.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						if adequate early follow up can be assured. It would be a little daunting to ensure that every member of nursing and medical staff could train a patient to use an epipen. By insisting on this, patients may end up with a longer stay for little clinical benefit. We suggest that a better form of words might be 'Patients should be offered an adrenaline injector and trained how to use this safely. This should be done soon after an episode of anaphylaxis.' We disagree that all of these interventions must occur before a patient is discharged from hospital.	
SH	Department of Health	7.00	General			Department of Health has no substantive comments to make, regarding this consultation.	Thank you
SH	Lincoln Medical Ltd	13.00	Full		53	You have omitted any mention of the 3rd auto-injector licensed and available in the UK since July 2001 namely ANAPEN. This should be corrected please since it is in fact second to market after Epipen and Jext is totally unknown and has never yet been prescribed to a patient in the UK. Given that ANAPEN is manufactured in the UK by a UK based company we can and do control the supply chain of ANAPEN in the UK and in fact show on a web site the labelled expiry date of fresh product supplied every month into the market. Lincoln Medical have never supplied product with less than 15 months of labelled shelf life remaining. In fact in certain European countries we guarantee that no patient will get less than 15 months and on that basis the prescription is fully reimbursed. We can offer similar guarantees in the UK because	Thank you. All trade names have been excluded from the guideline.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						of the uniqueness of the fact that we manufacture here in the UK and not as Epipen (manufactured for a Swedish company in the USA) or Jext (manufactured for a Danish company in Germany).	
SH	Meda Pharmaceuticals Ltd	24.00	Full	Introduction	4	MEDA Pharmaceuticals believes that the recommendation to refer prescribers to the BNF for drug dosage is not appropriate. The dosage guidelines in the BNF are based on the Resuscitation Council Guidelines for the emergency treatment of anaphylactic reactions. This document offers guidance to healthcare professionals in the active phase of treating an anaphylactic reaction and does not cover self-administration of adrenaline by patients; However the NICE Guidance deals with the assessment and treatment of a patient post a suspected anaphylactic episode, The Resuscitation Council themselves in their supplemental publication Frequently asked questions on "Emergency treatment of anaphylactic reactions Guidelines for healthcare providers" states that "Auto-injectors are recommended primarily for use by laypeople for self administration. Guidance for their use must allow a greater degree of safety in terms of dose and recommended dosing interval" We believe that HCPs should be offered advice on the appropriate dose of auto-injector to prescribe to patients. The current practice is as follows: Adults and children over 30kg - 0.3mg adrenaline; children between 15kg and 30kg - 0.15mg adrenaline.	Thank you for your comment. It is standard practice within NICE clinical guidelines to refer to the BNF. However, the recommendations have been amended to acknowledge that an appropriate adrenaline injector is offered. In addition the evidence to recommendations section has been update to reflect this point.
SH	Meda Pharmaceuticals Ltd	24.01	Full	Introduction	5	We feel that this section should also state that the guidance is intended to provide advice on	Thank you for your comment. It is not possible to state within the introduction what the

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						patient self-administration of adrenaline.	guideline does and does not cover. The areas under consideration are set out in the scope (Appendix C)
SH	Meda Pharmaceuticals Ltd	24.02	Full	Patient Centred Care	6	Suspected anaphylaxis should be replaced by severe allergic reaction in this section to ensure that all patients are managed appropriately and not only those with an actual diagnosis of anaphylaxis.	Thank you for your comment. The committee did consider the various terms currently used within the medical field and how anaphylactic reactions are sometimes termed severe allergic reactions. It was decided that to prevent any confusion as to the type of reaction that was covered by this guideline, that a definition for "suspected anaphylaxis" would be provided which listed the main clinical features of the reaction. Therefore it is not possible to alter the wording within this section.
SH	Meda Pharmaceuticals Ltd	24.03	Full	1.1.8	9	When discussing the 'specialist allergy service' it would be helpful if there was guidance on the grade, range and expected qualifications of healthcare professionals working within such a service.	Thank you for your comment. Unfortunately the makeup of a specialist allergy service is outside the remit of this guideline.
SH	Meda Pharmaceuticals Ltd	24.04	Full	3.3.4	41	When considering the cost effectiveness of adrenaline injectors there are clear cost implications around training. However these costs are magnified if a change to device is made and there are also risks to patients if they are not familiar with their device and need to use it in a life threatening situation. There are also significant resource implications associated with making a wholesale change of device across a health economy and additional risks associated with patients potentially having more than one different device at any one time.	Thank you for your comment. Though we appreciate that there may be cost implications of making a wholesale change of device, there is no evidence that this will be the case Also, because we were not looking at comparing individual devices, average estimates for both costs and health benefits were used in the model.
SH	Meda Pharmaceuticals	24.05	Full	3.3.4	46	Table 12:	Thank you for your comment.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	Ltd					The cost of auto-injectors is not £28.97.The EpiPen® Auto-Injector costs only £26.45 All brands are different and the EpiPen® Auto-Injector is the least expensive by approximately 14% The assumption of a six-month expiry date is wildly inaccurate and refers to an unusual period in supply where the previous distributor was winding down distribution in preparation for the launch of their own device (which is still yet to appear on the market) Based on our comments on 3.3.4 page 53 (number 8) we would challenge the need for 4 auto-injectors per year based on a 6 month expiry date.	The base-case shelf life for adrenaline injectors has been changed to 12 months, and it has been noted that this may represent a conservative estimate and the cost of the injector changed to £26.45.
SH	Meda Pharmaceuticals Ltd	24.06	Full	3.3.4	52	The base case cost of £28.97 is inaccurate because Meda has reduced the price of EpiPen® Auto-Injector by 8% to £26.45 per unit since we took over control of the product in April.	Thank you. The cost has been changed to £26.45.
SH	Meda Pharmaceuticals Ltd	24.07	Full	3.3.4	53	We believe that the paragraph beginning "There is uncertainty…" is not an accurate reflection of the norm and should be removed or at the very least revised considerably. The committee acknowledges that this draft guidance was put together when the previous distributor of EpiPen auto-injector were winding down distribution in preparation for the launch of their own device, however since MEDA have taken over the ownership and stewardship in April 2011 there has been significant improvement in the supply chain MEDA is concerned with how the shelf life of auto-injectors, and in particular the EpiPen® Auto-Injector, is being portrayed. These concerns are two fold, firstly the use of	Thank you for your comments. The base-case shelf life for adrenaline injectors has been changed to 12 months, and it has been noted that this may represent a conservative estimate.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						theoretical shelf life is meaningless and secondly the current situation is not current and based on qualitative thoughts. This also leads to inaccuracies of the economic model of the various devices. As a result we feel it is important to highlight the current situation with some facts: MEDA took over the distribution of the EpiPen® Auto-Injector in April 2011 with the aim of improving 'practical shelf life'. This is being achieved by reworking the supply chain. To back this with data we provide the following information (Jan to Jul 11) which relates to the most commonly prescribed strength 0.3mg and the deliveries of stock into the UK: MEDA had multiple deliveries of new stock every month into the UK: Delivery Month Expiry Apr (MEDA start) 30/06/2012 (3 batches) May 31/07/2012 (2 batches) Jun 29/09/2012 (1 batch) Jul 31/10/2012 (3 batches) (Source UDG Inventory System) In contrast we can compare this to the only other available 0.3mg auto-injector today, Anapen: In the period Jan to Jul 2011 there have been just 2 deliveries into the UK Delivery Month Expiry Jan 20/06/2012 Feb 20/06/2012 (same batch?) (Source: www.lincolnmedical.co.uk) 300mcg Anapen has a longer theoretical shelf life than the EpiPen® Auto-Injector (24 vs. 18 mths) but it is clear that this is meaningless	

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						when looking at 'practical shelf life'. Not only was the EpiPen® Auto-Injector supplied into the UK with comparable shelf life, our consistent regular deliveries are ensuring that fresh stock is entering the supply chain every month unlike Anapen where the stock being supplied to pharmacies is, at best, from the February delivery. In addition, we do not believe it is appropriate for NICE to mention/include products which are not currently available on the market for which there is no empirical evidence of usage, neither is it appropriate to infer a theoretical shelf-life to a product which has no track record of supply anywhere in the world and which has been repeatedly delayed. We are concerned that the NICE guidance could be quoted as a commercial vehicle and yet the contents are currently based on unfounded assurances. We would be keen for the committee to revisit health economics model with this new data. Within the model the committee asserts that a patient has two auto-injectors at any time; is it therefore the view of the committee that all patients should have available at least two auto-injectors at anytime and will they be including that in the recommendations? The Resuscitation Council in their supplement to the anaphylaxis treatment guidelines recommend that "A second device should be prescribed for school children if one is to be kept at school, or if there is history of requiring multiple doses, or if the patient spends prolonged periods in a remote area".	
SH	Meda Pharmaceuticals Ltd	24.08	Full	3.3.4	54	We would suggest that empirical data is available and that a different cost-utility picture	Thank you for your comment. The base-case shelf life for adrenaline

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						will emerge when the 12 month expiry and the correct price for EpiPen® Auto-Injector are considered.	injectors has been changed to 12 months, and it has been noted that this may represent a conservative estimate.
SH	Meda Pharmaceuticals Ltd	24.09	Full	3.3.5	55	In the second table we feel it is worth re-emphasising the importance of familiarity with devices in reducing the risk of harm associated with improper use of adrenaline injectors.	Thank you for your comment. The guidance document has been amended.
SH	Meda Pharmaceuticals Ltd	24.10	Full	3.3.5	56	Whilst we acknowledge the importance of good patient support and training in relation to the use of devices, because patients have confidence in, and are familiar with, a specific device there may be a negative impact from this point of view if patients are given a different device.	Thank you for your comment. However, the psychological aspects of using particular devices was not considered as part of this guideline.
SH	Meda Pharmaceuticals Ltd	24.11	Full	3.4.5	60	We would like to clarify where the evidence for needle stick injuries is taken from and ask that this comment be removed unless published, rather than anecdotal, evidence is available on this issue	Thank you for your comment. The risk of needle stick injury was raised through GDG experiences and consensus to highlight the importance of proper training. This section has now been amended to make this clear
SH	Meda Pharmaceuticals Ltd	24.12	Appendix	1.1	4	Appendix F As for comment 6 and 8 we would like to challenge the cost of individual auto-injectors and also the need for them to be replaced every 6 months	Thank you. Base case shelf life has been changed to 12 months.
SH	Medicines and Healthcare Products Regulatory Agency (MHRA)	8.00	General			We can confirm that we have no comments for this draft guideline as it has little to say about medicines.	Thank you
SH	National Allergy Strategy Group	20.00	Full	General		It would be useful to have a definition of a Specialist Allergy Service at the beginning of the document.	Thank you for your comment. The recommendations have been amended to define the type the areas of care that an individual requires following a referral.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							However, it is not possible to provide an exact definition of a specialist allergy service and its makeup as this is outside of the remit of this guideline.
SH	National Allergy Strategy Group	20.01	Full	General		Phrasing throughout the document should be amended to "anaphylaxis and severe allergic reaction". This is important as many patients will presenting with a severe reaction may not be treated as having anaphylaxis (due to mis-diagnosis) yet they would still benefit from following the guidelines.	Thank you for your comment. The definition of anaphylaxis has been clarified following consultation. The committee did consider the various terms currently used within the medical field and how anaphylactic reactions are sometimes termed severe allergic reactions. It was decided that to prevent any confusion as to the type of reaction that was covered by this guideline, that a definition for "suspected anaphylaxis" would be provided which listed the main clinical features of the reaction.
SH	National Allergy Strategy Group	20.02	Full	1.1.8	9	Need to reword the phrase "all patients who have been referred" as further down the page it states all patients should be referred.	Thank you for your comment. The recommendations have now been clarified.
SH	National Allergy Strategy Group	20.03	Full	1.1.9	9	Can we emphasise the importance of referral here? Whilst it is included in the list it should be made clearer as the most important part of the pathway.	Thank you for your comment. The recommendations have been amended.
SH	National Allergy Strategy Group	20.04	Full	1.1.12	9	Can we add "where possible" after age appropriate. If a specialist paediatrician is not available it is preferable for the child to see an adult with a speciality rather than a general paediatrician.	Thank you for your comment. The recommendations have been amended in line with this suggestion.
SH	National Allergy Strategy Group	20.05	Full	2	11	In the care pathway section, comments 2 and 5 should be considered – add severe allergic reaction to the last box and where possible after	Thank you for your comment. Following consultation the care pathway has been updated to reflect the amended

