assay, the substance-specific immunoglobulin will not be able to sufficiently bind to said substance, which results in a poor performance of the assay (e.g. low sensitivity).

Thus, in a first aspect the present invention provides:

A method for detecting the presence or absence of substance-specific immunoglobulin in a sample, said method comprising contacting said sample with a plurality of forms of said substance substantially simultaneously and determining whether an immune-complex is formed, wherein at least one form is a natural extract.

It is preferred that at least one form is an antigenic component or a combination of antigenic components.

It is preferred that said method can be used for the quantification of levels of substance-specific immunoglobulins in a sample. It is further preferred that said method can alternatively or additionally be used for the quantification of levels of antigenic component-specific immunoglobulin. The method of the invention can thus include one or more steps to quantify the levels of substance and/or antigenic component-specific immunoglobulin.

In another ~~preferred aspect~~ embodiment of the invention, the method may be used to enable the diagnosis of an allergy in an individual. The individual supplies the sample used in the method. The method of the invention can thus include one or more steps to determine the sensitisation status of an individual. Alternatively or additionally, the method can be used to determine the substance-specific or antigenic component-specific immunoglobulin status of an individual.

As used herein, sensitisation means that the patient has previously been exposed to a substance, and immunoglobulins have been raised against that substance. Further exposure may result in allergic symptoms as discussed previously.

In an embodiment ~~second aspect~~, there is provided a method for the quantification of levels of an substance-specific immunoglobulin in a sample, said method comprising contacting said sample with a plurality of forms of said substance and determining the level of reactivity of said immunoglobulin to said substance forms, wherein at least one form is a natural extract.

In an embodiment, ~~third aspect~~ there is provided a method for enhancing the binding capacity of a substance, comprising the selective removal of one or more components. It is preferred that the substance is prepared as a natural extract. The binding capacity relates to the ability of substance-specific binding members such as immunoglobulins to bind to the substance. Said substance (described herein as a modified or depleted substance) can be used in any method, array or kit of the invention.

In a second aspect of the present invention ~~fourth aspect~~, there is provided an array comprising a plurality of forms of a substance provided at discrete locations, wherein at least one form is a natural extract and at least one form is an antigenic component or a combination of antigenic components~~of said substance~~. Said array can be used in any of the methods or kits of the invention.

It is preferred that at least one antigenic component or a combination of antigenic components is provided as a form of said substance. Thus, 1 or more forms may be an antigenic component or antigenic component mix.

In ~~a fifth aspect~~an embodiment, there is provided a kit comprising an array which comprises a plurality of forms of a substance provided at discrete locations as described above and one or more detection binding agents.

In ~~a sixth aspect~~an embodiment, there is provided a method to determine the substance – specific immunoglobulin status of an individual comprising contacting a sample from said individual substantially simultaneously with a plurality of forms of said substance, wherein at least one form is a natural extract, and determining whether an immune complex is formed.

In ~~a seventh aspect~~an embodiment, there is provided a method for the diagnosis of an allergy to a substance in an individual, said method comprising contacting a sample from said individual substantially simultaneously with a plurality of forms of a substance, wherein at least one form is a natural extract, and the presence of an immune complex with one or more of the forms indicates the presence of a sensitisation or and/or allergy to that substance.

Brief description of figures

Figure 1: Figure 1 shows the results from Example 1. It is a bar chart showing the allergen-specific immunoglobulin (IgE) concentration (Reactivity in Class Score) versus average fluorescent signal for Dust Mite Extract (natural extract), Der p 1 and Der p 2 (both components).

Figure 2 is a further bar chart showing results from Example 1, and is similar to figure 1, except is shows negative or low reactive samples (allergen-specific immunoglobulin concentration < 0.35 kU/L). The bar chart show how both sensitivity (i.e. higher reactivity) and specificity (i.e. negative samples remain negative) can be improved by using the fluorescence signal derived from either the single antigen/allergen (e.g. natural extract) or a combination of them (e.g. Natural altered extract and/or single antigens)

Figure 3: shows the results from Example 1 plotted on a graph of IgE concentration versus Average fluorescent signal. To help the understanding of the plot, a trendline for each condition was superimposed to the data (e.g. higher slope value indicates higher assay sensitivity).

Figure 4: demonstrates pictorially the core of the invention that a plurality of forms of a substance are presented to the sample, including the natural extract. The natural extract is shown as a natural mix of antigens (antigenic components). Depicted are two minor antigens, an unknown antigen, major antigens, antibodies and the surface of the array. Example A shows an array for Patient 1 positive for major antigen 2. Example B shows an array for Patient 2 positive for minor antigens. Example C shows patient 3 positive for both major and minor/unknown antigens and Example D depicts Patient 4 who is positive for unknown antigens.

Figure 5: show select data from Example 1 that highlights the utility of the invention. 5 samples are presented where sensitivity to Dust Mite would not have been detected if natural

extract or individual components had been used in isolation. The data is presented as a bar chart of sample versus fluorescent signal.