

CAST[®] Allergens

for

CAST[®] ELISA
Flow CAST[®]

Inhalant Allergens
Venom Allergens
Food & Food Additives
Environmental Allergens

A Commitment to Diagnostics

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Intended Use

BÜHLMANN CAST® Allergens are optimized for *in vitro* Basophil Activation using BÜHLMANN CAST® assays: CAST® ELISA (EK-CAST) and Flow CAST® (FK-CCR).

CAST® Allergens are not included in BÜHLMANN CAST® assays. They are provided upon request. Refer to the allergen list.

Instruction for Use

The following instructions are intended for the following groups of allergens and mixes of them (refer to TOC page 2).

- Hymenoptera venoms
- Inhalants
- Food and food additives
- Environmental allergens

CAST® Protein allergens (hymenoptera venoms, inhalants food allergens, and environmental allergens) are delivered in liquid format (1 µL) Food additives are delivered dry. Before usage in CAST® assays, they are to be reconstituted / diluted with test specific Stimulation Buffer: CAST® ELISA: B-CAST-STB and Flow CAST®: B-CCR-STB.

- Add 250 µL Stimulation Buffer into the vial and vortex until the allergen (concentrated or dry) has completely dissolved.
- For some allergens we recommend an additional dilution with Stimulation Buffer (refer to the paragraph „Additional dilutions“ in the allergen specifications).
- E.g. an „additional dilution“ of 1:5 is carried out by adding 160 µL Stimulation Buffer to 40 µL allergen solution.
- For stimulation of cells, use these dilutions according to the respective CAST® IFU.

Remark: Some individuals react positive either at high or at low allergen concentrations, whereas others react positive over a broad range of concentration.

Storage and Stability

Unopened CAST® Allergens are to be stored at the temperature specified on the label until to the expiration date.

Important: Reconstituted or diluted allergens must not be stored and used again! Exception: Reconstituted bee venom (BAG2-I1) and wasp venom allergen (BAG2-I3) are stable for 1 month at ≤-20 °C.

Optimal time period for stimulation tests

For optimal results, CAST® assays should be run between 3 and 12 weeks after an allergic reaction to the presumed allergen [Lit.8], although specific basophil reaction is often being persistent over a longer time period.

Blood samples must be drawn for CAST® assays before carrying out a skin test or *in vivo* provocation with the presumed allergen as *in vivo* exposure to an allergen can cause an activation of the leucocytes.

Limitations

A negative CAST® assay result for a specific allergen does not exclude potential (even serious) clinical symptoms. Individuals who developed „allergic“ reactions towards protein or drug allergens in the past and whose CAST® assay was negative, should thus be verified with additional methods like the *in vivo* provocation or skin test before a drug is administered or a patient is exposed to the allergen.

Concentrations and cut-off

Concentrations and cut-off of these allergen groups were optimized regarding maximum specificity and sensitivity. Concentrations to be used in the test and cut-off of individual allergens are reported in the specifications of the allergens (refer to TOC pages 2-3).

For Flow CAST®, BÜHLMANN recommends the application of the stimulation index (SI) as an additional diagnostic criterion. The SI is defined as the ratio of allergen specific basophil activation and background activation.

Remarks:

- In order to apply allergen specific cut-offs, QC criteria published in the CAST® instructions must be fulfilled.
- Cut-offs should serve only as recommendations. Clinically defined cut-offs should be established by each laboratory or through clinical studies.

Application of CAST® allergens for the diagnosis of hymenoptera venom allergies

In order to identify persons allergic to bee or wasp venom we recommend using the allergens bee (BAG2-I1) and wasp venom (BAG2-I3) concentrations in the table for the respective allergen. The excellent sensitivity and specificity of the CAST® assays allows for unambiguous identification of the culprit allergen in most cases [3, 6, 8,9].

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- If double sensitivity to both, bee and wasp allergen, is suspected, we recommend an extended test procedure using different concentrations of the Check allergens: BAG2-I1CHK and BAG2-I3CHK and Flow CAST®. The dose response curves of bee and wasp allergen in 4-5 different dilutions are to be compared. If, for example, the concentration of bee venom needed to trigger 50% of the maximum signal intensity (EC50) is achieved at one-tenth or less of the wasp allergen, a predominant sensitization to bee venom is to be expected [5, 7]. Figure 1 and 2 on page 15 show examples using Flow CAST®.

Application of CAST® allergens for monitoring the specific immunotherapy (SIT) or during outgrow of allergies

- The efficacy of the immunotherapy can be monitored by establishing a dose-response curve with the culprit allergen [1, 15, 17]. Therefore, at least at the beginning and the end of SIT, a dose response curve using 4-5 allergen concentrations is established using Flow CAST®. Additional curves are to be done if needed. The course and success of SIT is measured by the change in the EC50. Changes by a factor of at least 10 towards higher allergen concentrations are considered to be significant (refer to figure 2).
- Check allergens BAG2-I1CHK (bee) and BAG2-I3CHK (wasp) are suitable for monitoring the desensitization of persons allergic to bee and wasp venom. [Refer to 10, 11, 12, 13, 14, 16, 18].
- Peanut extract BAG-F13, and the peanut components Ara h 1 (BAG2-ARAH1), Ara h 2 (BAG2-ARAH2), and Ara h 6 (BAG2-ARAH6) are suitable for monitoring the desensitization of peanut allergics [25].
- Children can outgrow their allergies. This can be monitored e.g. for milk allergy by a shift of the EC50 towards higher concentrations using milk allergen (BAG-F2) [20, 22].

Anwendungszweck

Die BÜHLMANN CAST® Allergene sind optimiert für die *in vitro* Leukozyten Stimulation in den BÜHLMANN CAST® Tests: CAST® ELISA (EK-CAST) und Flow CAST® (FK-CCR). CAST® Allergene sind als einzelne Reagenzien erhältlich und sind kein Bestandteil der CAST® Test Kits.

Gebrauchsanweisung

Die nachfolgende Anleitung gilt für die folgenden Allergene sowie deren Allergengemische (siehe Inhaltsverzeichnis auf Seite 2):

- Hymenopterengifte
- Inhalationsallergene
- Nahrungsmittel und Nahrungsmittelzusatzstoffe
- Umweltallergene

CAST® Protein - Allergene (Hymenopterengifte, Inhalations-Nahrungsmittel- und Umweltallergene) werden als Flüssigkonzentrat (1 µL) geliefert. Nahrungsmittelzusatzstoffe werden in getrockneter Form geliefert. Vor dem Gebrauch der Allergene in den CAST® Tests, werden diese mit dem Test spezifischen Stimulationspuffer (CAST® ELISA: B-CAST-STB und Flow CAST®: B-CCR-STB) verdünnt bzw. gelöst:

- Geben Sie 250 µL Stimulationspuffer in das Fläschchen mit dem getrockneten bzw. konzentrierten Allergen und vortexen Sie bis sich alles gelöst hat.
- Bei einigen Allergenen empfehlen wir eine zusätzliche Verdünnung mit Stimulationspuffer anzusetzen (siehe Angabe unter „Additional dilutions“ bei den Allergenbeschreibungen).
- Bei einer zusätzlichen Verdünnung von 1:5 („Additional dilutions“) mischen Sie zum Beispiel 40 µL Allergen Lösung mit 160 µL Stimulationspuffer.
- Setzen Sie diese Lösung(en) gemäss der entsprechenden CAST® Testarbeitsanleitung zur Stimulation der Zellen ein.

Bemerkung: Einzelne Patienten zeigen nur eine positive Stimulation entweder bei hohen oder tiefen Allergenkonzentrationen, während andere über einen breiten Konzentrationsbereich positiv reagieren.

Lagerung und Haltbarkeit

Ungeöffnete CAST® Allergene können bei der auf der Etikette angegebenen Temperatur bis zum Verfallsdatum gelagert werden.

Wichtig: Aufgelöste oder verdünnte Allergene sollen nicht aufbewahrt und wieder verwendet werden! Ausnahme: Die Allergene Bienengift (BAG2-I1) und Wespengift (BAG2-I3) können nach Auflösen im Stimulationspuffer bei ≤-20 °C für einen Monat aufbewahrt werden.

Zeitpunkt der Patientenmessung

Der optimale Zeitraum zur Durchführung eines CAST® Tests liegt zwischen 3 und 12 Wochen nach einer allergischen Reaktion auf ein vermutetes Allergen [Lit.4]. Dies, obwohl die spezifische Reaktivität der basophilen Zellen oft auch über einen noch längeren Zeitraum erhalten bleibt.