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						age appropriate.	recommendations.
SH	National Allergy Strategy Group	20.06	Full	General		There is no guidance on the numbers of AIs or the necessary dose. When the guidance states an AI should be offered before discharge there is no mention of what to do if the patient is a child under 10kg.	Thank you for your comment. As stated within the guidance document the guideline does not make recommendations on drug dosage; instead prescribers should refer to the 'British national formulary' for this information. The guideline also assumes that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients. However, the recommendations have been amended to acknowledge that an appropriate adrenaline injector is offered. In addition the evidence to recommendations section has been update to reflect this point.
SH	National Allergy Strategy Group	20.07	Evidence review		53	The economic model should be based on a longer than 6 months shelf life – 12 to 18 months is more realistic.	Thank you. The base-case shelf life for adrenaline injectors has been changed to 12 months, and it has been noted that this may represent a conservative estimate.
SH	National Allergy Strategy Group	20.08	Evidence review		53	Based on the comment above, if the economic model is reworked using the longer shelf life the paragraph which refers to brand names can be removed.	Thank you for your comment. The base-case shelf life for adrenaline injectors has been changed to 12 months, and it has been noted that this may represent a conservative estimate.
SH	NETSCC, Health Technology Assessment (Ref 1)	27.01	Full	General		**2.1 Please comment on the validity of the work i.e. the quality of the methods and their application (the methods should comply with NICE's Guidelines Manual available at http://www.nice.org.uk/page.aspx?o=guidelinesmanual).** In general the methods employed are appropriate.	Thank you.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	NETSCC, Health Technology Assessment (Ref 1)	27.02	Full	General		**2.2 Please comment on the health economics and/or statistical issues depending on your area of expertise** Total financial implications are not estimated nor are the number of patients treated per year? It is not clear from the information whether all-cause mortality has been accounted for in the model.	Thank you for your comments. The budget/cost impact is not usually considered in guideline development. See the guidelines manual 2009 (section 7, p. 81): 'Guideline recommendations should be based on the estimated costs of the treatment options in relation to their expected health benefits (that is, their 'cost effectiveness'), rather than on the total cost or resource impact of implementing them'. All cause mortality has been accounted for and derived from life tables. The mortality due to anaphylaxis is additional to this. This has been clarified in the guideline.
SH	NETSCC, Health Technology Assessment (Ref 1)	27.03	Full	3.3.4	41	**2.2 Please comment on the health economics and/or statistical issues depending on your area of expertise** A Markov model is used to determine the cost-effectiveness of four mutually exclusive treatment options. SC no AI, SC with AI, SS no AI and SS with AI. This is appropriate PSA is used and the distributions are well justified – this is appropriate.	Thank you
SH	NETSCC, Health Technology Assessment (Ref 1)	27.04	Full	3.3.4		**2.2 Please comment on the health economics and/or statistical issues depending on your area of expertise** An incremental analysis is undertaken – this is appropriate. The cost-effectiveness of SS is £18/QALY, which appears remarkable low. SC+AI is dominated by SS no AI (less effective, more costs) this seems appropriate. The results for children are similar to those	Thank you

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						presented for Adults.	
SH	NETSCC, Health Technology Assessment (Ref 1)	27.05	Full	3.3.4		**2.2 Please comment on the health economics and/or statistical issues depending on your area of expertise** The lifetime time horizon was chosen for the model, which may be ambitious considering the lack of evidence used to popular the model. This is particularly important since a main driver of the model is the future recurrence rate. Sensitivity analysis tests the time horizon, but the minimum time frame presented is 5 years. In addition (p27 Appendix F), why is SS no AI sensitivity to changes in the time horizon but SS plus AI is not?	Thank you for your comment. The effect of time horizon from 1 year has been tested. The model's sensitivity to time horizon alterations for SS but not AI arises because the costs of SS are predominantly "front-loaded", so a reduction in time horizon reduces benefits but not costs, whereas the provision of AIs provides ongoing costs and benefits; therefore, limiting them has little effect on the relative cost effectiveness of those strategies.
SH	NETSCC, Health Technology Assessment (Ref 1)	27.06	Full	3.3.4	44	**2.2 Please comment on the health economics and/or statistical issues depending on your area of expertise** Page 44 (and appendix G) In the base case analysis a higher QoL (utility) is given to the SS group, as a result of reduced anxiety about the potential impact of a recurrence. Whilst there may be reason to believe that some anxiety exists, it is difficult to believe the magnitude being suggested in the guideline. The evidence supporting this is minimal and the method used to derive the increment (a 0.25 factor relative to the decrement of recurrence) is not explained fully or supported. It is suggested that the base case analysis excludes this factor. The impact of anxiety should be explored in the sensitivity analysis only.	Thank you. An additional scenario analysis has been performed and reported removing this assumed benefit. This suggested that the cost effectiveness of both specialist services and adrenaline injectors could be expected to reduce; however, ICERs for each option remained within the range normally considered to represent effective use of NHS resources. This conservative analysis provides reassurance that model results are not solely dependent on the assumed day-to-day HRQoL benefit.
SH	NETSCC, Health Technology Assessment	27.07	Full	3.34	48	**2.2 Please comment on the health economics and/or statistical issues**	Thank you for your comment. It is conceivable that people under SC will

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	(Ref 1)					**depending on your area of expertise** The effect of SS is substantial (approximately 4 fewer days per 100 people treated). The effect of adrenaline injectors is less compelling. The main driver in the model unsurprisingly is the recurrence rates. Given the uncertainty in the model and more details sensitivity analysis around this value should be undertaken. At present the average person with SC will have 6 anaphylaxis episodes. The model does not allow for the fact that if an individual has a second anaphylaxis episode, there treatment pathway may change considerable, since they are now identified as being at higher risk. Therefore the estimated benefit may be substantially bias in favour of SS.	eventually end up under the care of SS. The effect of reducing the time horizon has now been tested. This suggests that immediate referral to SS remains cost effective unless it can be assumed that all affected individuals will find their way to specialist care within 3 years (adults) or 2 years (children). Given the modelled recurrence rates (6 recurrences in the average lifetime of a 30-year-old would approximate to one per 7–8 years), this does not appear plausible.
SH	NETSCC, Health Technology Assessment (Ref 1)	27.08	Full	3.3.4	49	**2.2 Please comment on the health economics and/or statistical issues depending on your area of expertise** The evaluators suggest that a comparison between SC no AI and SC plus AI is appropriate since this reflects providing adrenaline prior to SS care. This comparison is inappropriate because the majority of the benefit and costs occur after the proposed SS visit. A better comparison would be to include a 5th group, SC plus AI for x months and then SS no AI thereafter.	Thank you for your comment. It is precisely to exclude the cost and benefit of post-referral treatment that we believe it is appropriate to concentrate on the comparison between SC no AI and SC plus AI to address the question of interim prescription of AIs. In addition, it should be noted that this comparison was robust to alterations in the time horizon to 0.5 years, suggesting that the costs and benefits that are predicted to arise in the very short term support the use of AIs before a first SS appointment.
SH	NETSCC, Health Technology Assessment (Ref 1)	27.09	Full	3.3.4	53	**2.2 Please comment on the health economics and/or statistical issues depending on your area of expertise** Recurrence and utility are the main drivers of the model. The values used in the model were	Thank you. Though the evidence base is weak, sensitivity analyses around these parameters do not fundamentally change the results. The guideline has been updated to make this point clearer in the discussion and conclusion sections of the CEA. Additional

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						derived from expert opinion therefore there is considerable uncertainty regarding the true values. Consequently the conclusions should be treated with caution.	sensitivity analyses have been undertaken and reported, suggesting that these values would have to be extremely poor estimates to invalidate the model results.
SH	NETSCC, Health Technology Assessment (Ref 1)	27.10	Full	2.4.3	14	**2.2 Please comment on the health economics and/or statistical issues depending on your area of expertise** Appendix F - Table 5 is repeated twice	Thank you. This has now been amended.
SH	NETSCC, Health Technology Assessment (Ref 1)	27.11	Full	2.4.3	16	**2.2 Please comment on the health economics and/or statistical issues depending on your area of expertise** Appendix F - "For example, about 62% of cases of anaphylaxis from any cause would die in not less than 20 minutes…." Consider re-wording.	Thank you. This has been amended.
SH	NETSCC, Health Technology Assessment (Ref 1)	27.12	Full	General		**3.1 How far are the recommendations based on the findings? Are they a) justified i.e. not overstated or understated given the evidence? b) Complete? i.e. are all the important aspects of the evidence reflected?** A major limitation is that the recommendations are partly based on the published literature, where evidence is available, but mainly based on expert opinion.	Thank you for your comment.
SH	NETSCC, Health Technology Assessment (Ref 1)	27.13	Full	3.1	12-20	**3.1 How far are the recommendations based on the findings? Are they a) justified i.e. not overstated or understated given the evidence? b) Complete? i.e. are all the important aspects of the evidence reflected?** The aim of this section was to determine whether mast cell tryptase testing should be performed in patients with suspected anaphylaxis. The rationale for testing is to reduce the number of false negatives. There	Thank you for your comment. A separate recommendation has now been made regarding the use of mast cell tryptase tests in children.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						was some evidence presented (all low quality studies) to support mast cell tryptase testing in adults, but none identified for children.	
SH	NETSCC, Health Technology Assessment (Ref 1)	27.14	Full	3.1	21	**3.1 How far are the recommendations based on the findings? Are they a) justified i.e. not overstated or understated given the evidence? b) Complete? i.e. are all the important aspects of the evidence reflected?** The sensitivity and specificity of mast cell typtase testing varied considerably between studies. Therefore it is difficult to ascertain a true value.	Thank you for your comment. The evidence to recommendations section has now been amended to emphasise the role of GDG opinion in light of the low quality evidence.
SH	NETSCC, Health Technology Assessment (Ref 1)	27.15	Full	3.1	23	**3.1 How far are the recommendations based on the findings? Are they a) justified i.e. not overstated or understated given the evidence? b) Complete? i.e. are all the important aspects of the evidence reflected?** The evaluators comment that the economic costs of testing are negligible, this is rather simplistic as they fail to discuss the impact of false positives and false negatives	Thank you for your comment. In the economic model assessing the cost effectiveness of SS, sensitivity analysis demonstrated that referral to SS remained an effective use of NHS resources even when the initial appointment was assumed to cost £10,000 per person. This suggests that any failure to account fully for the costs of MCT testing would have no impact on recommendations.
SH	NETSCC, Health Technology Assessment (Ref 1)	27.16	Full	3.1	24	**3.1 How far are the recommendations based on the findings? Are they a) justified i.e. not overstated or understated given the evidence? b) Complete? i.e. are all the important aspects of the evidence reflected?** In general the evidence supporting mast cell tryptase testing is poor and the recommendations are mainly derived from the opinion of the GDG	Thank you for your comment. The evidence to recommendations section has now been amended to emphasise the role of GDG opinion in light of the low quality evidence.
SH	NETSCC, Health Technology Assessment (Ref 1)	27.17	Full	3.2	24-31	**3.1 How far are the recommendations based on the findings? Are they a) justified i.e. not overstated or understated given the**	Thank you for your comment. The role of GDG opinion in making this recommendation has been emphasised in the evidence to

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						evidence? b) Complete? i.e. are all the important aspects of the evidence reflected? No studies were identified that addressed the effectiveness of observation or the length of time that any observation period should last. The recommendation is therefore based on the opinion of the GDG.	recommendations section.
SH	NETSCC, Health Technology Assessment (Ref 1)	27.18	Full	3.2	32	**3.1 How far are the recommendations based on the findings? Are they a) justified i.e. not overstated or understated given the evidence? b) Complete? i.e. are all the important aspects of the evidence reflected?** No formal economic analysis was performed on the length of observation. A costing analysis should be performed since this may have significant resource implications.	Thank you. This question was not considered an economic priority, due to paucity of evidence. Moreover, the GDG felt that, because the recommendation did not represent a major departure from current common practice, the likely cost impact could be assumed to be relatively small. We acknowledge that health economic modelling, in this area, could be instructive; however, in order to make this feasible, it would be necessary to generate substantial additional evidence, such as that recommended in the research recommendations. If such data become available in future, we would expect formal economic consideration to be given to this question in any update of this guideline.
SH	NETSCC, Health Technology Assessment (Ref 1)	27.19	Full	3.3	33	**3.1 How far are the recommendations based on the findings? Are they a) justified i.e. not overstated or understated given the evidence? b) Complete? i.e. are all the important aspects of the evidence reflected?** No evidence is available to support what should be part of the review after a reaction to confirm diagnosis of anaphylaxis	Thank you for your comment. Searches were conducted as part of the review process, however, no applicable studies were found. Therefore recommendations were based on the clinical expertise and experience of the GDG.
SH	NETSCC, Health Technology Assessment	27.20	Full	3.3	33	**3.1 How far are the recommendations based on the findings? Are they a) justified i.e. not**	Thank you for your comment. Following consultation this section has been amended.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	(Ref 1)					**overstated or understated given the evidence? b) Complete? i.e. are all the important aspects of the evidence reflected?** The evidence suggests women are at greater risk of recurrence than men. Age and ethnicity are not risk factors. Atopic dermatitis, urticaria-angioedema are also risk factors for recurrence	Although women are at a higher risk of recurrent anaphylactic episodes than men, it was felt that a large proportion of men still suffer from recurrent reactions and that any decision on whether to refer or not should not be based on gender.
SH	NETSCC, Health Technology Assessment (Ref 1)	27.21	Full	3.3.5	54	**3.1 How far are the recommendations based on the findings? Are they a) justified i.e. not overstated or understated given the evidence? b) Complete? i.e. are all the important aspects of the evidence reflected?** What should be part of the review – There was no evidence to support this section, all based on GDG	Thank you.
SH	NETSCC, Health Technology Assessment (Ref 1)	27.22	Full	3.4	59	**3.1 How far are the recommendations based on the findings? Are they a) justified i.e. not overstated or understated given the evidence? b) Complete? i.e. are all the important aspects of the evidence reflected?** Patient information – the evidence provided suggests that patients lack the specific knowledge, however there is no evidence that demonstrates providing no information will improve patient outcomes.	Thank you for your comment. However, the GDG felt that in the absence of any evidence on the effectiveness of providing information that as a result of lack of knowledge within patients that information should be provided.
SH	NETSCC, Health Technology Assessment (Ref 1)	27.23	Full	3.5	61	**3.1 How far are the recommendations based on the findings? Are they a) justified i.e. not overstated or understated given the evidence? b) Complete? i.e. are all the important aspects of the evidence reflected?** Models of care – no evidence – based on GPG	Thank you.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						opinion	
SH	NETSCC, Health Technology Assessment (Ref 1)	27.24	Full	General		**3.2 Are any important limitations of the evidence clearly described and discussed?** The limitations of the published evidence are significant and in general these are described in the guideline. To compensate for the lack of evidence the evaluators rely of the opinion of the GDG. Unfortunately a complete narrative is not presented to validate this opinion.	Thank you for your comment. Where possible, further clarification has been added within the evidence to recommendation section.
SH	NETSCC, Health Technology Assessment (Ref 1)	27.25	Full	General		**4.1 Is the whole report readable and well presented? Please comment on the overall style and whether, for example, it is easy to understand how the recommendations have been reached from the evidence.** The report is well written and easy to follow.	Thank you.
SH	NETSCC, Health Technology Assessment (Ref 1)	27.26	Full	33.2	33	**4.1 Is the whole report readable and well presented? Please comment on the overall style and whether, for example, it is easy to understand how the recommendations have been reached from the evidence.** The evidence is provided in table format, but not summarized in the corresponding text. The actual written summary of the table is found in the next section 333.2	Thank you for your comment. Throughout the document evidence is presented in a table format and then summarised into evidence statements in the subsequent section.
SH	NETSCC, Health Technology Assessment (Ref 1)	27.27	Full	3.2.1	24	**4.2 Please comment on whether the research recommendations, if included, are clear and justified.** No research recommendations have been suggested for the use or timing of mast cell tryptase testing. This is surprising given the paucity of evidence presented in the guideline	Thank you for your comment. The evidence to recommendations section has now been amended to emphasise the role of GDG opinion in light of the low quality evidence.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	NETSCC, Health Technology Assessment (Ref 1)	27.28	Full	General		**4.2 Please comment on whether the research recommendations, if included, are clear and justified.** Further work is required to estimate the recurrence rate. Further work is required to estimate the utility of anxiety associated with fear on anaphylaxis	Thank you for your comment. The committee have considered other areas for research recommendations and these have been included within the final guideline.
SH	NETSCC, Health Technology Assessment (Ref 2)	27.29	Full	General		**1.1 Are there any important ways in which the work has not fulfilled the declared intentions of the NICE guideline (compared to its scope – attached)** The areas of the scope are broadly covered by the guideline however the document generated is not likely to be of practical value in practice.	Thank you for your comment. NICE produce a set of implementation tools which help with the putting the recommendations into practice.
SH	NETSCC, Health Technology Assessment (Ref 2)	27.30	Full	General		**2.1 Please comment on the validity of the work i.e. the quality of the methods and their application (the methods should comply with NICE's Guidelines Manual available at http://www.nice.org.uk/page.aspx?o=guidelinesmanual).** The methods used comply with NICE's Guidelines Manual. However, it is not clear why recommendations have been made in the absence of evidence. If consensus has been used, this needs to be more clearly demonstrated.	Thank you for your comment. Where possible, further clarification has been added within the evidence to recommendation section.
SH	NETSCC, Health Technology Assessment	27.31	Full	General	2	**2.1 Please comment on the validity of**	Thank you for your comment. The care pathway has been amended following

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	(Ref 2)					**the work i.e. the quality of the methods and their application (the methods should comply with NICE's Guidelines Manual available at http://www.nice.org.uk/page.aspx?o=guidelinesmanual).** (Care pathway) - There are some inconsistencies in wording. For example, the flow diagram suggests 'offering' an adrenaline injector whereas elsewhere it states to "give" an adrenaline auto-injector	consultation.
SH	NETSCC, Health Technology Assessment (Ref 2)	27.32	Full	General		**2.2 Please comment on the health economics and/or statistical issues depending on your area of expertise.** It is noted that the evidence base is weak/low.	Thank you.
SH	NETSCC, Health Technology Assessment (Ref 2)	27.33	Full	General		**2.2 Please comment on the health economics and/or statistical issues depending on your area of expertise.** The side effects of adrenaline autoinjectors does not appear to have been considered.	Thank you for your comment. The committee did consider the potential side effects of providing adrenaline injectors. However, they felt that the risk of harm was offset by the considerable benefits of preventing adverse outcomes from a recurrent anaphylactic episode
SH	NETSCC, Health Technology Assessment (Ref 2)	27.34	Full	General		**3.1 How far are the recommendations based on the findings? Are they a) justified i.e. not overstated or understated given the evidence? b) Complete? i.e. are all the important aspects of the evidence reflected?** The evidence base does not translate to the strength of the wording used in the	Thank you for your comment. Following consultation the wording of some of the recommendations has been revised.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						recommendations.	
SH	NETSCC, Health Technology Assessment (Ref 2)	27.35	Full	1.1.4 3.1.3.1		**3.1 How far are the recommendations based on the findings? Are they a) justified i.e. not overstated or understated given the evidence? b) Complete? i.e. are all the important aspects of the evidence reflected?** Recommendation 1.1.4 recommends the use of mast cell tryptase despite a weak/low evidence base.	Thank you for your comment. The evidence to recommendations section has now been amended to emphasise the role of GDG opinion in light of the low quality evidence.
SH	NETSCC, Health Technology Assessment (Ref 2)	27.36	Full	1.1.6		**3.1 How far are the recommendations based on the findings? Are they a) justified i.e. not overstated or understated given the evidence? b) Complete? i.e. are all the important aspects of the evidence reflected?** It is not clear from the evidence why recommendation 1.1.6 recommends keeping all children in hospital.	Thank you for your comment. The evidence to recommendations section (section 3.2.5) has now been amended to clarify the reasoning behind this recommendation.
SH	NETSCC, Health Technology Assessment (Ref 2)	27.37	Full	1.1.8		**3.1 How far are the recommendations based on the findings? Are they a) justified i.e. not overstated or understated given the evidence? b) Complete? i.e. are all the important aspects of the evidence reflected?** Weak evidence base for a strong recommendation to offer everyone an adrenaline autoinjector.	Thank you for your comment. Although the evidence base was weak the GDG felt that following a suspected anaphylactic reaction it was important to ensure that those waiting for a referral appointment were able to prevent any adverse outcomes of a second suspected anaphylactic reaction. Therefore they felt that as an interim measure the offering of an adrenaline injector should be recommended.
SH	NETSCC, Health Technology Assessment	27.38	Full	1.1.9		**3.1 How far are the recommendations based on the findings? Are they a)**	Thank you for your comment. Following consultation the recommendation has

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	(Ref 2)					**justified i.e. not overstated or understated given the evidence? b) Complete? i.e. are all the important aspects of the evidence reflected?** It is not clear what the appropriate skills and competencies are. Also, who is being referred to in the recommendation (an A&E consultant, nurse, specialist allergist).	amended. The GDG did not consider which specific skills and competencies were necessary to carry out each of the stated functions. The order of the recommendations has been amended, therefore making it clear that any referral should occur following emergency treatment and prior to discharge.
SH	NETSCC, Health Technology Assessment (Ref 2)	27.39	Full	General		**3.2 Are any important limitations of the evidence clearly described and discussed?** It is noted that the evidence base is weak/low and this is not always clear in the evidence to recommendations sections.	Thank you for your comment. Where appropriate the weak evidence base has been acknowledged within the evidence to recommendations sections.
SH	NETSCC, Health Technology Assessment (Ref 2)	27.40	Full	1.1		**4.1 Is the whole report readable and well presented? Please comment on the overall style and whether, for example, it is easy to understand how the recommendations have been reached from the evidence.** The order of the recommendations does not flow. For example, recommendations 1.1.8 mentions those who have been referred to a specialist allergy service while a later recommendation (1.11) then asks the healthcare professional to refer people to a specialist allergy service	Thank you for your comment. The recommendations have now been clarified to address this issue.
SH	NETSCC, Health Technology Assessment	27.41	Full	General		**Section five – additional comments** **Please make any additional comments**	Thank you for your comment. The definition of anaphylaxis has been clarified following

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	(Ref 2)					**you want the NICE Guideline Development Group to see, feel free to use as much or as little space as you wish.** The definition of anaphylaxis is not clear and so the recommendations cannot be put into context and are not clear.	consultation.
SH	NETSCC, Health Technology Assessment (Ref 2)	27.42	Full	General		**Section five – additional comments** **Please make any additional comments you want the NICE Guideline Development Group to see, feel free to use as much or as little space as you wish.** There is no definition of emergency treatment, so would this include treatment such as antihistamine?	Thank you for your comment. Unfortunately the treatment required for any suspected anaphylactic reaction was not considered as it was outside the remit of this guideline.
SH	NETSCC, Health Technology Assessment (Ref 2)	27.43	Full	General		**Section five – additional comments** **Please make any additional comments you want the NICE Guideline Development Group to see, feel free to use as much or as little space as you wish.** There is no clear guidance on which patients to include/exclude in this guideline.	Thank you for your comment. The definition of anaphylaxis has been clarified following consultation. The guidance document has been amended to provide details on the typical presenting signs and symptoms.
SH	NETSCC, Health Technology Assessment (Ref 2)	27.44	Full	General		**Section five – additional comments** **Please make any additional comments you want the NICE Guideline Development Group to see, feel free to use as much or as little space as you wish.**	The guidance document has been amended to provide details on the typical presenting signs and symptoms. Thank you for your comment. The definition of anaphylaxis has been clarified following consultation.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						The guideline does not make it clear how doctors should reach decisions as to which pt has or does not have an anaphylactic reaction, when it is life threatening, which emergency treatments warrant tertiary referral, or which patients should have injectors or what "appropriate competences" are needed to allow patient instruction. This lack of definition makes it impossible to apply to a current AED dept or a walk in centre.	The committee did consider the various terms currently used within the medical field and how anaphylactic reactions are sometimes termed severe allergic reactions. It was decided that to prevent any confusion as to the type of reaction that was covered by this guideline, that a definition for "suspected anaphylaxis" would be provided which listed the main clinical features of the reaction.
SH	NETSCC, Health Technology Assessment (Ref 2)	27.45	Full	General		**Section five – additional comments** **Please make any additional comments you want the NICE Guideline Development Group to see, feel free to use as much or as little space as you wish.** Some recommendations may not be feasible in practice and have consequences that are not intended. For example; • should all people receive adrenaline autoinjectors (would somebody with a cardiac history be suitable?) • will all hospitals have facilities to undertake Mast cell tryptase testing and should this be performed on all patients (even those without anaphylaxis) ?	Thank you for your comment. While developing the recommendations the committee did consider the potential unintended consequences of the recommendations. In terms of prescriptions the guideline assumes that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients In addition the recommendations set out what is best practice; an assessment of the ability of services to meet demand is outside of the remit of guideline.
SH	NETSCC, Health Technology Assessment (Ref 2)	27.46	Full	General		**Section five – additional comments** **Please make any additional comments you want the NICE Guideline**	Thank you for your comment. Recommendation 1.1.3 does recommend the recording of the circumstances prior to reaction as a means of identifying a possible

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						Development Group to see, feel free to use as much or as little space as you wish. There is no advice on how to detect a specific trigger.	trigger. The actual diagnosis of the trigger is carried out by the specialist service.
SH	NETSCC, Health Technology Assessment (Ref 2)	27.47	Full	General	1.1.3	**Section five – additional comments** **Please make any additional comments you want the NICE Guideline Development Group to see, feel free to use as much or as little space as you wish.** It is not clear what information needs to be recorded.	Thank you for your comment. Due to the wide range of circumstances that are possible it was not possible to provide any further details.
SH	NETSCC, Health Technology Assessment (Ref 2)	27.48	Full	General	1.1.6 1.1.7	**Section five – additional comments** **Please make any additional comments you want the NICE Guideline Development Group to see, feel free to use as much or as little space as you wish.** Subgroups of patients are identified (children and young people) although the age ranges of these groups are not defined.	Thank you for your comment. The definitions of children and you people are defined with the patient centred care section of the guidance document.
SH	NETSCC, Health Technology Assessment (Ref 2)	27.49	Full	General	1.1.9	**Section five – additional comments** **Please make any additional comments you want the NICE Guideline Development Group to see, feel free to use as much or as little space as you wish.** There is no advice on when to use an autoinjector.	Thank you for your comment. The advice as to when to use the auto-injector is to be provided by the professional prior to discharge.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	NETSCC, Health Technology Assessment (Ref 2)	27.50	Full	General	1.1.11	**Section five – additional comments** **Please make any additional comments you want the NICE Guideline Development Group to see, feel free to use as much or as little space as you wish.** Specialist allergy services are unlikely to have the capacity to manage all the referrals that the guideline is suggesting	Thank you for your comment. The recommendations set out what is best practice; an assessment of the ability of services to meet demand is outside of the remit of guideline.
SH	NETSCC, Health Technology Assessment (Ref 1)	27.00	Full	General		**1.1 Are there any important ways in which the work has not fulfilled the declared intentions of the NICE guideline (compared to its scope – attached)** The guidelines are comprehensive and generally adhere to the scope of the assignment. Adults and young children are dealt with separately. The populations are further divided by the underlying cause of anaphylaxis. The majority of the key clinical issues have been addressed. The major limitation pertains to the lack of supporting clinical evidence, therefore the conclusion rely upon expert opinion	Thank you.
SH	NHS Direct	16.00	Full	Care pathway	11	Patient information and support Include note that carers of children should ensure access to adrenaline injector available in school and that expiry dates of injector are checked and replacement injectors ae supplied as required. This may be included in section 5 when it is completed but there was no text on which to comment.	Thank you for your comment. The adrenaline injector prescribed is an interim measure only. This information would be relayed at the specialist appointment but it is outside the scope of the guideline.
SH	Resuscitation Council	21.00	Full	General	1	A more concise lead title would be helpful,	Thank you for your comment. The title is

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	(UK)					perhaps with a longer subtitle.	derived from the referral received from the Department of Health.
SH	Resuscitation Council (UK)	21.01	Full	General		Anaphylaxis presents as a spectrum of clinical features and severity. It is not a single entity and overlaps with severe allergic reaction. The term severe allergic reaction is more often used instead of anaphylaxis. The severity of reactions varies from one reaction to another. It would therefore be of value to users to include the phrase 'or severe allergic reaction' after anaphylaxis in the guideline and recommendations. This is important as anyone with a severe allergic reaction should be referred for specialist investigation – only those with life-threatening features i.e., anaphylaxis need adrenaline.	Thank you for your comment. The definition of anaphylaxis has been clarified following consultation. The committee did consider the various terms currently used within the medical field and how anaphylactic reactions are sometimes termed severe allergic reactions. It was decided that to prevent any confusion as to the type of reaction that was covered by this guideline, that a definition for "suspected anaphylaxis" would be provided which listed the main clinical features of the reaction.
SH	Resuscitation Council (UK)	21.02	Full	General		Using a clinically useful definition for anaphylaxis as used in the RCUK Guidelines may make distinction between anaphylaxis (life-threatening) and other severe allergic reactions. It would also prevent the need to talk about allergic/non-allergic mechanisms. There is not a precise definition for anaphylaxis and international definitions include supplementary and explanatory statements. The definition given in the guideline is unhelpful. Suggest add further clinical detail, to provide a more balanced picture: patients either have respiratory difficulty or hypotension, usually with cutaneous features. For example the RCUK modification of the European Academy of Allergology and Clinical Immunology Nomenclature Committee definition: *Anaphylaxis is a severe, life-threatening, generalised or systemic hypersensitivity*	Thank you for your comment. The definition of anaphylaxis has been clarified following consultation to describe the key clinical features of the reaction which include the life-threatening problems : the airway (pharyngeal or laryngeal oedema) and/or breathing (bronchospasm with tachypnoea) and/or circulation (hypotension and/or tachycardia).