Die Blutproben für die CAST® Tests müssen abgenommen werden, bevor ein Hauttest oder eine *in vivo* Provokation mit dem verdächtigen Allergen durchgeführt wurde. Die *in vivo* Exposition gegenüber einem Allergen kann eine Aktivierung der Patientenleukozyten zur Folge haben.

Einschränkungen

Ein negatives CAST® Test Resultat für ein spezifisches Allergen schliesst die Möglichkeit einer (auch schweren) klinischen Reaktion beim Patienten nicht aus. Patienten, die früher „allergische“ Reaktionen gegenüber Protein- oder Medikamenten-Allergenen gezeigt haben und die ein negatives CAST® Test Resultat haben, sollten deswegen wenn möglich, mit weiteren Methoden wie *in vivo* Provokation oder Hauttestung getestet werden, bevor ein Medikament verabreicht wird oder der Patient dem Allergen ausgesetzt wird.

Konzentrationen und Grenzwert

Die Konzentrationen und Grenzwert (cut-off) der CAST® Allergene wurden optimiert bezüglich höchst möglicher Spezifität und Sensitivität [Lit.2,3]. Die in den Test einzusetzenden Konzentrationen und den Grenzwert finden Sie bei der Beschreibung der einzelnen Allergene (siehe Seiten 2-3, Inhaltsverzeichnis).

Beim Flow CAST® wird die Anwendung eines Stimulationsindex (SI) als zusätzliches Kriterium durch BÜHLMANN vorgeschlagen. Der SI ist definiert als der Quotient aus allergenspezifischer Basophilenaktivierung und dem Basalwert.

Hinweise:

- Um die Allergen spezifischen Grenzwerte anzuwenden, müssen die in der CAST® Testarbeitsanleitung beschriebenen Qualitätskontroll-Kriterien erfüllt werden.
- Diese Grenzwerte dürfen nur als Empfehlungen betrachtet werden. Klinisch relevante Grenzwerte sollten durch jedes Labor oder durch weitere Studien ermittelt werden.

Einsatz von CAST® Allergenen in der Diagnostik von Hymenopterengift Allergien

Zur diagnostischen Identifikation von Bienen- oder Wespengift Allergikern empfehlen wir die Anwendung des Bienengifts (BAG2-I1) und des Wespengifts (BAG2-I3) in der Konzentration, die in der Tabelle für das jeweilige Allergen vorgegeben ist. Die sehr gute Sensitivität und Spezifität der CAST® Tests ermöglicht eine eindeutige Identifikation des auslösenden Allergens in den allermeisten Fällen [Lit. 3, 6, 8, 9].

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- Bei Patienten mit vermuteten Doppel-Sensibilisierungen gegen Biene- und Wespengift, empfehlen wir eine erweiterte Austestung mit mehreren Allergenkonzentrationen mit Hilfe der Check-Allergene: BAG2-I1CHK (Biene) und BAG2-I3CHK (Wespe) und Flow CAST®. Dazu werden Dosis-Wirkungskurven mit 4-5 Verdünnungen des Bienen- und des Wespengift-Allergens miteinander verglichen. Kann zum Beispiel die Halbmaximale-Stimulierbarkeit (EC50) durch das Bienengift-Allergen durch eine 10fach kleinere Dosis des Wespengift-Allergens oder weniger erreicht werden, kann von einer prädominanten Sensibilisierung durch das Bienengift-Allergen ausgegangen werden [Lit. 5 , 7]. Beispiele mit Flow CAST® sind in Abbildung 1 und 2 auf Seite 15 dargestellt.

Einsatz von CAST® Allergenen im Monitoring von spezifischen Immuntherapien (SIT) oder beim Auswachsen von Allergien

- Anhand von Dosis-Wirkungskurven mit dem zu therapeutierenden Allergen kann der Effekt und die Wirkung der Immuntherapie beobachtet werden [Lit. 1, 15, 17]. Dazu werden mindestens vor und nach Abschluss (bei Bedarf auch während) der SIT, Dosis-Wirkungskurven über 4-5 Allergenkonzentrationen im CAST® Test gemessen und anhand der Veränderung der halbmaximalen Stimulierbarkeit (EC50) der Therapieverlauf bzw. -erfolg gemessen. Änderungen des EC50 von mehr als einen Faktor von 10 hin zu grösseren Allergenkonzentrationen können als signifikant betrachtet werden. Siehe Abbildung 2.
- Für das Monitoring von Desensibilisierungen bei Bienen- und Wespengift Allergikern werden die Check-Allergene: BAG2-I1CHK (Biene) und BAG2-I3CHK (Wespe) eingesetzt (siehe auch [Lit. 10, 11, 12, 13, 14, 16, 18]).
- Für das Monitoring von Desensibilisierungen bei Erdnussallergie können der Erdnussextrakt BAG-F13, sowie die Erdnusskomponenten Ara h 1 (BAG2-ARAH1), Ara h 2 (BAG2-ARAH2) sowie Ara h 6 (BAG2-ARAH6) eingesetzt werden [Lit. 25]
- Bei Kindern können sich Allergien „auswachsen“. Das kann z.B. bei Milchallergie über die Verschiebung des EC50 von Milchallergen (BAG-F2) zu höheren Allergenkonzentrationen gemessen werden [Lit. 20, 22].

Utilisation prévue

Les allergènes CAST® de BÜHLMANN sont optimisés pour l'activation des basophiles *in vitro* dans les tests CAST® de BÜHLMANN : CAST® ELISA (EK-CAST) et Flow CAST® (FK-CCR) .

Les allergènes CAST® ne sont pas fournis dans les kits de dosage CAST® de BÜHLMANN, mais vendus séparément. Consulter la liste d'allergènes.

Mode d'emploi

Les instructions suivantes se réfèrent aux groupes d'allergènes ci-dessous et à leurs mélanges (consulter le sommaire à la page 2).

- Venins d'hyménoptères
- Pneumallergènes
- Aliments et additifs alimentaires
- Allergènes environnementaux

Les allergènes protéiques CAST® (venins d'hyménoptères, pneumallergènes, aliments et allergènes environnementaux) sont vendus sous forme liquide (1 µL). Les additifs alimentaires sont vendus sous forme déshydratée. Ils doivent être reconstitués ou dilués dans le tampon de stimulation correspondant au test avant emploi dans les tests CAST® : CAST® ELISA B-CAST-STB et Flow CAST® : B-CCR-STB.

- Ajouter 250 µL de tampon de stimulation dans le flacon. Vortexer jusqu'à dissolution complète de l'allergène (concentré ou déshydraté).
- Dans le cas de certains allergènes, nous recommandons une dilution supplémentaire dans le tampon de stimulation. Consulter le paragraphe « Additional dilutions » dans les spécifications de l'allergène.
- Par exemple, une dilution au 1/5 («Additional dilution») est réalisée en ajoutant 160 µL de tampon de stimulation à 40 µL de solution d'allergène.
- Pour la simulation de cellules, utiliser ces dilutions conformément aux instructions d'utilisation du test CAST® correspondant.

Remarque : certains individus ne réagissent positivement à l'allergène qu'à faible ou forte concentration, tandis que d'autres réagissent positivement sur une large plage de concentrations.

Stockage et stabilité

Conserver les allergènes CAST® non ouverts à la température indiquée sur l'étiquette, sans dépasser la date de péremption.

Important : ne jamais stocker ni réutiliser un allergène reconstitué ou dilué ! Exception : les allergènes reconstitués de venin d'abeille (BAG2-I1) et de venin de guêpe (BAG2-I3) sont stables pendant un mois à une température ≤ - 20 °C.

Délai optimal pour les tests de stimulation

Pour obtenir des résultats optimaux, il convient de réaliser les tests CAST® 3 à 12 semaines après la réaction allergique à l'allergène présumé [Lit.8], bien que la réaction spécifique des basophiles puisse être observée sur une durée plus importante.

Prélever les échantillons sanguins pour les tests CAST® avant le test cutané ou la provocation *in vivo* avec l'allergène présumé. En effet, toute exposition *in vivo* à un allergène peut entraîner l'activation des leucocytes.

Limites

Un résultat négatif au test CAST® pour un allergène spécifique n'écarte pas la possibilité de symptômes cliniques, y compris graves. Pour les individus ayant présenté par le passé des réactions « allergiques » vis-à-vis de protéines ou de médicaments allergènes dont le test CAST® se révèle négatif, le résultat doit être vérifié par d'autres méthodes, comme la provocation *in vivo* ou un test cutané avant l'administration d'un médicament ou d'un allergène.