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						reaction. This is characterised by rapidly developing life-threatening airway and/or breathing and/or circulation problems usually associated with skin and mucosal changes.	
SH	Resuscitation Council (UK)	21.03	Full	Introduction	3,4	It would be helpful to say in the introduction that the emergency treatment of anaphylaxis is covered in the Resuscitation Council (UK) Guidelines (2008) – www.resus.org.uk	Thank you for your comment. Unfortunately it is not possible to refer to guidelines which have not been appraised as part of the NICE development process and which are outside the scope of this guideline.
SH	Resuscitation Council (UK)	21.04	Full	Introduction	3	The third paragraph contradicts the first by saying anaphylaxis may be allergic or non-allergic, when the definition in the first paragraph states it is a serious allergic reaction. In the context of patients presenting for emergency treatment, whether the sudden illness was allergic or non-allergic is a secondary consideration to recognising the event was anaphylaxis/severe allergy. '50% of patients referred to my specialist anaphylaxis clinic had an alternative more likely diagnosis'.	Thank you for your comment. The definition has now been amended and the apparent contradiction removed.
SH	Resuscitation Council (UK)	21.05	Full	Introduction	3, 4	The sentence ' In the UK there have been 1 million recorded cases of venom anaphylaxis and 0.4 million recorded cases of nut anaphylaxis in people under the age of 45' is clearly wrong and a misquote from the reference which says this is worldwide data..	Thank you for your comment. The statistics in question are taken from the referenced document. We have re-examined this document and amended the statistic appropriately.
SH	Resuscitation Council (UK)	21.06	Full	Introduction	3, 4	Contradiction between the assertion that anaphylaxis is potentially life threatening, with lots of episodes (e.g. "1 million " cases of venom anaphylaxis), and yet fatal anaphylaxis is rare. Throughout the document, this point is under-emphasised and needs more balance. Example from feedback to RCUK 'It should prominently be in the introduction to allow balance - one viewpoint (mine and many others)	Thank you for your comment. The definition of anaphylaxis has been clarified following consultation and has been amended to provide details on the typical presenting signs and symptoms. This definition builds on that provided by the UK resuscitation council. The purpose of the guideline is to help clinicians, who are presented with an

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						is that most cases described as "anaphylaxis" are either misdiagnosed or were not life-threatening or both. So milder allergic reactions are being over-diagnosed as anaphylaxis, or there is an unfounded worry that the milder reaction (untreated) will become life-threatening (true anaphylaxis). The view in the introduction is biased ++. It reads anaphylaxis is very bad, very common and under-reported and the only reason for so few recorded deaths is that the latter are under-reported. This is weak / does not stand scrutiny. The converse is more likely (in my view true) - anaphylaxis is grossly over-diagnosed because in fact life-threatening reactions are rare which is why deaths are rare.'	allergic reaction, to accurately categorise the reaction. Thereby ensuring that in the future fewer cases are misdiagnosed.
SH	Resuscitation Council (UK)	21.07	Full	Introduction	General	The introduction fails to make the point that about half of deaths are iatrogenic & generally in hospital/clinical settings (Pumphrey data). This is important as 1. no need for adrenaline injector in the iatrogenic groups. 2. Need to include the fact that health care workers need training to recognise and treat anaphylaxis 3. That iatrogenic harm by healthcare workers misdiagnosing anaphylaxis and wrong route errors for adrenaline are well documented (Giving large dose IV adrenaline instead of IM).	Thank you for your comment. The introduction section has been amended.
SH	Resuscitation Council (UK)	21.08	Full		8	A key point is missed in the recommendations – may be it is too obvious to make – documentation, investigation and follow up should only start once emergency resuscitation and life-threatening problems dealt with. We note it is the first box on the flow chart.	Thank you for your comment. The guidance addresses what should be done following emergency treatment and this is made clear within the care pathway.
SH	Resuscitation Council (UK)	21.09	Full		8	Specify serum (clotted) sample required for tryptase test.	Thank you for your comment. The type of sample that needs to be collected is outside

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							the remit of this guidance.
SH	Resuscitation Council (UK)	21.10	Full	1.1.8	9	Is it necessary to give an adrenaline injector to all cases of suspected anaphylaxis? When there is an obvious trigger that can be avoided, this may not be necessary, e.g. IV contrast, anaesthetic drugs etc. This point needs clarification as the guidance is intended for primary, secondary, and tertiary settings. As a general comment the needs of patients who suffer from anaphylaxis in the different settings is not explicit. The recommendation that adrenaline auto-injectors should be given to all who present for emergency treatment of an illness thought to be anaphylaxis will result in many inappropriate prescriptions. Once prescribed, it is very difficult to "unprescribe" an auto-injector. 'Although adrenaline by any route will ameliorate reactions and may prevent progression of an allergic reaction to anaphylaxis, despite studying fatal anaphylaxis for 20 years I can find no evidence that auto-injectors have saved lives. I think the dangers of inappropriate prescription are greater than the dangers of delaying prescription until proper assessment of the condition they are intended to treat. I find no evidence to the contrary in this guideline.'	Thank you for your comment. As the final determination of the suspected trigger is undertaken following referral the committee felt that the risk of harm from prescribing adrenaline injectors was offset by the considerable benefits of preventing adverse outcomes from a recurrent anaphylactic episode.
SH	Resuscitation Council (UK)	21.11		1.1.8	9	When an adrenaline injector is prescribed how many should they be given (1 or 2 or more? E.g. carry 2 in case one fails, one breaks, and one for school or work etc). This is one of the commonest queries received by the RCUK from	Thank you for your comment. The committee did consider how many injectors should be prescribed for each person but felt that due to varying circumstances that this should be left to the judgement of the clinician in question.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						both healthcare professionals and laypersons. Patients like to have a spare one just in case. It does not appear to have been explicitly addressed in this document or the mathematical modelling. Any recommendation is likely to have a cost impact so important. We know that many patients do get prescribed more than 1.	
SH	Resuscitation Council (UK)	21.12	Full	1.1.8	9	'All patients who have been referred…' This is confusing, as all patients are to be referred. Suggest reword. Important actions required after emergency treatment are - all people should be given information about the need for referral to a specialist allergy service and the referral process; - and (or, as appropriate, their parent and/or carer) offered an adrenaline injector as an interim measure pending the referral appointment. As written, the referral tend to be lost in a long list of actions This has been identified as the major block in the care pathway	Thank you for your comment. The recommendations have now been clarified.
SH	Resuscitation Council (UK)	21.13	Full	1.1.9	9	Remove the referral to 1.1.8 (see 21.12). This is where the care pathway stops. This does not get sufficient emphasis where it is sited.	Thank you for your comment. The recommendations have been amended.
SH	Resuscitation Council (UK)	21.14	Full	1.1.10	9	Suggest add 'or severe allergic reaction'. There are several reasons for suggesting this. This is how anaphylaxis is commonly labelled. These reactions involve a spectrum of severity, and there is no exact differential point between anaphylaxis and severe allergic reaction. The patient who has suffered a severe allergic reaction may be worse in the next reaction and warrants referral for diagnosis and management to prevent reactions.	Thank you for your comment. The definition of anaphylaxis has been clarified following consultation. The committee did consider the various terms currently used within the medical field and how anaphylactic reactions are sometimes termed severe allergic reactions. It was decided that to prevent any confusion as to the type of reaction that was covered by this guideline, that a definition for "suspected

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							anaphylaxis" would be provided which listed the main clinical features of the reaction.
SH	Resuscitation Council (UK)	21.15	Full	1.1.12	9	Suggest change to 'Refer people to a specialist allergy service, age-appropriate where possible' The reason is that when there is a lack of paediatric allergy services, referral to an adult allergy service is preferable to referral to a generalist without allergy skills. This allows for referral to a paediatric allergist when one is available.	Thank you for your comment. Following consultation this recommendation has been amended, however this aspect has been retained.
SH	Resuscitation Council (UK)	21.16	Full	Care pathway	11	Towards the end, after…."Refer people who have an initial anaphylactic episode'', suggest add 'or severe allergic reaction'.	Thank you for your comment. The definition of anaphylaxis has been clarified following consultation. The committee did consider the various terms currently used within the medical field and how anaphylactic reactions are sometimes termed severe allergic reactions. It was decided that to prevent any confusion as to the type of reaction that was covered by this guideline, that a definition for "suspected anaphylaxis" would be provided which listed the main clinical features of the reaction.
SH	Resuscitation Council (UK)	21.17	Full	2	11	Last box Revise "Refer people to an age-appropriate specialist allergy service that has" to "Refer people to a specialist allergy service, age-appropriate where possible, that has"	Thank you for your comment. Following consultation the care pathway has been updated to reflect the amended recommendations.
SH	Resuscitation Council (UK)	21.18	Full		16	Suggest re-word	Thank you for your comment. The beginning of this section has been amended.
SH	Resuscitation Council (UK)	21.19	Full	3	16	This page is confusing. It assumes the test should always be positive in anaphylaxis which	Thank you for your comment. This section is intended to describe the impact of these

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						is not the case.	outcomes (ie. true positives, false positives, etc) from any potential diagnostic test for anaphylaxis. This has now been clarified in the guideline. The purpose is to set the context for assessing evidence on diagnostic accuracy. The evidence to recommendations section describes the application of these terms in the context of mast cell tryptase tests.
SH	Resuscitation Council (UK)	21.20	Full	3.1.2	12-20	Since around 1997 all tests for mast cell tryptase in routine UK laboratories have been based on the B12 antibody that detects the native form of alpha-protryptase and beta tryptase. There is therefore no need to wait 30 minutes for the peak level of denatured beta tryptase that was detected by the G5 antibody in older assays. When considering the timing of sampling for tryptase why did the review look at papers based on the older technology?	Thank you for your comment. Section 3.1.2 of the guidance acknowledges that the evidence available on the timing of acute mast cell tryptase release includes methods not currently used in the UK. No studies about mast cell tryptase timing were found on the newer technology currently used in the UK. The GDG have not made recommendations requiring a 30-minute wait to detect the peak level. The recommendations about the appropriate timing of the blood samples were based on GDG opinion, informed by the evidence of when the peak or half-life occurred in most patients in the studies.
SH	Resuscitation Council (UK)	21.21	Full	3.1.3.2	17	The studies in anaesthesia are suspected anaphylaxis so all are not necessarily anaphylaxis and may/will include non-allergic events. Evaluating the usefulness of a test in a mixed population creates errors. The evidence statement should reflect this. This is not clear	Thank you for your comment. The evidence to recommendations section has been amended to comment on the diversity of causes of anaphylaxis in the studies and the potential problems in interpretation of the results.
SH	Resuscitation Council (UK)	21.22	Full		26	In clinical practice biphasic reactions are not common. The data here is at variance with experience. The evidence should be scrutinised e.g. the Scranton 2009 study was of immunotherapy induced reactions and not community anaphylaxis. The "biphasic	The Scranton study met the inclusion criteria as the initial presentation of the reaction met the definition of suspected anaphylaxis. The GDG acknowledged (and it was highlighted in the evidence to recommendations section) that the varying criteria used to classify a

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						reactions" were mild, and included minor reactions, some not suggestive of allergic reactions, and not requiring treatment. These cannot be counted as biphasic reactions. Data on the incidence of severe biphasic reactions is required.	biphasic reaction had likely contributed to the high rates of biphasic reactions. Furthermore, removing this study will not have a large impact on the range off biphasic rates currently reported and, given that these studies were included as indirect evidence, it was decided that this study would remain included.
SH	Resuscitation Council (UK)	21.23	Full		43	Mathematical modelling – reactions occurring in healthcare settings secondary to interventions should not be included in the modelling – as clinically irrelevant – many drug deaths appear to occur in hospital (anaesthetics, antibiotics) and hence self administered adrenaline irrelevant.	Thank you for your comment. A sensitivity analysis which excludes the effect of specialist allergy service on drug induced anaphylaxis was undertaken, and showed that SS remained cost effective, with ICERs less than £2000 per QALY.
SH	Resuscitation Council (UK)	21.24	Full	Table 11	45	Specialist care should reduce further costs in idiopathic anaphylaxis by medical management preventing or controlling reactions (footnote).	Thank you for your comment. Although this rationale sounds reasonable, in the absence of evidence, it was not practical to account for this effect in the base-case economic analysis. However, we have added a note to the discussion that the analysis may be conservative with regard to the efficiency of SS.
SH	Resuscitation Council (UK)	21.25	Full	Table 12	46	The shelf life of adrenaline auto-injectors in use is incorrect and should be longer. For currently available devices it is approx 18 months. A further licensed device with 24 month shelf life will be available in Sept 2011. Model uses 6 months.	Thank you for your comment. The base-case shelf life for adrenaline injectors has been changed to 12 months, and it has been noted that this may represent a conservative estimate.
SH	Resuscitation Council (UK)	21.27	Full	General		Models of care. There is data from UK on the effect of specialist allergy care compared to general care in nut allergy, which is the commonest food cause of severe allergic reactions/anaphylaxis. This provides evidence of reduced incidence of severe reactions and	Thank you for your comment. Unfortunately the effectiveness of specialist care is outside of the scope of the main review questions.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						decreased use of NHS resources We suggest this should be included as support for specialist care.	
SH	Resuscitation Council (UK)	21.28	Full		60-61	Information to patients: production of a standard hand out for universal use would be helpful. This would help staff who will not likely have the appropriate expertise and improve standards of care.	Thank you for your comment. NICE does not produce this type of material however we acknowledge the use of a standard hand out would be helpful. NICE does produce an understanding guidance booklet which provides further details to patients about allergy organisations.
SH	Resuscitation Council (UK)	21.29	Full	3.4.6	61	Recommendation 1.1.9 Same comment as 21.28.	
SH	Resuscitation Council (UK)	21.30	Full	3.5	61-62	Models of care. Suggest include evidence (see comment 21.19) on effectiveness of specialist care. In these studies, nut allergy was the cause of severe reactions/anaphylaxis and is known to have a high rate of further reactions. Specialist care substantially reduced the incidence of severe reactions.	Thank you for your comment. Unfortunately the effectiveness of specialist care is outside of the scope of the main review and as such it is not possible to include these papers.
SH	Resuscitation Council (UK)	21.31	Full	10	73	Suggest revise the definition of anaphylaxis (as suggested in comments 21.01 and 21.02).	Thank you for your comment. The definition of anaphylaxis has been clarified following consultation.
SH	Resuscitation Council (UK)	n	Full	Table 12	46	When an adrenaline injector is prescribed, how many should they be given (1 or 2 or more? E.g. carry 2 in case one fails, one breaks, and one for school or work etc). This is one of the commonest queries received by the RCUK from both healthcare professionals and laypersons. Patients like to have a spare one just in case. It does not appear to have been explicitly addressed in this document but should be. The mathematical modelling suggests person has 2 at any one time – doe this mean they should all be prescribed 2. Needs to be made clearer.	Thank you. This parameter has been revised, with children requiring 4 adrenaline injectors at any one time. Please also note that sensitivity analysis tested the effect of increased cost.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	Royal College of General Practitioners	22.00	Full	Title	1	This will be impenetrable to most people – please simplify	Thank you for your comment. We have amended the title so it reflects the recommendations.
SH	Royal College of General Practitioners	22.01	Full	Introduction	3-4	This section is very poorly referenced, in relation to the diagnosis, aetiological factors and how these vary with age, and more generally the epidemiology; please make a more thorough review of the relevant UK literature	Thank you for your comment. Following consultation the introduction has been amended. The introduction briefly sets out the need for guidance in this area. It is not intended to be an exhaustive review of the literature in this area.
SH	Royal College of General Practitioners	22.02	Full	Introduction	3	This definition is confusing as it refers to anaphylaxis as being 'a serious allergic reaction' and then later on in Para 3 on the same page it says that anaphylaxis may be caused by a 'non-allergic response'. I suggest that the UK Resuscitation Council definition is used, to promote a degree of consistency in the UK.	Thank you for your comment. The definition has now been amended and the apparent contradiction removed.
SH	Royal College of General Practitioners	22.03	Full	Introduction	3	Please cite the full reference as this otherwise limits accessibility to the UK Resuscitation Council guidelines	Thank you for your comment. The reference has been amended.
SH	Royal College of General Practitioners	22.04	Full	1.1.8	9	Make clear that all patients with a working diagnosis of anaphylaxis should be given an adrenaline auto-injector	Thank you for your comment. The guidance document does state that all patients who have suffered a suspected anaphylactic reaction should be offered an adrenaline injector.
SH	Royal College of General Practitioners	22.05	Full	1.1.10	9	Make clear that pathways need to be available for both children and adults; suggest referring to the RCPCH pathway for anaphylaxis that has already been developed for children	Thank you for your comment. The recommendations have been amended to state that separate referral pathways should be available for adults and children. Unfortunately it is not possible to refer to pieces of non-NICE based guidance within the recommendations.
SH	Royal College of General Practitioners	22.06	Full	Care pathway	11	Suggest that direct reference is made to the UK Resuscitation Council and or World Allergy Organization Anaphylaxis Guidelines when	Thank you for your comment. Unfortunately the provision of emergency treatment was outside the scope of this guideline. As such it

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						referring to emergency treatment (i.e. first box)	is not possible to refer to guidelines which have not been appraised as part of the NICE process.
SH	Royal College of General Practitioners	22.07	Full	Care pathway	11	It is important that there is appropriate documentation of the suspected/confirmed anaphylaxis in the patient's written/electronic medical records, with appropriate coding so as to enable decision support functionality	Thank you for your comment. The committee felt that the recording of the suspected/confirmed anaphylaxis would be standard practice and that the appropriate information would be part of any referral.
SH	Royal College of General Practitioners	22.08	Full	3	16	Need to point out that tryptase is less likely to be elevated in food allergy.	Thank you for your comment. The evidence to recommendations has been amended to acknowledge this.
SH	Royal College of General Practitioners	22.09	Full	3	16	Note that tryptase is most unlikely to be undertaken in a general practice setting	Thank you for your comment. The GDG considered the practicalities of this recommendation but felt that blood should be taken regardless of setting.
SH	Royal College of General Practitioners	22.10	Full	Table 12	46	Please check estimates of shelf-life of adrenaline; this varies with the different products	Thank you for your comment**.** The base-case shelf life for adrenaline injectors has been changed to 12 months, and it has been noted that this may represent a conservative estimate.
SH	Royal College of General Practitioners	22.11	Full	References	69	The reference to Estelle et al is incorrect; it should be Simons	Thank you for your comment. The guidance document has been amended.
SH	Royal College of General Practitioners	22.12	Full	General		The guidance is rather cumbersome and does not address many of the problems GPs grapple with – e.g. how to code suspect reactions, who to refer to in the absence of specialist services locally; how many adrenaline auto-injectors to provide; how to ensure adequate training etc	Thank you for your comment. The recommendations have been amended following consultation to provide more detail on the signs and symptoms of a suspected anaphylactic reaction. However, issues pertaining to dosages, training and the provision of specialist services are outside of the scope of this guideline.
SH	Royal College of General Practitioners	22.13	Full	General		Given the real paucity of evidence uncovered, please make a much fuller set of research recommendations and advise which funders should help move this agenda on	Thank you for your comment. Following consultation additional research recommendations have been added to the document.
SH	Royal College of Nursing	32.00	Full	General		The RCN welcomes proposals to develop the	Thank you.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						anaphylaxis guideline. The recommendations seem very sensible, clear to follow and based on the information currently available.	
SH	Royal College of Nursing	32.01	Full	2	11	The care pathway on page 11 will be very helpful to A&E units.	Thank you.
SH	Royal College of Nursing	32.02	Full	1.17	32	We are pleased to see the recommendation for holding the patient for 6-12 hours post reaction as currently many patients are discharged early appearing to ignore the biphasic risks.	Thank you for your comment.
SH	Royal College of Nursing	32.03	Full	3.34	41	Referral to specialist clinics and the prescribing of an interim adrenaline pen is also welcome	Thank you.
SH	Royal College of Nursing	32.04	Full	General		We feel that overall the recommendations should improve the diagnosis and on-going care of a patient with anaphylaxis	Thank you.
SH	Royal College of Paediatrics and Child Health	30.00	Full	3.1.2	12-20	Since around 1997 all tests for mast cell tryptase in routine UK laboratories have been based on the B12 antibody that detects the native form of alpha-protryptase and beta tryptase. There is therefore no need to wait 30 minutes for the peak level of denatured beta tryptase that was detected by the G5 antibody in older assays. When considering the timing of sampling for tryptase why did the review look at papers based on the older technology?	Thank you for your comment. Section 3.1.2 of the guidance acknowledges that the evidence available on the timing of acute mast cell tryptase release includes methods not currently used in the UK. No studies about mast cell tryptase timing were found on the newer technology currently used in the UK. The GDG have not made recommendations requiring a 30-minute wait to detect the peak level. The recommendations about the appropriate timing of the blood samples were based on GDG opinion, informed by the evidence of when the peak or half-life occurred in most patients in the studies.
SH	Royal College of Paediatrics and Child Health	30.01	Full	Introduction	3	The third paragraph contradicts the first by saying anaphylaxis may be allergic or non-allergic, when the definition in the first paragraph states it is a serious allergic reaction. In the context of patients presenting for emergency treatment, whether the sudden illness was allergic or non-allergic is a	Thank you for your comment. The definition has now been amended and the apparent contradiction removed.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						secondary consideration to recognising the event was anaphylaxis: 50% of patients referred to a specialist anaphylaxis clinic had an alternative more likely diagnosis.	
SH	Royal College of Paediatrics and Child Health	30.02	Full	General		The recommendation that adrenaline auto-injectors should be given to all who present for emergency treatment of an illness thought to be anaphylaxis will result in many inappropriate prescriptions. Once prescribed, it is very difficult to "unprescribe" an auto-injector. Although adrenaline by any route will ameliorate reactions and may prevent progression of an allergic reaction to anaphylaxis, despite studying fatal anaphylaxis for 20 years we can find no evidence that auto-injectors have saved lives. We think the dangers of inappropriate prescription are greater than the dangers of delaying prescription until proper assessment of the condition they are intended to treat. We find no **evidence** to the contrary in this guideline.	Thank you for your comment. The guidance document has been amended to provide details on the typical presenting signs and symptoms, which would limit the number of inappropriate prescriptions. The committee did consider the potential harmful effects of prescribing adrenalin injectors. However they concluded that the risk of harm was offset by the considerable benefits of preventing adverse outcomes from a recurrent anaphylactic episode.
SH	Royal College of Paediatrics and Child Health	30.03	Full	Care pathway	11	Patient information and support. Information for families and carers of infants on a suitable replacement diet if cow's milk elimination is advised.	Thank you for your comment. This information is provided at specialist follow up and is therefore outside the scope of the guideline.
SH	Royal College of Paediatrics and Child Health	30.04	Full	3.4.6	61	Recommendation 1.1.9 Families and carers of infants on an exclusion diet should receive follow up from a specialist paediatric dietician to ensure that the replacement diet is adequate and monitor growth.	Thank you for your comment. This is outside the scope of the guideline.
SH	Royal College of Paediatrics and Child Health	30.05	Full	3.1	12-24	**Use and timing of mast cell tryptase testing in the anaphylaxis diagnostic pathway** The GDG accept that the evidence is poor and has not included studies in children. Use of	Thank you for your comments. A separate recommendation has now been made regarding the use of mast cell tryptase tests in children. It is now recommended that testing

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						tryptase to diagnose anaphylaxis seems to have reasonable specificity (90) but poor sensitivity (as low as 35%). Despite this poor quality evidence the GDG recommends that everyone with suspected anaphylaxis has tryptase measured immediately and at 2 hours. They then leave interpretation up to the 'allergy expert'. If the GDG recommends measuring tryptase, then they should provide guidance in interpretation. So, if a child has a typical anaphylactic reaction to nuts – for example, widespread urticaria, mouth swelling, wheeze and respiratory distress – how is measuring the tryptase going to affect management? Doing 2 blood tests on children is not without some difficulty, both for the medical staff and for the child. The GDG needs to provide a clearer rationale for recommending this test in everyone.	only be carried out in children where the cause is thought to be venom-related, drug-related or idiopathic. The aim of the test is to provide the allergy specialist, following referral, with additional information to aid their assessment of whether the reaction was truly anaphylaxis. It is acknowledged within the evidence to recommendations that as a result of the low false negative rate and because the results from mast cell tryptase tests would normally be interpreted by an allergy specialist in conjunction with a clinical assessment, the GDG felt that the use of mast cell tryptase was warranted. Unfortunately providing guidance about the interpretation of these tests which occurs after the point of referral and the subsequent mangement is beyond the scope of this guideline.
SH	Royal College of Paediatrics and Child Health	30.06	Full	3.3.6	56	2 areas where guidance was much needed from the medical community was clarity of which patients warrant AIs (beyond those who have had clear anaphylaxis) and also how many should be prescribed. Whilst there is a lack of evidence to guide this decision, can expert consensus not be used to end the current geographical variability. Both EAACI and WAO guidelines on anaphylaxis broach these issues.	Thank you for your comment. The population of interest for this guideline was those who have received treatment for suspected anaphylaxis. Therefore, it is outside the scope of this guideline to comment on whether other groups should receive adrenaline injectors The committee did consider how many injectors should be prescribed for each person but felt that due to varying