Concentrations et seuil

Les concentrations et la valeur seuil (cut-off) des présents groupes d'allergènes ont été optimisées pour une spécificité et une sensibilité maximales. Les concentrations utilisées dans le test et la valeur seuil de chacun des allergènes sont indiquées dans les spécifications correspondantes (consulter le sommaire aux pages 2-3).

Dans le cas du test Flow CAST®, BÜHLMANN recommande d'utiliser un critère de diagnostic supplémentaire, l'indice de stimulation (IS). L'IS est défini comme le quotient entre l'activation spécifique des basophiles et leur activation de base.

Remarques :

- Pour appliquer le seuil spécifique de l'allergène, il convient de respecter les critères de contrôle qualité publiés dans les instructions des tests CAST®.
- Les valeurs seuils ne sont fournies qu'à titre indicatif. Chaque laboratoire doit définir ses propres valeurs de seuil clinique, soit directement, soit en s'appuyant sur des études cliniques.

Utilisation des allergènes CAST® dans le diagnostic des allergies aux venins d'hyménoptères

Pour identifier les individus allergiques au venin d'abeille ou de guêpe, nous recommandons l'emploi des allergènes abeille (BAG2-I1) et guêpe (BAG2-I3) dans les concentrations indiquées dans la table de l'allergène respective. Caractérisés par une excellente sensibilité et spécificité, les tests CAST® permettent d'identifier sans ambiguïté l'allergène responsable de l'allergie dans la plupart des cas [3, 6, 8, 9].

- En cas de double sensibilité suspectée aux allergènes d'abeille et de guêpe, il est conseillé de procéder à un protocole de test allongé en utilisant plusieurs concentrations des allergènes « check » : BAG2-I1CHK et BAG2-I3CHK et Flow CAST®. Comparer ensuite les courbes dose-réponse obtenues pour les deux allergènes avec 4 ou 5 concentrations différentes. Si, par exemple, la concentration de venin d'abeille requise pour obtenir une réponse égale à 50 % du signal maximal (EC50) est au moins 10 fois inférieure à la concentration de l'allergène de venin de guêpe, on pourra s'attendre à une sensibilisation prédominante au venin d'abeille [5, 7. Les figures 1 et 2, page 15, illustrent l'utilisation du test Flow CAST®.

Utilisation des allergènes CAST® dans le suivi d'immunothérapies spécifiques (ITS) ou de la disparition naturelle d'une allergie

- L'efficacité de l'immunothérapie peut être vérifiée en établissant une courbe dose-réponse pour l'allergène responsable [1, 15, 17]. Une courbe dose-réponse déterminée à partir de 4 ou 5 concentrations de l'allergène doit ainsi être déterminée au minimum au début et à la fin de l'ITS avec le test Flow CAST®. Des courbes supplémentaires peuvent être réalisées si besoin. La progression et la réussite de l'ITS sont indiquées par la modification de la EC50. L'augmentation de la concentration d'au moins un facteur 10 vers la concentration la plus élevée d'allergène est considérée comme significative (voir la figure 2).

- Les «check-allergènes» BAG2-I1CHK (abeille) et BAG2-I3CHK (guêpe) permettent de suivre la désensibilisation des individus allergiques au venin d'abeille et de guêpe. [Voir 10, 11, 12, 13, 14, 16, 18].
- L'extrait d'arachide BAG-F13 et les composants de l'arachide Ara h 1 (BAG2-ARAH1), Ara h 2 (BAG2-ARAH2) et Ara h 6 (BAG2-ARAH6) permettent de suivre la désensibilisation des individus allergiques à l'arachide [25].
- Les allergies survenant chez l'enfant peuvent disparaître avec l'âge. Cette évolution peut être suivie, par exemple pour une allergie au lait, en étudiant le décalage de la EC50 vers des concentrations plus élevées en utilisant un allergène de lait (BAG-F2) [20, 22].

Uso previsto

Gli Allergeni CAST® della BÜHLMANN sono ottimizzati per l'attivazione dei basofili *in vitro* mediante i seguenti dosaggi BÜHLMANN CAST®: CAST® ELISA (EK-CAST) e Flow CAST® (FK-CCR).

Gli Allergeni CAST® non sono inclusi nei dosaggi BÜHLMANN CAST® e vengono forniti su richiesta. Fare riferimento all'elenco degli allergeni.

Istruzioni per l'uso

Queste istruzioni sono relative ai seguenti gruppi di allergeni e a combinazioni degli stessi (consultare l'indice a pagina 2).

- Veleni di imenotteri
- Inalanti
- Alimenti e additivi alimentari
- Allergeni ambientali

Gli allergeni proteici CAST® (veleni di imenotteri, inalanti, allergeni alimentari e allergeni ambientali) sono forniti in forma liquida (1 µL), mentre gli additivi alimentari sono forniti secchi. Prima dell'utilizzo nei dosaggi CAST®, devono essere ricostituiti/diluiti con il tampone di stimolazione specifico del test: CAST® ELISA: B-CAST-STB e Flow CAST®: B-CCR-STB.

- Aggiungere 250 µL di tampone di stimolazione al flacone e vortexare fino a completa dissoluzione dell'allergene (concentrato o secco).
- Per alcuni allergeni si consiglia un'ulteriore diluizione con tampone di stimolazione (consultare il paragrafo "Additional dilutions" nelle specifiche degli allergeni).
- Ad esempio: per ottenere una diluizione 1:5 («Additional dilution»), aggiungere 160 µL di tampone di stimolazione a 40 µL di soluzione di allergene.
- Per la stimolazione di cellule, utilizzare queste diluizioni secondo le istruzioni per l'uso per il rispettivo CAST®.

Nota: alcuni individui hanno una reazione positiva ad alte oppure a basse concentrazioni di allergene, mentre altri hanno una reazione positiva in un ampio intervallo di concentrazioni.

Conservazione e stabilità

Gli allergeni CAST® non aperti devono essere conservati alla temperatura indicata sull'etichetta fino alla data di scadenza.

Importante: non conservare né riutilizzare allergeni ricostituiti o diluiti! Eccezione: gli allergeni ricostituiti del veleno d'ape (BAG2-I1) e del veleno di vespa (BAG2-I3) sono stabili per 1 mese a ≤-20 °C.

Tempo ottimale per i test di stimolazione

Per ottenere risultati ottimali, eseguire i dosaggi CAST® tra 3 e 12 settimane dopo una reazione allergica al presunto allergene [Bibl. 8], sebbene la specifica reazione basofila spesso persista per un periodo di tempo più lungo.

È necessario prelevare campioni di sangue per i test CAST® prima di eseguire un test cutaneo o un test di provocazione *in vivo* con il presunto allergene, dal momento che l'esposizione *in vivo* ad un allergene può causare un'attivazione dei leucociti.

Limitazioni

Il risultato negativo di un test CAST® per un allergene specifico non esclude la possibilità di sintomi clinici (anche seri). I pazienti con anamnesi di reazioni "allergiche" ad allergeni proteici o a farmaci e CAST® negativi dovrebbero quindi essere studiati con ulteriori metodi, come test di provocazione *in vivo* o test cutanei prima della somministrazione del farmaco o dell'allergene.

Concentrazioni e cut-off

I valori di concentrazioni e cut-off di questi gruppi di allergeni sono stati ottimizzati per quanto riguarda la massima specificità e sensibilità. Le concentrazioni utilizzati nel test e il valore dei cut-off dei singoli allergeni sono riportati nelle specifiche degli allergeni (consultare l'indice alle pagine 2-3).

Per Flow CAST®, BÜHLMANN propone l'uso dell'indice di stimolazione (SI) come ulteriore criterio discriminante. Lo SI è definito come il quoziente tra la attivazione basophila specifica e la attivazione aspecifica.

Osservazioni:

- Per poter applicare valori di cut-off specifici dell'allergene in questione, è necessario che siano soddisfatti i criteri di QC pubblicati nelle istruzioni per i CAST®.
- I valori di cut-off devono essere considerati come indicativi. Il cut-off clinico deve essere stabilito da ogni singolo laboratorio o attraverso studi clinici.

Applicazione degli allergeni CAST® per la diagnosi di allergie al veleno di imenotteri

Per identificare i pazienti allergici al veleno d'ape o di vespa, si consiglia di utilizzare gli allergeni veleno d'ape (BAG2-I1) e vespa (BAG2-I3) nelle concentrazioni riportate nella tabella corrispondente. Nella maggior parte dei casi, l'eccellente sensibilità e specificità dei dosaggi CAST® consentono di identificare senza ambiguità l'allergene responsabile [3, 6, 8, 9].