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
							circumstances that this should be left to the judgement of the clinician in question.
SH	Royal College of Paediatrics and Child Health	30.07	Full	General		For most practitioners, the distinction between anaphylaxis and severe allergic reactions is somewhat arbitrary and perhaps the terminology should be extended to 'Anaphylaxis and severe allergic reactions'.	Thank you for your comment. The definition of anaphylaxis has been clarified following consultation. The committee did consider the various terms currently used within the medical field and how anaphylactic reactions are sometimes termed severe allergic reactions. It was decided that to prevent any confusion as to the type of reaction that was covered by this guideline, that a definition for "suspected anaphylaxis" would be provided which listed the main clinical features of the reaction.
SH	Royal College of Paediatrics and Child Health	30.08	Full	1.1.8	9	No guidance given for infants/children <10kg where adrenaline injectors would not be appropriate.	Thank you for your comment. It is standard practice within NICE clinical guidelines to refer to the BNF. However, the recommendations have been amended to acknowledge that an appropriate adrenaline injector is offered. In addition the evidence to recommendations section has been update to reflect this point.
SH	Royal College of Paediatrics and Child Health	30.09	Full	1.1.9	9	As well as specialist referral, there is no reason why, if food allergy is suspected, that a referral to a registered dietician for allergen avoidance advice should not be instigated (as suggested in the Food Allergy guideline).	Thank you for your comment. The committee felt that dietetic advice would, if applicable, be part of any specialist appointment and therefore it was not necessary to recommend this.
SH	Royal College of Paediatrics and Child Health	30.10	Full	General		Another issue is the recommendation to supply (with training) an injectable adrenaline device for anyone who presents to ED with anaphylaxis. The definition of anaphylaxis is fairly loose/broad in the document. I would be	Thank you for your comment. The guidance document has been amended to provide details on the typical presenting signs and symptoms, which would limit the number of inappropriate prescriptions.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						concerned about a couple of consequences: a) that Epipens would be given to people with milder reactions and without an appropriate risk assessment/ complete package of care/appropriate follow up. It is also not necessarily that straightforward to stop an Epipen prescription once started. b) some schools/nurseries may (and do) stop a child from attending with an Epipen until a formal care plan is in place. Thus the prescription of the Epipen (rightly or wrongly as noted above) without the full allergy team input first may not necessarily protect the child nor be in their best interests if their education is disrupted.	The committee did consider issues around school attendance. However, they did not agree that the provision of an adrenaline injector would bar a child from attending school.
SH	Royal College of Paediatrics and Child Health	30.11	Full	General		There is no evidence mentioned to support (or refute) the recommendation to check trytase twice in Emergency Dept in paediatrics; there are technical and other issues in regards to invasive tests in children; There are also the cost and capacity issues.	Thank you for your comment. A separate recommendation has now been made regarding the use of mast cell tryptase tests in children.
SH	Royal College of Paediatrics and Child Health	30.12	Full	Introduction	3	Anaphylaxis, suspected anaphylaxis, mild and moderate allergic reactions should be defined in the introduction. The reader is referred to the Sampson 2006 reference. The document is asking the ED physician to differentiate a moderate allergic reaction from suspected anaphylaxis, and, on the basis of this, may request that a child be admitted for observation. It would be useful if these terms could be included in the guideline rather than forcing the physician to consult another document which she/he may not have access to.	Thank you for your comment. The introduction section has been amended and the definition of anaphylaxis revised to provide additional detail. As a result mild and moderate presentations are those people who do not meet the definition of anaphylaxis.
SH	Royal College of Paediatrics and Child	30.13	Full	General		It is disappointing that the management of children who have had a mild or moderate	Thank you for your comment. The topics that NICE develops guidance on are referred from

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	Health					allergic reaction and are potentially at risk of anaphylaxis is not covered. Could this be the focus of another guideline?	the Department of Health. As such it is not within NICE's remit to determine which areas guidance is developed on. Currently NICE are seeking consultation on the library of topics please see link for details on how to comment. http://www.nice.org.uk/newsroom/pressreleases/QualityStandardsEngagementExercise.jsp
SH	Royal College of Paediatrics and Child Health	30.14	Full	1.1.9	9	Need to prescribe antihistamines as well.	Thank you for your comment. The committee considered this but did not feel it necessary to recommend the prescription of antihistamines as this is part of routine practice.
SH	Royal College of Paediatrics and Child Health	30.15	Full	1.1.9	9	If asthmatic need to optimise asthma management.	Thank you for your comment. Unfortunately the management of associated co-morbidities was outside the scope of this guideline.
SH	Royal College of Paediatrics and Child Health	30.16	Full	1.1.9	9	Need to specify if need 1 or 2 adrenalin injectors.	Thank you for your comment. The committee did consider how many injectors should be prescribed for each person but felt that due to varying circumstances that this should be left to the judgement of the clinician in question.
SH	Royal College of Paediatrics and Child Health	30.17	Full	First paragraph	First section	Definition of anaphylaxis: "***can lead to potentially*** life-threatening breathing and circulatory problems or both." The use of *can lead to* and *potentially* is confusing. Replacing *can lead to* with *involves*, or removing the word *potentially* could clarify the definition.	Thank you for your comment. The definition of anaphylaxis has been clarified following consultation.
SH	Royal College of Paediatrics and Child Health	30.18	Full	Introduction	3	"***Foods*** are common precipitants" might be qualified by "*Certain foods* are…" as only some foods are responsible for the vast majority of anaphylaxis.	Thank you for your comment. The introduction section has been amended.
SH	Royal College of Paediatrics and Child Health	30.19	Full	1.1.8 &1.1.11	9	"All people ***who have been referred***…" There is an implication that all would not be referred in section 1.1.8, whereas the recommendation in 1.1.11 is that all should be referred.	Thank you for your comment. The recommendations have been clarified.
SH	Royal College of	30.20	Full	1.1.9	9	"***a healthcare professional with appropriate***	Thank you for your comment. The committee

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	Paediatrics and Child Health					***skills and competencies***…" may need further clarification in the case of children (being admitted under a paediatric team): who of the following would be considered appropriate: allergy specialist/general paediatrician/senior trainee/allergy nurse (as expertise may be very limited in the paediatric team).	did not feel it appropriate to designate a specific individual to deliver this intervention. Instead all that was necessary was that individual had the skills and competencies necessary to deliver the interventions in question.
SH	Royal College of Paediatrics and Child Health	30.21	Full	Care Pathway	11	*Duration* and *place* of admission for children unclear; the guideline says admit under paediatric team: ? observation for minimum 8 hrs (or 24 hrs)? Where: day unit/acute ward.	Thank you for your comment. The recommendation has been clarified to state that this is a paediatric medical team. The committee did not feel it appropriate to provide a minimum time for the admission of any child as the time that any child should be admitted would vary on a case by case basis. Instead the length of any admission should be left to the clinician in question.
SH	Royal College of Paediatrics and Child Health	30.22	Full	3.1.4.1	23	Grammatical error: "should ***be*** interpreted".	Thank you. This has been amended.
SH	Royal College of Paediatrics and Child Health	30.23	Full	General		We should welcome these guidelines which in general are well co-ordinated with the RCPCH care pathways. This is a reflection of appropriate membership on the guideline development group. One concern is that the guidelines do not consider the very common situation of a patient presenting with an acute allergic reaction which is not full-blown anaphylaxis. Many such patients are at risk of future anaphylaxis and an assessment of risk is required to make decisions on management. This is a much more common scenario than is addressed in these guidelines. Furthermore, it is the area for which management is most variable, thus requiring a guideline. Once a patient has	Thank you for your comment. Unfortunately as stated within the introductory section, those presenting with mild or moderate reactions are outside the scope of this guideline.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						suffered anaphylaxis the management is much more consistent.	
SH	Royal College of Paediatrics and Child Health	30.24	Full	3.1	12	The section on Mast cell tryptase does not discuss the sensitivity of the assays which vary from study to study.	Thank you for your comment. The evidence to recommendations section has now been amended to highlight the variability of the sensitivities reported in the studies.
SH	Royal College of Paediatrics and Child Health	30.25	Full	3.1.4	22	There is no statement about Mastocytosis as an important condition which will have persistent raised tryptase. Not all baseline raised levels are "natural" as suggested in the evidence of recommendations table.	Thank you for your comment. The evidence to recommendations section has been amended to clarify that this is 'unexplained' rather than 'natural' high levels of mast cell tryptase. This section has also been amended to point out that mastocytosis is an example of unexplained high levels of tryptase.
SH	Royal College of Paediatrics and Child Health	30.26	Full	3.1.5	24	It is disappointing that there are no research recommendations. Given the poor sensitivity of tryptase assays, particularly in children reacting to foods, surely more work is required to improve sensitivity and to investigate other mast cell mediators which may improve diagnosis. This includes carboxypeptidase and the use of saliva as an alternative to blood.	Thank you for your comments. Following consultation the committee have drafted additional research recommendations. This includes a research recommendation on other potential mediators.
SH	Royal College of Paediatrics and Child Health	30.27	Full	3.3.2	33	No effort was made to review papers identifying risk factors for anaphylactic deaths or recurrence of severe reaction which would influence assessment and management. These include; unknown allergen, co-existent asthma (particularly if poorly controlled), nut, milk and sesame allergy.	Thank you for your comment. The aim of the question was to identify risk factors for recurrent anaphylactic reactions, not risk factors for anaphylactic deaths. Therefore these papers would have been excluded from the review.
SH	Royal College of Paediatrics and Child Health	30.28	Full	3.3.13		Many studies highlight the absolute indication of adrenalin prescription for those with asthma.	Thank you for your comment. Although some papers may highlight the absolute indication of adrenalin prescription for those with asthma, no papers were found which met the inclusion criteria set out in assessment group report (Appendix G)
SH	Royal College of	30.29	Full	3.3.4	41	The economic modelling assumes a cost of	Thank you.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	Paediatrics and Child Health					£200 per specialist consultation. The actual cost is very much higher. Even a general paediatric first consult commands a higher tariff. Given the need for testing patient/parent education, specialist nurse and dietician input in food allergy the cost is around £400. The other assumption is a follow-up every 2 years. This is very unsatisfactory. Review of outcomes suggests that the current practice does not work. A high percentage of patients having a subsequent anaphylactic episode either are not carrying their adrenalin injector, do not use it, or use it incorrectly. The consequence is a higher risk of death. Much more frequent follow-up is required to ensure the management plan is agreed, understood and that there is maintained concordance.	The costs have been amended according to NHS Reference costs (2009/10) ((initial, follow-up) Children (£266, £234), Adults (£321,£450)). Rate of follow-up was based on expert opinion and also subjected to sensitivity analysis, which showed no change in results up to once per month.
SH	Royal College of Paediatrics and Child Health	30.30	Full	3.3.5	56	There was no review of the number of injectors recommended. This is an issue of great concern and dispute. However, the economic modelling did suggest that 2 prescriptions every 6 months was a standard.	Thank you for your comment. The Base case shelf life has been changed to 12 months and based on GDG opinion; adults receive 2 injectors at a time and up to 4 for children.
SH	Royal College of Paediatrics and Child Health	30.31	Full	3.5	61	We recommend that there should be reference to the RCPCH care pathways.	Thank you for your comment. We do not cross refer to non NICE guidance in our recommendations.
SH	Royal College of Paediatrics and Child Health	30.32	Full	1.1.4	8	The document suggests that all individuals with suspected anaphylaxis should have serial tryptase measurements. Tryptase level rise frequently does not occur in children and individuals with food induced anaphylaxis. Therefore should this be a universal recommendation? Anaphylaxis is a clinical diagnosis and although tryptase measurement can be useful (e.g. drug induced anaphylaxis)	Thank you for your comment. A separate recommendation has now been made regarding the use of mast cell tryptase tests in children.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						we are not convinced it should be a universal recommendation.	
SH	Royal College of Paediatrics and Child Health	30.33	Full	1.1.8	9	We are aware of a number of children seen in allergy clinic after an episode of anaphylaxis who are not prescribed an adrenaline auto-injector. This is especially true when the allergen is uncommon and easily avoidable. In these cases parents often find it easier to simply control their child's environment rather than been subjected to the stresses of ensuring at least 2 auto-injectors follow their child everywhere they go. Given that several studies have shown the variability in health professionals' ability to use auto-injectors themselves should we be advocating that all children are set up with the devices? Even if we attempt to train all acute physicians and paediatricians to teach parents how to administer adrenaline there will still be issues regarding training nursery and school staff and the provision of written anaphylaxis plans to accompany the auto-injector. Would it not be better to advocate review by an allergy specialist prior to discharge if the child is felt to be at high risk of meeting the allergen again or avoidance until seen in allergy outpatients?	Thank you for your comment. The committee did consider the issues pertaining to the provision of adrenaline injectors to children. However, they felt that prior to referral with a specialist allergy service that it was necessary to offer the injectors.
SH	Royal College of Pathologists	12.00	Full	Introduction	3	Paragraph 3, line 6: suggest change 'known' to 'readily identifiable'.	Thank you for your comment. The introduction has been amended.
SH	Royal College of Pathologists	12.01	Full	Introduction	3	Paragraph 3/4: text might usefully indicate that there are a number of known intrinsic and extrinsic risk/co-factors which contribute to anaphylactic reactions (some of which are modifiable) which are particularly important to	Thank you for your comment. The risk factors associated with the recurrence of anaphylactic reactions were considered as part of the evidence review.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						consider in the context of idiopathic anaphylaxis.	
SH	Royal College of Pathologists	12.02	Full	1.1	8	Recommendations: An additional useful quality recommendation might be that tryptase measurements are only undertaken in accredited laboratories which participate in an appropriate external quality assurance scheme.	Thank you for your comment. Recommendations about how the measurement of mast cell tryptase should be performed, including the quality assurance requirements of the laboratories that perform these tests, are beyond the scope of this guideline.
SH	Royal College of Pathologists	12.03	Full	3.1.2	13	Line 1: suggest insert 'in-vitro' between. '…tests' and 'IgE tests) alone…'.	Thank you for your comment. This has been amended.
SH	Royal College of Pathologists	12.04	Full	3.1.2	13	Table 1: the term 'RAST' used to denote in-vitro detection/measurement of allergen-specific IgE is outdated. 'Specific IgE', 'in-vitro Specific IgE' or 'sIgE' should be used as preferred alternatives (with definition of abbreviation if the last is selected).	Thank you for your comment. This has been written in the guideline as it was reported in the studies. This has now been updated.
SH	Royal College of Pathologists	12.05	Full	3.1.2	16	*False negative* section: existing text '…but who have a diagnosis of not considered to be anaphylaxis…' is nonsensical (? remove 'of' from text).	Thank you for your comment. This is a typo which has been amended.
SH	Royal College of Pathologists	12.06	Full	3.1.4.1	23	*Relative value of different outcomes* section, paragraph 3: the use of the term 'naturally' to describe high basal levels of mast cell tryptase in some patients may be misleading. The phrasing of this sentence might usefully be altered to 'It was also noted that some patients had high basal levels of mast cell tryptase for other reasons and therefore…'.	Thank you for your comment. The evidence to recommendations section has been amended to clarify that this is 'unexplained' rather than 'natural' high levels of mast cell tryptase. This section has also been amended to point out that mastocytosis is an example of unexplained high levels of tryptase.
SH	Royal College of Pathologists	12.07	Full	3.1.4.1	23	*Economic considerations* section: 'negligible' is a subjective, undefined term. In the context of the whole patient journey the cost of 3 mast cell tryptase assessments may be minor. However, the unit cost of tryptase measurement is	Thank you for your comment. We have now provided additional detail outlining the health economic consequences of this recommendation. Although MCT testing represents a non-negligible cost to the NHS, it