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- Se si sospetta una doppia sensibilità a entrambi gli allergeni, ape e vespa, si consiglia di adottare una procedura di analisi estesa utilizzando diverse concentrazioni degli allergeni di controllo: BAG2-I1CHK, BAG2-I3CHK e Flow CAST®. Le curve di risposta alla dose di allergeni d'ape e di vespa in 4-5 diverse diluizioni devono essere confrontate. Se, per esempio, la concentrazione di veleno d'ape necessaria a innescare il 50% dell'intensità massima del segnale (EC50) viene già raggiunta a un decimo o meno dell'allergene di vespa, si dovrà prevedere una sensibilizzazione predominante al veleno d'ape [5,7]. Le figure 1 e 2 a pagina 15 mostrano esempi relativi all'uso di Flow CAST®.

Applicazione degli allergeni CAST® per il monitoraggio dell'immunoterapia specifica (ITS) o durante il superamento delle allergie con la crescita

- L'efficacia dell'immunoterapia può essere monitorata stabilendo una curva dose-risposta con l'allergene responsabile [1, 15, 17]. Pertanto, almeno all'inizio e alla fine dell'ITS, viene stabilita mediante Flow CAST® una curva dose-risposta utilizzando 4-5 concentrazioni di allergene. Se necessario, devono essere realizzate ulteriori curve. Il decorso e il successo della ITS si misurano in base alla variazione di EC50. Una variazione è considerata significativa quando c'è un fattore di variazione pari almeno a 10 verso concentrazioni maggiori di allergene (vedere la figura 2).
- Gli allergeni 'check' BAG2-I1CHK (ape) e BAG2-I3CHK (vespa) sono idonei per il monitoraggio della desensibilizzazione dei pazienti allergici al veleno d'ape e di vespa [fare riferimento a 10, 11, 12, 13, 14, 16, 18].
- L'estratto d'arachide BAG-F13 e i componenti delle arachidi Ara h1 (BAG2-ARAH1), Ara h2 (BAG2-ARAH2) e Ara h6 (BAG2-ARAH6) sono idonei per il monitoraggio della desensibilizzazione dei pazienti allergici alle arachidi [25].
- Crescendo, i bambini riescono a risolvere spontaneamente le loro allergie. Questo può essere monitorato, ad esempio, nel caso dell'allergia al latte con uno spostamento della EC50 verso concentrazioni più alte utilizzando l'allergene latte (BAG-F2) [20, 22].

Uso previsto

Los alérgenos BÜHLMANN CAST® están optimizados para la activación de basófilos *in vitro* utilizando los tests BÜHLMANN CAST®: CAST® ELISA (EK-CAST) y Flow CAST® (FK-CCR).

Los alérgenos CAST® no vienen incluidos en los ensayos BÜHLMANN CAST®. Se facilitan previa solicitud. Véase la lista de alérgenos.

Instrucciones de uso

Las instrucciones siguientes se refieren a los siguientes grupos de alérgenos y mezclas de ellos (véase el índice en la página 2).

- Venenos de himenópteros
- Inhalantes
- Alimentos y aditivos alimentarios
- Alérgenos ambientales

Los alérgenos proteicos CAST® (venenos de himenópteros, inhalantes, alimentos y alérgenos ambientales) se entregan en formato líquido (1 µL); los aditivos alimentarios se entregan secos. Antes de usarlos en tests CAST®, deben ser reconstituídos / diluidos con el tampón de estimulación específico de la prueba: CAST® ELISA: B-CAST-STB y Flow CAST®: B-CCR-STB.

- Añada 250 µL de tampón de estimulación al vial y sométalo a vórtice hasta que el alérgeno (concentrado o seco) se haya disuelto completamente.
- Para algunos alérgenos, recomendamos una dilución adicional con tampón de estimulación (véase el párrafo “Additional dilutions” en las especificaciones de alérgenos).
- P.ej. Se lleva a cabo una dilución “1:5” («Additional dilution») añadiendo 160 µL de tampón de estimulación a 40 µL de solución de alérgeno.
- Para la estimulación celular, utilice esas diluciones conforme a lo indicado en las respectivas Instrucciones de uso de CAST®.

Observación: Algunas personas reaccionan positivamente bien a altas o a bajas concentraciones de alérgeno, mientras que otras reaccionan positivamente en un amplio rango de concentraciones.

Almacenamiento y estabilidad

Los alérgenos CAST® sin abrir deben almacenarse a la temperatura especificada en la etiqueta hasta su fecha de caducidad.

Importante: ¡Los alérgenos reconstituídos o diluidos no deben ser almacenados y reutilizados! Excepción: Los alérgenos de veneno de abeja (BAG2-I1) y veneno de avispa (BAG2-I3) reconstituídos son estables durante 1 mes a ≤-20 °C.

Período de tiempo óptimo para los tests de estimulación

Para obtener unos resultados óptimos, los tests CAST® se deben llevar a cabo entre 3 y 12 semanas después de una reacción alérgica al supuesto alérgeno [Ref.8], pese a que la reacción específica de los basófilos suele persistir a menudo durante un período de tiempo más largo.

Las muestras de sangre para tests CAST® se deben extraer antes de llevar a cabo tests cutáneos o de provocación *in vivo* con el supuesto alérgeno, ya que la exposición *in vivo* a un alérgeno puede provocar una activación de los leucocitos.

Limitaciones

Un resultado negativo en una prueba CAST® para un determinado alérgeno no excluye posibles síntomas clínicos (incluso de gravedad). Para las personas que hayan presentado reacciones “alérgicas” frente a alérgenos proteicos o medicamentosos con anterioridad y cuyo resultado en un test CAST® sea negativo, debería verificarse ese resultado con métodos adicionales como la provocación *in vivo* o prueba cutánea antes de que les sea administrado un medicamento o alérgeno.

Concentraciones y punto de corte

Las concentraciones y el punto de corte (cut-off) de estos grupos de alérgenos se optimizaron con respecto a la máxima especificidad y sensibilidad. Las concentraciones utilizadas en el test y el punto de corte específico correspondientes a los distintos alérgenos se indican en las especificaciones de los mismos (véase el índice en las páginas 2-3).

Para Flow CAST®, BÜHLMANN recomienda la aplicación del índice de estimulación (IE o SI por las siglas en inglés) como criterio diagnóstico adicional. El IE o SI se define como el cociente entre la activación específica de los basófilos y la activación básica.

Observaciones:

- Para aplicar el punto de corte específico para cada alérgeno, deben cumplirse los criterios de control de calidad recogidos en las instrucciones de CAST®.
- Los puntos de corte deben servir únicamente como recomendaciones. Deben establecerse umbrales clínicamente definidos en cada laboratorio o mediante estudios clínicos.

Aplicación de alérgenos CAST® en el diagnóstico de alergias a venenos de himenópteros

Para determinar si una persona es alérgica al veneno de abeja o de avispa, recomendamos utilizar los alérgenos de veneno de abeja (BAG2-I1) y veneno de avispa (BAG2-I3) en las concentraciones indicadas en la tabla del alérgeno correspondiente. La excelente sensibilidad y especificidad de los tests CAST® permite identificar sin lugar a duda el alérgeno responsable en la mayoría de los casos [3,6,8,9].

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- Cuando se sospeche una doble sensibilidad a ambos alérgenos, de abeja y de avispa, recomendamos llevar a cabo un procedimiento de prueba ampliado utilizando distintas concentraciones de los alérgenos de comprobación: BAG2-I1CHK y BAG2-I3CHK, y Flow CAST®. Deben compararse las curvas dosis-respuesta de los alérgenos de abeja y avispa en 4 o 5 diluciones diferentes. Si, por ejemplo, la concentración de veneno de abeja necesaria para desencadenar el 50% de la intensidad de señal máxima (EC50) se alcanza a una décima parte o menos del alérgeno de avispa, cabe esperar una sensibilización predominante al veneno de abeja [5,7]. Las figuras 1 y 2 en la página 15 muestran ejemplos utilizando Flow CAST®.
 - Las alergias infantiles pueden remitir y desaparecer cuando los niños crecen. Eso puede monitorizarse, por ejemplo en el caso de una alergia a la leche a través del desplazamiento del valor EC50 hacia concentraciones más altas cuando se utiliza el alérgeno de la leche (BAG-F2) [20, 22].