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						relatively high in comparison to many other laboratory investigations (e.g. routine biochemistry or haematology) and would not be considered negligible in operational budget terms. Suggest 'definable' might be used in preference to 'negligible'.	is currently conducted as part of the management plan during follow-up at specialist allergy clinics. For this reason, the cost of MCT testing is assumed to be incorporated in the cost of a visit to a specialist allergy service in the health economic model described in section 3.3.4. Conducting a separate analysis here would run the risk of double-counting.
SH	Royal College of Pathologists	12.08	Full	3.1.4.1	23	Evidence to recommendations, 'Other considerations' section: An additional useful quality recommendation might be that tryptase measurements are only undertaken in accredited laboratories which participate in an appropriate external quality assurance scheme.	Thank you for your comment. Recommendations about how the measurement of mast cell tryptase should be performed, including the quality assurance requirements of the laboratories that perform these tests, are beyond the scope of this guideline.
SH	Royal College of Pathologists	12.09	Full	3.1.5	24	Recommendations: An additional useful quality recommendation might be that tryptase measurements are only undertaken in accredited laboratories which participate in an appropriate external quality assurance scheme.	Thank you for your comment. Recommendations about how the measurement of mast cell tryptase should be performed, including the quality assurance requirements of the laboratories that perform these tests, are beyond the scope of this guideline.
SH	Royal College of Pathologists	12.10	Full	3.3.4	53	Wording of the text suggest that there are (or will) be only two adrenaline autoinjector devices available. This is not the case, with at least one other BNF-listed preparation (Anapen) also being available for prescription.	Thank you. All trade names have been excluded from the guideline.
SH	Royal College of Physicians London	28.00	Full	General		The RCP is grateful for the opportunity to comment on this consultation. Overall, our experts broadly concur but would like to emphasise the following issues: (1) Because the profile of allergy in undergraduate and postgraduate training is	Thank you for your comments. The guidance document has been amended to provide details on the typical presenting signs and symptoms. However, undergraduate and

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						typically low, many health professionals are uncertain how to make a diagnosis of anaphylaxis and how to differentiate it from other less serious conditions which may mimic it, particularly idiopathic urticaria and angioedema. Thus while it is important to recognise life threatening anaphylaxis and treat it promptly it is also important not to frighten the patient unnecessarily if this diagnosis is not correct and give adrenaline unnecessarily. This is an important training issue which should be addressed through NICE or other means such as CQUIN standards of care. This also touches on correct tuition in the use of adrenaline injectors. (2) The critical observations to make in A&E are for the 3 potentially life threatening features of anaphylaxis: profound hypotension, bronchospasm especially in an exisiting asthmatic and laryngeal oedema (the vocal cords should always be inspected in A&E). Just about all patients should have urticaria with or without angioedema. It is surprising how difficult it is to find such data documented in A&E records. (3) Our experts agree that serum tryptase is helpful if taken according to the guidelines expounded. (4) Agree that prompt referral to an expert allergist (adult or paediatric) is essential: only such professionals can make the diagnosis, initiate appropriate investigations, interpret them and liaise efficiently with other field workers such as school nurses. This may be difficult when there are vast swathes of the country without one: We trust NICE will take due note of	postgraduate training curriculums and the provision of specialist allergy services were outside the remit of this guideline.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						this and hopefully initiate action.	
SH	Royal Victoria Infirmary Newcastle upon Tyne	14.00	Full	General	3	Anaphylaxis is not defined; this is essential as there is major problem of less allergic reactions such as localised angioedema being called 'anaphylaxis' and Epipens being inappropriately issued. This causes specialist services difficulty when explaining to patients that they do NOT have anaphylaxis and do NOT require Epipens	Thank you for your comment. The definition of anaphylaxis has been clarified following consultation.
SH	Royal Victoria Infirmary Newcastle upon Tyne	14.01	Full	General		It would have been helpful if the acute management of anaphylaxis be covered. Intravenous adrenaline is STILL being administered inappropriately in A&E Departments. Definitive statements on the use of Steroids and anti-histamines acutely would be valuable in the light of the Cochrane Reviews. Australasian practice no longer includes these drugs in management	Thank you for your comment. Unfortunately the acute management of anaphylaxis was outside the scope of this guideline.
SH	Royal Victoria Infirmary Newcastle upon Tyne	14.02	Full	3.1	23	The recommendations on Tryptase will have signiifcant economic implications for diagnostic laboratories as it will lead to a very large increase in requests for tryptase assays. This has not been adequately assessed and no health economic modelling has been carried out. This is unacceptable. Tryptase is not required in the majority of reactions and its use should be restricted to cases where there is clinical doubt. The sensitivity and specificity of the assay is not particularly impressive.	Thank you for your comment. We have now provided additional detail outlining the health economic consequences of this recommendation. Although MCT testing represents a non-negligible cost to the NHS, it is currently conducted as part of the management plan during follow-up at specialist allergy clinics. For this reason, the cost of MCT testing is assumed to be incorporated in the cost of a visit to a specialist allergy service in the health economic model described in section 3.3.4. Conducting a separate analysis here would run the risk of double-counting.
SH	Royal Victoria Infirmary Newcastle upon Tyne	14.03	Full	3.2	31	The issue of biphasic reactions and therefore the duration of the period of observation is tied in to the question of whether corticosteroids should be given, as it is believed that they work	Thank you for your comment. The GDG was unable to make an evidence-based recommendation about the use of corticosteroids to prevent biphasic reactions.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						to prevent the late phase reactions. Delay in initial treatment may be a factor in late phase reactions. The requirement for hospital attendance and a period of observation may lead to patients delaying adrenaline administration and subsequently causing a more severe reaction. Some patients can be safely self-managed at home.	The guideline states that patients given emergency treatment should be admitted or observed in order to be clear that these patients will have received emergency treatment first. The GDG felt that all patients given emergency treatment should be either observed (young people and adults) or admitted (children).
SH	Royal Victoria Infirmary Newcastle upon Tyne	14.04	Full	3.3.4	53	The assessment of adrenaline shelf-life is now out-of-date. Jext has not been launched in the UK yet and the new distributor of Epipen (Meda) has addressed the short-shelf life of Epipens, so that there will be little difference in shelf-life between products. This section does not address the fact children and young adults may require 4 pens, as schools and colleges usually insist on keeping 2 pens in a place of safety accessible to teachers; these pens are in addition to the pens that the family will keep at home The economic analysis does not take into consideration the large number of inappropriate prescriptions for adrenaline pens; this guideline will make this problem worse not better.	Thank you for your comments. The base-case shelf life for adrenaline injectors has been changed to 12 months, and it has been noted that this may represent a conservative estimate.. The base-case analysis has been amended to reflect the likelihood of people having up to 4 pens. The economic model does take account of inappropriate use in that cost is incurred for injector regardless of effectiveness, but benefit due to mortality reduction is only incurred with proper and timely use.
SH	Royal Victoria Infirmary Newcastle upon Tyne	14.05	Full	3.3.5	55	Do not support the view that giving out adrenaline for self injection to all patients with a reaction prior to specialist review is justified. This will increase the inappropriate use. Patients with an entirely avoidable allergen do not require adrenaline, nor do patients with non-	Thank you for your comment. However, the committee felt that the risk of harm was offset by the considerable benefits of preventing adverse outcomes from a recurrent anaphylactic episode.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						systemic reactions. However, patients with underlying asthma should be viewed as high risk and prioritised for adrenaline.	
SH	South Western Ambulance Service NHS Foundation Trust	10.00	Full	1.1.7	8	It is often difficult to apply NICE guidelines, as the ambulance phase has either not specifically been mentioned, or it is unclear how it exactly applies. In this case, it is unclear whether if the patient recovers promptly following medication they need to be admitted, or whether they can remain on-scene after a period of monitoring. As, in reality this period is unlikely to exceed 30 minutes at most, it would be extremely useful if the guidelines could specify whether all anaphylaxis patients must be admitted to an ED? Happy to provide data on the current conveyance rates across the South West if that is useful.	Thank you for your comment. It is the expectation that when a patient presents with suspected anaphylaxis and are treated by an emergency team, that they should be admitted into an emergency department in order to be observed for the period described in the recommendations.
SH	UK Clinical Pharmacy Association (UKCPA) & Royal Pharmaceutical Society of Great Britain	18.00	Full	General		There appears to be a lack of emphasis on the responsibility of professionals to communicate information about identified causes of anaphylaxis/severe allergic reaction in a patient to other professionals involved in the care of the patient.	Thank you for your comment. This is a valid comment .The committee considered that if the trigger was readily identifiable that the provision of this information would be standard practice within any referral process.
SH	UK Clinical Pharmacy Association (UKCPA) & Royal Pharmaceutical Society of Great Britain	18.01	Full	General		Further clarification is needed as to who is responsible for referral to the specialist allergy service- is it the professional who has identified the anaphylaxis?	Thank you for your comment. The recommendations have been clarified to make it clear that the referral should take place following emergency treatment and prior to discharge.
SH	UK Clinical Pharmacy Association (UKCPA) & Royal Pharmaceutical Society of Great Britain	18.02	Full	General		There is no mention of using the MHRA Yellow Card Scheme for newly identified anaphylaxis	Thank you for your comment. Unfortunately the process of reporting any adverse drug reactions is outside of the scope of this guideline.
SH	UK Clinical Pharmacy Association (UKCPA) &	18.03	Full	General		There are no details about the documentation /communication between the interfaces of	Thank you for your comment. This is a valid comment and the guideline does make

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
	Royal Pharmaceutical Society of Great Britain					primary/secondary and tertiary care	recommendations on the information that needs to be recorded during the suspected anaphylactic reaction, such as the signs and symptoms and the circumstances prior to the reaction. It was felt that the communication of this information would be standard practice in any referral to specialist services..
SH	UK Clinical Pharmacy Association (UKCPA) & Royal Pharmaceutical Society of Great Britain	18.04	Full	General		There is no reference to the Anaphylaxis algorithm (Resuscitation Council UK) or the APLS anaphylaxis algorithm used in Paediatrics	Thank you for your comment. However, the treatment for anaphylaxis is outside of the scope of this guideline.
SH	UK Clinical Pharmacy Association (UKCPA) & Royal Pharmaceutical Society of Great Britain	18.05	Full	General		There are no definitions of anaphylaxis/severe allergy presenting symptoms	Thank you for your comment. The guidance document has been amended to provide details on the typical presenting symptoms.
SH	UK Clinical Pharmacy Association (UKCPA) & Royal Pharmaceutical Society of Great Britain	18.06	Full	General		There is no mention of Hereditary angioedema / C1-estarase inhibitor deficiency which regularly gets mistaken for anaphylaxis, when the mainstay or treatment should be C1-esterase inhibitor or, in its absence, Fresh Frozen Plasma.	Thank you for your comment. The committee do acknowledge within the evidence to recommendations that the aim of the clinical review after an anaphylactic episode is to rule out other potential diagnoses. However, it is not within the remit of this guideline to detail the various other possible diagnoses.
SH	UK NEQAS for Immunology and Immunochemistry	11.00	Full	1.1.4	8	The blood sampling guidance is different form recommended practice in many centres. This should be phrased to ensure that this is the **minimum** sample requirement and to clarify that a single sample as soon as possible after the reaction onset is the essential sample and ideally within the first hour. The use of a second sample within 1-2 hours to enhance the change of getting a better estimation of the "peak" level is interesting but	Thank you for your comment. The GDG felt that the wording of the current recommendation was sufficient to demonstrate the importance of taking a sample as soon as possible after the reaction following emergency treatment. The evidence to recommendations section has been changed so that it is clear that the need for the second sample is not to estimate the peak of tryptase but to help understand the tryptase