Aplicación de alérgenos CAST® en la monitorización de inmunoterapias específicas (ITE o SIT por las siglas en inglés) o durante la remisión / desaparición de alergias

- La eficacia de la inmunoterapia puede monitorizarse estableciendo una curva dosis-respuesta con el alérgeno responsable [1, 15, 17]. Por lo tanto, cuando menos al comienzo y al final de la ITE o SIT, se establece una curva dosis-respuesta con 4 o 5 concentraciones de alérgeno utilizando Flow CAST®; puede ser necesario obtener curvas adicionales. El transcurso y el éxito de la inmunoterapia específica se mide a través del cambio en el valor EC50. Se consideran significativos los cambios en un factor de al menos 10 hacia concentraciones de alérgeno más altas (véase la figura 2).
- Los alérgenos “check” BAG2-I1CHK (abeja) y BAG2-I3CHK (avispa) son aptos para monitorizar la desensibilización de personas alérgicas a los venenos de abeja y avispa. [Véanse las referencias 10, 11, 12, 13, 14, 16, 18].
- El extracto de cacahuete BAG-F13 y los componentes del cacahuete Ara h 1 (BAG2-ARAH1), Ara h 2 (BAG2-ARAH2) y Ara h 6 (BAG2-ARAH6) son aptos para monitorizar la desensibilización de alérgicos al cacahuete [25].

General

1. Patil SU et al.: Immunology in the clinic review series; focus on allergies: basophils as biomarkers for assessing immune modulation. *Clin Exp Immunol* 2011, 167: 59–66.
2. Wolanczyk-Medrala A. et al.: A new variant of the basophil activation test for allergen-induced basophil CD63 upregulation. The effect of cetirizine. *J Investig Allergol Clin Immunol* 2009, 19(6): 465-73.
3. Schneider M. et al.: Towards a clinical validation of the BÜHLMANN Flow2 CAST® basophil activation test for drug and protein allergy. Poster presented at XXV. EAACI annual meeting, Warsaw, 06.-10. June 2009.
4. Ebo DG et al.: Basophil activation test by flow cytometer: present and future applications in allergology. *Cytometry B Clin Cytom* 2008, 74: 201-10.
5. Int Arch Allergy Immunol. 2008, 146: 248-54.
15. Korosec P. et al.: Predicting side-effects in venom immunotherapy by basophil activation: basophil sensitivity vs maximal response. *Allergy* 2007, 62: 81.
16. Ebo DG et al.: Flow-assisted quantification of in vitro activated basophils in the diagnosis of wasp venom allergy and follow-up of wasp venom immunotherapy. *Cytometry B Clin Cytom* 2007, 72: 196-203.
17. Kosnik M. et al.: High sensitivity of basophils predicts side-effects in venom immunotherapy. *Allergy* 2005, 60: 1401-6.
18. Erdmann SM et al.: The basophil activation test in wasp venom allergy: sensitivity, specificity and monitoring specific immunotherapy. *Allergy* 2004, 59: 1102-9

Insect Venom Allergy

5. Eberlein B. et al.: Double positivity to bee and wasp venom: Improved diagnostic procedure by recombinant allergen-based IgE testing and basophil activation test including data about CCDs. *J Allergy Clin Immunol* 2012, 130: 155-61.
6. Kosnik M. et al.: Importance of basophil activation testing in insect venom allergy. *Allergy, Asthma & Clinical Immunol* 2009, 5: 11.
7. Hausmann O. et al.: Double positivity in insect venom allergy – diagnostic approach with basophil activation test. Poster presented at XXV. EAACI annual meeting, Warsaw, 06.-10. June 2009.
8. Scherer K. et al.: Cellular in vitro assay in the diagnosis of hymenoptera venom allergy. *Intl Arch Allergy and Immunol* 2008, 146: 122-32.
9. Ebo DG. et al: Hymenoptera venom allergy: taking the sting out of difficult cases. *J Investig Allergol Clin Immunol* 2007, 17: 357-60.

Insect Venom Immunotherapy

10. Zitnik SEK et al.: Monitoring honeybee venom immunotherapy in children with the basophil activation test. *Pediatr Allergy Immunol* 2012, 23: 166–172.
11. Kucera Pet al.: Basophil activation can predict clinical sensitivity in patients after venom immunotherapy. *J Investig Allergol Clin Immunol*. 2010, 20: 110-6.
12. Mikkelsen S. et al.: Basophil sensitivity through CD63 or CD203c is a functional measure for specific immunotherapy. *Clin Mol Allergy* 2010, 8: 2.
13. Hausmann O. et al.: Usefulness of the basophil activation tests in monitoring the immune response to bee venom immunotherapy controlled by sting challenge – pilot phase results. Poster presented at XXV. EAACI annual meeting, Barcelona, 06.-10. June 2008.
14. Peternelj A. et al.: Basophil sensitivity in patients not responding to venom immunotherapy. *Allergy* 2004, 59: 1102-9
19. Glaumann S. et al.: Basophil allergen threshold sensitivity, CD-sens, IgE-sensitization and DBPCFC in peanut-sensitized children. *Allergy* 2012, 67: 242-7.
20. Rubio A. et al.: Benefit of the basophil activation test in deciding when to reintroduce cow's milk in allergic children. *Allergy* 2010, 66: 92-100.
21. Octman A. et al: Basophil activation tests for the diagnosis of food allergy in children. *Clin & Exp Allergy* 2009, 39: 1234-45.
22. Wanich N. et al.: Allergen-specific basophil suppression associated with clinical tolerance in patients with milk allergy. *J Allergy Clin Immunol* 2009, 123: 789-94.
23. Ebo DG: Basophil activation tests in food allergy. *Clin & Exp Allergy* 2009, 39: 1115-6.
24. Caruso M. et al.: Effects of a new nutraceutical ingredient on allergen-induced sulphidoleukotrienes production and CD63 expression in allergic subjects. *Int Immunopharmacol* 2008, 20: 1781-6.
25. Jones SM. et al.: Clinical efficacy and immune regulation with peanut oral immunotherapy. *J Allergy Clin Immunol* 2009; 124:292–300, e1-97.
26. Shreffler WG: Evaluation of basophil activation in food allergy: present and future applications. *Curr Opin Allergy Clin Immunol* 2006; 6: 226-33.

Insect Venoms

Order Code	Name	Taxonomic	DE	FR	IT	ES
BAG2-I1	Honey Bee Venom	Apis mellifera	Bienengift	Venin d'abeille	Veleno d'api	Veneno de abeja
BAG2-I3	Yellow Jacket Venom	Vespula spp.	Wespengift	Venin de guêpe	Veleno de vespa	Veneno de avispa
BAG2-I75	European Hornet Venom	Vespa crabro	Hornissengift	Venin de frelon	Veleno de calabrone	Veneno de avispon
BAG2-I77	European Paper Wasp Venom	Polistes dominula	Feldwespengift	Venin de guêpe poliste gaulois	Veleno de vespa gallica	Veneno de avispa galica

	Content per vial	CAST® ELISA		Flow CAST®	
		Conc. in stim.	Cut-off	Conc. in stim.	Cut-off (CD63)
BAG2-I1	12.5 ng	10 ng/mL	≥270 pg/mL	11.5 ng/mL	≥10%
BAG2-I3	12.5 ng	10 ng/mL	≥270 pg/mL	11.5 ng/mL	≥10%
BAG2-I75	12.5 ng	10 ng/mL	≥200 pg/mL	11.5 ng/mL	≥10%
BAG2-I77	12.5 ng	10 ng/mL	≥200 pg/mL	11.5 ng/mL	≥10%

Insect Venom Check

Order Code	Name	Taxonomic	DE	FR	IT	ES
BAG2-I1CHK	Honey Bee Venom Check	Apis mellifera	Honigbiene- gift Check	Venin d'abeille Check	Veleno d'api Check	Veneno de abeja
BAG2-I3CHK	Yellow Jacket Venom Check	Vespula spp.	Wespengift Check	Venin de guêpe Check	Veleno de vespa Check	Veneno de avispa Check

Use a fresh allergen vial each time a new stimulation is performed.

Dissolve the allergen prior use as follows:

Add 250 µL of Stimulation Buffer to vial, vortex briefly. (=c1)

Mix 40 µL of allergen solution c1 with 160 µL of stimulation buffer (=c2)

Mix 40 µL of allergen solution c2 with 160 µL of stimulation buffer (=c3)

Mix 40 µL of allergen solution c3 with 160 µL of stimulation buffer (=c4)

Use the allergen solutions according to the test protocol.

1 vial is sufficient for up to 3 stimulations.

Content per vial: 312.5 ng

Conc. After reconstitution: 1250 ng/mL

Conc. In stimulation (Flow CAST®): c1: 284 ng/mL, c2: 57 ng/mL; c3: 11 ng/mL; c4: 2.3 ng/mL

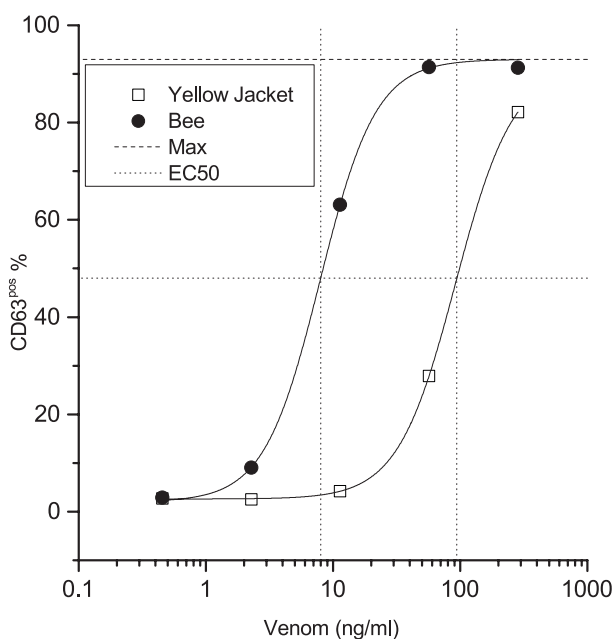


Figure 1: Determination of the half maximal stimulation. Maximal stimulation: 93.9% CD63. Minimal stimulation: 2.5% CD63. EC50 (Yellow Jacket venom): 100 ng/mL; EC50 (Bee venom): 7 ng/mL; Ratio EC50 (Yellow Jacket venom/Bee venom) = 14.3. Conclusion: Patient shows reactivity to Bee venom (adapted from [5]).

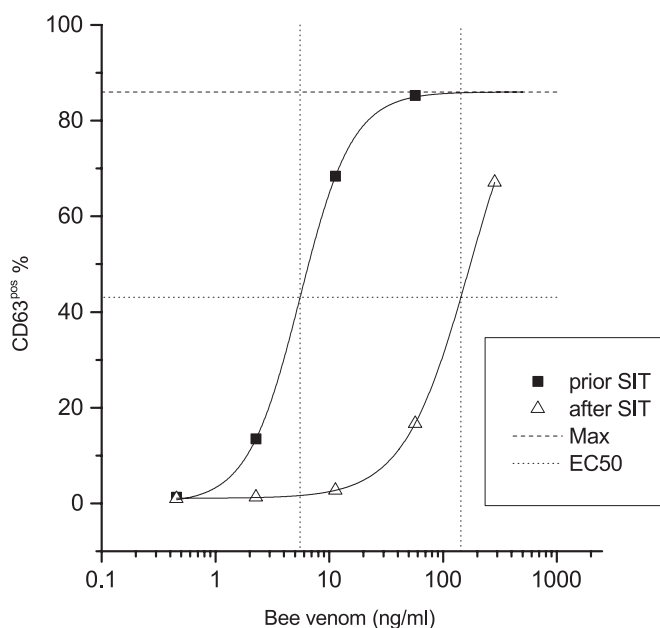


Figure 2: Flow CAST® with Bee venom Check allergen (BAG2-I1CHK) of a patient before (prior SIT) and after 3 years of specific immunotherapy (after SIT). EC50 (prior SIT): 5 ng/mL; EC50 (after SIT): 120 ng/mL; Ratio EC50 (prior SIT/after SIT) = 24.

Grasses

Order Code	Name	Taxonomic	DE	FR	IT	ES
BAG-G6	Timothy Grass	Phleum pratense	Lieschgras	Fléole des Prés	Codolina	Fleo

	Content per vial	CAST® ELISA		Flow CAST®	
		Conc. in stim.	Cut-off	Conc. in stim.	Cut-off (CD63)
BAG-G6	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%

Order Code	Name	Components	Content per vial (ng)	Conc. in stim. (ng/mL)
BAG-GX1	6-Grass Mix	Orchard Grass (G3)	4.2	17
		Meadow Fescue (G4)	4.2	17
		Rye Grass (G5)	4.2	17
		Timothy Grass (G6)	4.2	17
		Meadow Grass (G8)	4.2	17
		Velvet Grass (G13)	4.2	17
		Total content	25	100

Assay	CAST® ELISA	Flow CAST®
Conc. in stimulation	20 ng/mL	22.5 ng/mL
Cut-off	≥200 pg/mL	≥15% CD63

Weeds

Order Code	Name	Taxonomic	DE	FR	IT	ES
BAG-W19	Pellitory	Parietaria officinalis	Aufrechtes Glaskraut	Pariétaire Officinale	Erba Vetriola	Morella Roque- ra

Order code	Content per vial	CAST® ELISA		Flow CAST®	
		Conc. in stim. (ng/mL)	Cut-off (pg/mL)	Conc. in stim. (ng/mL)	Cut-off (CD63)
BAG-W19	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%

Trees

Order Code	Name	Taxonomic	DE	FR	IT	ES
BAG-T3	Common Birch	Betula pendula	Birke	Bouleau	Betulla	Abedul
BAG-T4	Hazel	Corylus avellana	Gemeine Hasel	Noisetier	Nocciolo	Avellano

	Content per vial	CAST® ELISA		Flow CAST®	
		Conc. in stim.	Cut-off	Conc. in stim.	Cut-off (CD63)
BAG-T3	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG-T4	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%

Molds

Order Code	Name	Taxonomic	DE	FR	IT	ES
BAG-M1	Penicillium	Penicillium notatum	Schimmel, Penicillium	Moisissures, Penicillium	Muffe, Penicillium	Mohos, Penicillium
BAG-M2	Cladosporium	Cladosporium herbarum	Schimmel, Cladosporium	Moisissures, Cladosporium	Muffe, Cladosporium	Mohos, Cladosporium
BAG-M3	Aspergillus	Aspergillus fumigatus	Schimmel, Aspergillus	Moisissures, Aspergillus	Muffe, Aspergillus	Mohos, Aspergillus
BAG-M5	Candida albicans	Candida albicans	Candida, Hefen	Candida, Levures	Candida, Lieviti	Candida, Levaduras
BAG-M6	Alternaria	Alternaria alternata	Schimmel, Alternaria	Moisissures, Alternaria	Muffa, Alternaria	Mohos, Alternaria

	Content per vial	CAST® ELISA		Flow CAST®	
		Conc. in stim.	Cut-off	Conc. in stim.	Cut-off (CD63)
BAG-M1	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG-M2	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG-M3	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG-M5	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG-M6	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%

Mites / Animals

Order Code	Name	Taxonomic	DE	FR	IT	ES
BAG-D1	House dust mite	Dermatophagoides Pteronyssinus	Hausstaubmilbe	Acarien de la Poussière de Maison	Acaro della polvere di casa	Ácaro del polvo de la casa
BAG-D2	Am. House dust mite	Dermatophagoides farinae	Amerik. Staubmilbe	Acarien de la Poussière	Acaro della polvere	Ácaro del polvo
BAG-E1	Cat Epithelium	Felis domesticus; epitilium	Katzenepithel	Epithélium de chat	Epitelio di gatto	Epitelio de gato
BAG-E2	Dog Epithelium	Canis familiaris; epitilium	Hundeepithel	Epithélium de chien	Epitelio di cane	Epitelio de perro
BAG2-FELD1	rFel d 1 Cat	Felinis domesticus; Cat Major Allergen				

	Content per vial	CAST® ELISA		Flow CAST®	
		Conc. in stim.	Cut-off	Conc. in stim.	Cut-off (CD63)
BAG-D1	250 ng	200 ng/mL	≥200 pg/mL	225 ng/mL	≥15%
BAG-D2	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG-E1	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG-E2	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG2-FELD1	250 ng	200 ng/mL	≥200 pg/mL	225 ng/mL	≥15%

Order Code	Name	Components	Content per vial (ng)	Conc. after reconst. (ng/mL)
BAG-DX1	Mites Mix	Acarus siro (D70)	6.25	25
		Lepidoglyphus destructor (D71)	6.25	25
		Tyrophagus putrescentia (D72)	6.25	25
		Glycyphagus domesticus (D73)	6.25	25
		Total content	25	100

Assay	CAST® ELISA	Flow CAST®
Conc. in stimulation	20 ng/mL	22.5 ng/mL
Cut-off	≥200 pg/mL	≥15% CD63

Order Code	Name	Components	Content per vial (ng)	Conc. after reconst. (ng/mL)
BAG-IX1	Inhalant Mix	6-Grass Mix (GX1)	25	100
		cult. Rye Grass (G12)	25	100
		Birch (T3)	25	100
		Hazel (T4)	25	100
		Mugwort (W6)	25	100
		Ribwort (W9)	25	100
		Alternaria (M6)	25	100
		House dust mite (D1)	25	100
		Am. House dust mite (D2)	25	100
		Cat Epithelium (E1)	25	100
		Dog Epithelium (E2)	25	100
		Total content	275	1100