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						not likely to be terribly reliable due to individual differences in half life of the analyte and the text should be re-written to state that its purpose is to determine if the Tryptase rises further in the 1-2 hour period (which is useful clinically).	levels trends after a reaction.
SH	UK NEQAS for Immunology and Immunochemistry	11.01	Full	1.1.5	8	A 24 hour baseline sample should be recommended wherever possible to exclude the possibility of Mastocytosis. If admitted overnight, a sample prior to discharge could be *recommended* if possible. I understand the need to make the guidance simple but ensuring a baseline result is available before discharge would ensure that Mastocytosis is not missed.	Thank you for your comment. Recommendation 1.1.5 has been amended so it is clearer that the purpose of this additional blood sample at specialist follow-up is to measure mast cell tryptase concentration at baseline. The evidence to recommendations section has also been amended to point out that mastocytosis is an example of unexplained high levels of tryptase.
SH	UK NEQAS for Immunology and Immunochemistry	11.02	Full	1.1.8	9	Suggest the text is clarified to ensure that all individuals issued an adrenaline injector are also *trained* in its use. This does appear later in the document but would potentially benefit from repetition.	Thank you for your comment. Where possible within the recommendations repetition is avoided. The need for training in the use of adrenaline injectors is addressed in recommendation1.1.12.
SH	UK NEQAS for Immunology and Immunochemistry	11.03	Full	3.1.4	23	The low quality evidence makes any threshold recommended rather hard to defend, but the median T1/2 is 90 minutes therefore making a 4 hour limit would seem less consistent than a 6 hour limit in terms of ensuring a maximum sensitivity (and low false-negativity" as stated in the aims on page 23, section 3.1.4.	Thank you for your comment. The GDG felt that the few cases with a half-life or peak up to 5 or 6 hours were atypical and that measuring mast cell tryptase at this time would be too late in most patients. The evidence to recommendations section is now clearer about this.
SH	UK NEQAS for Immunology and Immunochemistry	11.04	Full	3.1.4	23	The statement that some individuals have "naturally" high tryptase levels needs to balanced against the observation that false-positive tryptase levels with the current assay have been well described and are not uncommon, at least with the previous formulation of the assay. The	Thank you for your comment. The evidence to recommendations section has been amended to clarify that this is 'unexplained' rather than 'natural' high levels of mast cell tryptase. This section has also been amended to point out that mastocytosis is an example of unexplained high levels of tryptase.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						use of the word natural is inappropriate and unexplained would be preferable. Reference: "Raised tryptase without anaphylaxis or mastocytosis: heterophilic antibody interference in the serum tryptase assay. R. Sargur et al, Clinical and Experimental Immunology 2011;**163**:339-345".	
SH	UK NEQAS for Immunology and Immunochemistry	11.05	Full	3.1.3	21	*"While it was noted that most studies employed methods that are not currently being used in the UK, the GDG did not consider the type of test used to significantly impact upon an overall assessment of the clinical utility of measuring mast cell tryptase."* This is not strictly correct. I should however make it clear that I would agree with the statement that there is no reason to suppose that "αβ" tryptase does not effectively detect acute phase tryptase release in allergic reactions, but any attempt to examine thresholds and ROC curves is futile and not valid unless data related to the current assay is used. The new assay (and there is only one monopoly supplier) is different and utilises different detector antisera (against "αβ" tryptase rather than "β" (mature) tryptase). The new assay was shown from it introduction to tend towards increased positivity in comparison with the former in laboratories, with very different reference ranges, yet a good overall correlation. This is well described, although the assays are thought to be of similar utility in detecting acute phase release.	Thank you for your comment. We have now confirmed with the manufacturer that the test currently available in the UK is the new name for the test that was used in the four studies included for diagnostic accuracy. However, the studies included for timing of mast cell tryptase release used tests (such as ELISA and RIA) which are currently not used in the UK. The GDG considered, despite the differing methods used to measure mast cell tryptase, that they still provided useful information about the timing of mast cell tryptase release. The recommendations about the appropriate timing of the blood samples were based on GDG opinion, informed by the evidence of when the peak or half-life occurred in most patients in the studies. The statement in section 3.1.2 about the tests used in the evidence has been clarified.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						The "β" Tube RIA and "αβ" FEIA (fluorescent enzyme immunoassay) assays are entirely different from each other and use different detector antibodies and have different characteristics. Therefore the sensitivity and specificity data are not directly transferrable and the data has been over-analysed. Only one assay has been available in the UK since the late 1990s (approximately 1996 in the UK).	
SH	UK NEQAS for Immunology and Immunochemistry	11.06	Full	3.1.2	14	Table 2 is interesting and possibly incorrect in places (or the authors incorrect in their method statements) as the UNICAP method was an FEIA even in 1999-2000 (and has always been since introduction in the mid 1990s to my recollection). Some of the papers may also use ELISA technology instead. The authors Mertes and Malinowsky however state that they were using a UNICAP RIA. This is unlikely to be correct unless they were using a modification of the commercially available method. Perhaps they are simply uncertain about the technology used. This should be checked with the authors. Both references (Mertes and Malinowsky) are from the same group and the method details are not extensive in the primary papers.	Thank you for your comment. The table has been updated to state that UniCAP is a fluoroenzymeimmunoassay.
SH	UK NEQAS for Immunology and Immunochemistry	11.07	Full	1.1.2	11	The care pathway makes recommendations for the use of a test in clinical practice without considering Q**uality Assurance** or the lack of a **tryptase reference preparation** to validate the calibration of the assay. This is a major deficiency in many NICE documents. There is no standard reference preparation for tryptase and thus no traceable calibration to ensure that	Thank you for your comment. Recommendations about how the measurement of mast cell tryptase should be performed, including the quality assurance requirements of the laboratories that perform these tests, are beyond the scope of this guideline. While the GDG acknowledged that there is

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						all these assays are producing comparable results. In this case there is only one supplier and the issue of inter-assay comparability is not relevant to current testing practice (there is a monopoly). Since the assay is only from one manufacturer there is a de-facto possibility of concordance between results and assay performance, but it cannot be assumed. If you are recommending an assay is used throughout the country you should include an assessment of comparability between the assays available and involve experts in External Quality Assessment. In this case there should be a clear statement in the text that participation in External Quality Assessment schemes for the measurement of Tryptase should be mandatory for any laboratory providing Tryptase assays. There is an EQA (External Quality Assessment Scheme) for Tryptase and it should be recommended that all providers of the assay participate in EQA to ensure comparability of results between centres. This is core to good practice, mandatory for laboratory accreditation in the UK and essential if NICE is to recommend the use of a test in routine clinical practice.	currently only one method of mast cell tryptase measurement available for use in the UK, the current guideline only recommends that the blood samples are taken for mast cell tryptase tests. They do not make specific recommendations about one type of assay.
SH	UK NEQAS for Immunology and Immunochemistry	11.08	Full	3.1.3.2	21	"Other thresholds showed different sensitivities and specificities" should be removed because it is a statement which is obvious to anyone who understands how tests work and implies a lack of understanding how performance characteristic are calculated. The observation	Thank you for your comment. This statement was included to be clear that only the sensitivities and specificities for some of the thresholds have been reported in this text. This statement has now been removed.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						that changing a threshold changes your calculated false and true positives is actually the basis for plotting ROC curves, it is how 2x2 tables for calculating sensitivities, specificities and predictive values are derived. The extensive data analysis of the thresholds is irrelevant in the absence of a traceable standard, and the fact that many of these assays probably utilise the same antibodies only partly mitigates that problem.	The evidence to recommendations section has now been amended to emphasise the role of GDG opinion in light of the low quality evidence.
SH	UK NEQAS for Immunology and Immunochemistry	11.09	Full	3.3.4	53	The text should be careful not to imply that there are only 2 autoinjectors on the UK market including the "Epipen™". The "Anapen™" is not mentioned. The "Jext™" is not yet in frequent use. While it is reasonable to base your analysis on the cost of the dominant product in the market, NICE should be careful to avoid apparent bias.	Thank you. All trade names will be excluded from the guideline.
SH	UK NEQAS for Immunology and Immunochemistry	11.10	Full	General		Experts in the laboratory analysis of tryptase and the External Quality Assurance of tryptase should have been consulted in any guideline development process where the use of laboratory tests is being promulgated as a key part of the patient pathway. This is often neglected.	Thank you for your comment. Recommendations about how the measurement of mast cell tryptase should be performed, including the quality assurance requirements of the laboratories that perform these tests, are beyond the scope of this guideline.
SH	University of Glamorgan	29.00	Full	Introduction	3-4	No reference to the Resuscitation Council UK anaphylaxis algorithim.	Thank you for your comment. The introduction details the need for the guidance and is not able to refer to specific content of other pieces of guidance.
SH	University of Glamorgan	29.01	Full	1.1.8	9	This section mentions that following emergency treatment all people who have been referred to a specialist allergy service should be offered an adrenaline injector. This statement is unclear.	Thank you for your comment. The recommendations have now been clarified.

Type	Stakeholder	Order No	Document	Section No	Page No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
						What about the use of medi- alerts post emergency treatment-where do these fit in?	
SH	University of Glamorgan	29.02	Full	Care Pathway	11	The Care Pathway states that an adrenaline injector will be offered as an interim measure pending an referral appointment. Emergency care nurses offer these injectors therefore the supply and education of staff is critically important.	Thank you for your comment. Recommendation 1.1.12 does state that before discharge a healthcare professional with the appropriate skills and competencies should offer people a demonstration and information on the appropriate use of an adrenaline injector.

These organisations were approached but did not respond:

ALK Abello
Allergy UK
Association of Anaesthetists of Great Britain & Ireland
Association of Clinical Pathologists
Association of Paediatric Anaesthetists of Great Britain and Ireland
Barchester Healthcare
BMJ
BOC Healthcare
British Medical Association (BMA)
British National Formulary (BNF)
British Paediatric Allergy, Immunity & Infection Group
British Psychological Society, The
British Society of Immunology
British Society of Interventional Radiology
Camden Link
Care Quality Commission (CQC)
Central London Community Healthcare
Citizens Commission on Human Rights
Connecting for Health
Dental Practitioners Association
Department for Communities and Local Government

Department for Education
Department of Health Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI)
Department of Health, Social Services & Public Safety, Northern Ireland (DHSSPSNI)
Dorset Cancer Network
Dorset PCT
Education for Health
Faculty of Dental Surgery
Faculty of General Dental Practice
Faculty of Intensive Care Medicine
George Eilot Hosptal Trust
Gloucestershire Hospitals NHS Trust
Gloucestershire LINk
Great Western Hospitals NHS Foundation Trust
Greater Manchester and Cheshire Cancer Network
Greater Manchester West Mental Health NHS Foundation Trust
Healthcare Improvement Scotland
Healthcare Inspectorate Wales
Healthcare Quality Improvement Partnership
Humber NHS Foundation Trust
Intensive Care Society
Interhealth Canada
JBOL Ltd
Lambeth Community Health
Leeds PCT
Liverpool Community Health
Lothian University Hospitals Trust
Luton & Dunstable Hospital NHS Foundation Trust
Ministry of Defence (MoD)
National Day Nurseries Association
National Patient Safety Agency (NPSA)
National Treatment Agency for Substance Misuse
NHS Clinical Knowledge Summaries Service (SCHIN)
NHS Milton Keynes
NHS Pathways
NHS Plus
NHS Sheffield
NHS Western Cheshire
North Tees & Hartlepool NHS Foundation Trust
North West Allergy and Clinical Immunology Network
Northampton Primary Care NHS Trust

Northumberland Hills Hospital, Ontario
Nottingham Support Group for Carers of Children with Eczema
Paediatric Intensive Care Society
PERIGON Healthcare Ltd
Phadia Ltd
Pharmacosmos
Poole and Bournemouth PCT
Public Health Wales
Queen Anne St Medical Centre
RCPCH Allergy Care Pathways Project
Rotherham NHS Foundation Trust
Royal Berkshire NHS Foundation Trust
Royal Brompton & Harefield NHS Foundation Trust
Royal College of Anaesthetists
Royal College of General Practitioners Wales
Royal College of Midwives
Royal College of Obstetricians and Gynaecologists
Royal College of Psychiatrists
Royal College of Radiologists
Royal College of Surgeons of England
Royal Free Hospital NHS Trust
Royal Society of Medicine
Royal United Hospital
Salford Royal Hospitals Foundation NHS Trust
Scarborough and North Yorkshire Healthcare NHS Trust
Scottish Intercollegiate Guidelines Network (SIGN)
Sheffield Children's NHS Foundation Trust
Sheffield Teaching Hospitals NHS Foundation Trust
Social Care Institute for Excellence (SCIE)
Social Exclusion Task Force
Society for Acute Medicine
Society of Chiropodists & Podiatrists
Solent Healthcare
South Asian Health Foundation
South East Coast Ambulance Service
South London Cardiac and Stroke Network
South Tees Hospitals NHS Trust
Swansea University
Trafford Primary Care Trust
UK Ophthalmic Pharmacy Group

UNISON
United Lincolnshire Hospitals NHS Trust
Welsh Assembly Government
Welsh Scientific Advisory Committee (WSAC)
West Midlands Ambulance Service NHS Trust
Western Health and Social Care Trust
Wirral University Teaching Hospital NHS Foundation Trust
Wirrall Community NHS Trust
Wye Valley NHS Trust
York Teaching Hospital NHS Foundation Trust