Assay	CAST® ELISA	Flow CAST®
Conc. in stimulation	220 ng/mL	250 ng/mL
Cut-off	≥200 pg/mL	≥15% CD63

Latex

Order Code	Name	Taxonomic	DE	FR	IT	ES
BAG-K82	Latex		Latex	Latex	Lattice	Latex

Assay	CAST® ELISA	Flow CAST®
Conc. in stimulation	20 ng/mL	22.7 ng/mL
Cut-off	≥200 pg/mL	≥10% CD63

Egg / Milk

Order Code	Name	Taxonomic	DE	FR	IT	ES
BAG-F1	Egg White	Gallus domesticus	Hühnereieiweiss	Blanc d'oeuf	Bianco d'uovo	Clara de huevo
BAG-F75	Egg Yolk	Gallus domesticus	Eigelb	Jaune f'oeuf	Tuorlo d'uovo	Yema de huevo
BAG-F2	Cow Milk	Bos domesticus	Kuhmilch	Lait de vache	Latte di mucca	Leche de vaca
BAG-F76	α -Lactalbumin	Bos domesticus	α -Lactalbumin	α -Lactalbumine	α -Lactalbumina	α -Lactalbumina
BAG-F77	β -Lactoglobulin	Bos domesticus	β -Lactoglobulin	β -Lactoglobuline	β -Lactoglobulina	β -Lactoglobulina
BAG-F78	Casein	Bos domesticus	Kasein	Caséin	Caseina	Caseína

	Content per vial	CAST® ELISA		Flow CAST®	
		Conc. in stim.	Cut-off	Conc. in stim.	Cut-off (CD63)
BAG-F1	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG-F75	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG-F2	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG-F76	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG-F77	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG-F78	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%

Fish / Meat

Order Code	Name	Taxonomic	DE	FR	IT	ES
BAG-F3	Codfish	Gadus callarias	Dorsch	Morue	Merluzzo	Bacalao
BAG-F24	Shrimp	Pandalus borealis	Garnele	Crevette	Gambero	Gamba
BAG-F27	Beef	Bos domesticus	Rind	Boeuf	Manzo	Ternera
BAG2-GAL	alpha-Gal-HSA	-				

	Content per vial	CAST® ELISA		Flow CAST®	
		Conc. in stim.	Cut-off	Conc. in stim.	Cut-off (CD63)
BAG-F3	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG-F24	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG-F27	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG2-GAL	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%

Fruits / Vegetables

Order Code	Name	Taxonomic	DE	FR	IT	ES
BAG-F25	Tomato	Solanum lycopersicum	Tomate	Tomate	Pomodoro	Tomate
BAG2-MALD1	rMal d 1 Apple	Malus domestica; Apple				

	Content per vial	CAST® ELISA		Flow CAST®	
		Conc. in stim.	Cut-off	Conc. in stim.	Cut-off (CD63)
BAG-F25	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG2-MALD1	250 ng	200 ng/mL	≥200 pg/mL	225 ng/mL	≥15%

Seeds, Beans / Nuts

Order Code	Name	Taxonomic	DE	FR	IT	ES
BAG-F10	Sesame	Sesamum indicum	Sesam	Sésame	Sesamo	Sesamo
BAG-F13	Peanut	Arachis hypogaea	Erdnuss	Cacahuète	Noccioline Americane	Cacahuete
BAG2-ARAH1	nAra h 1 Peanut	Ara h 1				
BAG2-ARAH2	nAra h 2 Peanut	Ara h 2				
BAG2-ARAH6	nAra h 6 Peanut	Ara h 6				
BAG-F14	Soybean	Glycine soja	Soja	Soja	Soia	Soya
BAG-F17	Hazelnut	Corylus avellana	Haselnuss	Noisette	Nocciola	Avellana
BAG-F20	Almond	Prunus amygdalus	Mandel	Amande	Mandorla	Almendra
BAG-F202	Cashew Nut	Anacardium occidentale	Cashewnuss	Noix de Cajou	Anacardio	Anacardo
BAG-F203	Pistachio Nut	Pistacia vera	Pistazie	Pistache	Pistacchio	Pistacho
BAG-F256	Walnut	Juglans regia	Wallnuss	Noix	Noce	Nuez

	Content per vial	CAST® ELISA		Flow CAST®	
		Conc. in stim.	Cut-off	Conc. in stim.	Cut-off (CD63)
BAG-F10	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG-F13	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG2-ARAH1	250 ng	200 ng/mL	≥200 pg/mL	227 ng/mL	≥10%
BAG2-ARAH2	5 ng	4 ng/mL	≥200 pg/mL	4.5 ng/mL	≥10%
BAG2-ARAH6	5 ng	4 ng/mL	≥200 pg/mL	4.5 ng/mL	≥10%
BAG-F14	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG-F17	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG-F20	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG-F202	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG-F203	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥10%
BAG-F256	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥10%

Cereals

Order Code	Name	Taxonomic	DE	FR	IT	ES
BAG-F4	Wheat	Triticum aestivum	Weizen	Blé	Grano	Trigo
BAG-F5	Rye Flour	Secale cereale	Roggen	Seigle	Segale	Centeno
BAG-F6	Barley Flour	Hordeum sativum	Gerste	Orge	Orzo	Cebada
BAG-F7	Oat Flour	Avena sativa	Hafer	Avoine	Avena	Avena
BAG-F45	Baker's Yeast	Saccharomyces cerevisiae	Backhefe	Levure de bière	Lievito	Levadura
BAG-F79	Gluten - Wheat	Triticum aestivum	Gluten - Weizen	Gluten - Blé	Glutine - Frumento	Gluten - Trigo
BAG-F98	Gliadin - Wheat	Triticum aestivum	Gliadin - Weizen	Gliadine - Blé	Gliadina - Frumento	Gliadina - Trigo

	Content per vial	CAST® ELISA		Flow CAST®	
		Conc. in stim.	Cut-off	Conc. in stim.	Cut-off (CD63)
BAG-F4	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG-F5	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG-F6	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG-F7	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG-F45	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥15%
BAG-F79	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥10%
BAG-F98	25 ng	20 ng/mL	≥200 pg/mL	22.5 ng/mL	≥10%

Order Code	Name	Components	Content per vial (ng)	Conc. after reconst. (ng/mL)
BAG-FX1	Food Mix	Egg White (F1)	12.5	50
		Egg Yolk (F75)	12.5	50
		Cow Milk (F2)	25	100
		Codfish (F3)	25	100
		Wheat (F4)	25	100
		Peanut (F13)	25	100
		Soybean (F14)	25	100
		Hazelnut (F17)	25	100
		Shrimp (F24)	25	100
		Total content	200	800

Assay	CAST® ELISA	Flow CAST®
Conc. in stimulation	180 ng/mL	205 ng/mL
Cut-off	≥200 pg/mL	≥15% CD63

Food Colorant Mixes

Order Code	Name	Components	Content per vial (µg)	Conc. after reconst. (µg/mL)
BAG2-C101	Food Colorant Mix I	Quinoline Yellow (CE104)	25	100
		Sunset Yellow (CE110)	25	100
		Chromotrope FB (CE122)	25	100
		Amaranth (CE123)	25	100
		New Coccine (CE124)	25	100
		Total content	125	500

Assay	CAST® ELISA	Flow CAST®
Conc. in stimulation	100 µg/mL	115 µg/mL
Cut-off	≥160 pg/mL	≥5% CD63, SI≥2

Order Code	Name	Components	Content per vial (µg)	Conc. after reconst. (µg/mL)
BAG2-C102	Food Colorant Mix II	Erythrosine (CE127)	1.25	5
		Patent Blue V (CE131)	6.25	25
		Indigo Carmine (CE132)	6.25	25
		Brilliant Black (CE151)	6.25	25
		Total content	20	80

Assay	CAST® ELISA	Flow CAST®
Conc. in stimulation	16 µg/mL	18 µg/mL
Cut-off	≥100 pg/mL	≥5% CD63, SI≥2

Order code	Name
BAG2-C103	Tartrazine

$C_{16}H_9N_4Na_3O_9S_2$
MW 534.4

Name E102; Hydrazine yellow; Acid yellow 23; FD&C yellow No. 5; C.I. Food yellow 4

Content per vial	625 µg	Conc after reconst.	2.5 mg/mL
Additional dilutions	1:5		
Assay	CAST® ELISA	Flow CAST®	
Conc. in stimulation	500 µg/mL	570 µg/mL	
Cut-off	≥120 pg/mL	≥5% CD63; SI*≥2	

Order code	Name
BAG2-C111	Sodium Benzoate

$C_7H_5NaO_2$
MW 144.1

Name E211

Content per vial	625 µg	Conc after reconst.	2.5 mg/mL
Additional dilutions	1:5		
Assay	CAST® ELISA	Flow CAST®	
Conc. in stimulation	500 µg/mL	570 µg/mL	
Cut-off	≥90 pg/mL	≥5% CD63; SI*≥2	

Order code	Name
BAG2-C112	Sodium Nitrite

$NNaO_2$
MW 69.0

Name E250; Na-Nitrite; Nitrous acid sodium salt; Erinirit

Content per vial	25 µg	Conc after reconst.	100 µg/mL
Additional dilutions	1:5		
Assay	CAST® ELISA	Flow CAST®	
Conc. in stimulation	20 µg/mL	22.7 µg/mL	
Cut-off	≥60 pg/mL	≥5% CD63; SI*≥2	

Order code	Name		$K_2S_2O_5$
BAG2-C113	Potassium Metabisulfite		MW 222.3

Name E224; Potassium disulfite; Potassium pyrosulfite

Content per vial	12.5 µg	Conc after reconst.	50 µg/mL
Additional dilutions	1:5		
Assay	CAST® ELISA	Flow CAST®	
Conc. in stimulation	10 µg/mL	11.5 µg/mL	
Cut-off	≥40 pg/mL	≥5% CD63; SI*≥2	

Order code	Name		$C_7H_5NaO_3$
BAG2-C114	Sodium Salicylate		MW 160.1

Name E 218, Alysine; Ardall; Clin; Idocyl novum; Enterosalicyl; Entersalil; Magsalyl; Parbocyl-Rev

Content per vial	250 µg	Conc after reconst.	1 mg/mL
Additional dilutions	1:5		
Assay	CAST® ELISA	Flow CAST®	
Conc. in stimulation	200 µg/mL	227 µg/mL	
Cut-off	≥120 pg/mL	≥5% CD63; SI*≥2	

Order code	Name		$C_{18}H_8NNa_3O_{11}S_3$
BAG2-CE104	Quinoline Yellow		MW 579.4

Name E104; Acid yellow 3; D&C yellow No.10; Food yellow 13

Content per vial	125 µg	Conc after reconst.	500 µg/mL
Additional dilutions	1:5		
Assay	CAST® ELISA	Flow CAST®	
Conc. in stimulation	100 µg/mL	115 µg/mL	
Cut-off	≥300 pg/mL	≥5% CD63; SI*≥2	

Order code **Name**
BAG2-CE110 **Sunset Yellow FCF**

$C_{16}H_{10}N_2Na_2O_7S_2$
 MW 452.4

Name E110; FD&C yellow No.6; C.I. Food yellow 3

Content per vial 125 µg Conc after reconst. 500 µg/mL

Additional dilutions 1:5

Assay **CAST® ELISA** **Flow CAST®**

Conc. in stimulation 100 µg/mL 115 µg/mL

Cut-off ≥40 pg/mL ≥5% CD63; SI*≥2

Order code **Name**
BAG2-CE122 **Chromotrope FB**

$C_{20}H_{12}N_2Na_2O_7S_2$
 MW 502.4

Name E122; C.I. Food red 176

Content per vial 250 µg Conc after reconst. 1 mg/mL

Additional dilutions 1:5

Assay **CAST® ELISA** **Flow CAST®**

Conc. in stimulation 200 µg/mL 227 µg/mL

Cut-off ≥80 pg/mL ≥5% CD63; SI*≥2

Order code **Name**
BAG2-CE123 **Amaranth**

$C_{20}H_{11}N_2Na_3O_{10}S_3$
 MW 604.5

Name E123; C.I. Food red 9; Acid red 27; FD&C red No. 2

Content per vial 25 µg Conc after reconst. 100 µg/mL

Additional dilutions 1:5

Assay **CAST® ELISA** **Flow CAST®**

Conc. in stimulation 20 µg/mL 22.7 µg/mL

Cut-off ≥40 pg/mL ≥5% CD63; SI*≥2

Order code	Name
BAG2-CE124	New Coccine

$C_{20}H_{11}N_2Na_3O_{10}S_3$
MW 604.5

Name E124; C.I. Food red 7; Acid red 18; Ponceau 4R

Content per vial	625 µg	Conc after reconst.	2.5 mg/mL
Additional dilutions	1:5		
Assay	CAST® ELISA	Flow CAST®	
Conc. in stimulation	500 µg/mL	570 µg/mL	
Cut-off	≥60 pg/mL	≥5% CD63; SI*≥2	

Order code	Name
BAG2-CE127	Erythrosine

$C_{20}H_6I_4N_2Na_2O_5$
MW 879.9

Name E127; Erythrosine BS; Erythrosine B; FD&C Red No. 3; C.I. Food Red 14; Acid Red 51

Content per vial	1.25 µg	Conc after reconst.	5 µg/mL
Additional dilutions	1:5		
Assay	CAST® ELISA	Flow CAST®	
Conc. in stimulation	1 µg/mL	1.15 µg/mL	
Cut-off	≥60 pg/mL	≥5% CD63; SI*≥2	

Order code	Name
BAG2-CE131	Patent Blue V

$C_{27}H_{31}N_2NaO_7S_2$
MW 582.7

Name E131; C.I. Food blue 5; Acid Blue 3 Sodium salt; Acid Blue V Sodium salt

Content per vial	62.5 µg	Conc after reconst.	250 µg/mL
Additional dilutions	1:5		
Assay	CAST® ELISA	Flow CAST®	
Conc. in stimulation	50 µg/mL	57 µg/mL	
Cut-off	≥70 pg/mL	≥5% CD63; SI*≥2	

Order code	Name
BAG2-CE132	Indigo Carmine

$C_{16}H_8N_2Na_2O_8S_2$
MW: 466.4

Name E132; Sodium indigotin disulfonate; soluble indigo blue; Indigotine; Acid Blue 74; C.I. Food Blue 1; FD&C Blue No. 2

Content per vial	62.5 µg	Conc after reconst.	250 µg/mL
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Additional dilutions 1:5

Assay	CAST® ELISA	Flow CAST®
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Conc. in stimulation	50 µg/mL	57 µg/mL
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Cut-off	≥50 pg/mL	≥5% CD63; SI*≥2
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Order code	Name
BAG2-CE151	Brilliant Black BN

$C_{28}H_{17}N_5Na_4O_{14}S_2$
MW 867.7

Name E151; C.I. Food black 1; Black PN

Content per vial	62.5 µg	Conc after reconst.	250 µg/mL
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Additional dilutions 1:5

Assay	CAST® ELISA	Flow CAST®
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Conc. in stimulation	50 µg/mL	57 µg/mL
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Cut-off	≥40 pg/mL	≥5% CD63; SI*≥2
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Order code	Name
BAG2-CE202	Sorbic acid

$C_6H_7KO_2$
MW 150.2

potassium salt

Name E200, E202

Content per vial	0.5 mg	Conc after reconst.	2 mg/mL
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Additional dilutions 1:5

Assay	CAST® ELISA	Flow CAST®
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Conc. in stimulation	400 µg/mL	455 µg/mL
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Cut-off	≥40 pg/mL	≥5% CD63; SI*≥2
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Order code	Name
BAG2-CE466	Carboxymethylcellulose

Name Cellulose glycolate; Cethylose; CMC; Carmethose; Cel-O-Brandt; Glykocellon; Carbose D; Xylo-Mucine; Tylose MGA; Cellolax; Polycell

Content per vial	5 µg	Conc after reconst.	20 µg/mL
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Additional dilutions	1:5
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Assay	CAST® ELISA	Flow CAST®
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Conc. in stimulation	4 µg/mL	4.5 µg/mL
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Cut-off	≥150 pg/mL	≥5% CD63; SI*≥2
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Order code	Name
BAG2-CE621	Glutamate

$C_5H_8NNaO_4$
MW 187.1

Name E621; Chinese seasoning; MSG; RL-50; Accent; Ajinomoto; Glutacyl; Glutavene; Vetsin

Content per vial	2.5 mg	Conc after reconst.	10 mg/mL
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Additional dilutions	1:5
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Assay	CAST® ELISA	Flow CAST®
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Conc. in stimulation	2 mg/mL	2.27 mg/mL
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Cut-off	≥70 pg/mL	≥5% CD63; SI*≥2
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