Portable Food Allergen Tester and Tracker

An automated portable device designed to test foods for possible allergens

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Executive Summary

This document demonstrates the interest among people with food allergies for a food allergen intake tracking device, proposes the design of such a wearable health device, and outlines the regulatory strategy required to market the device as a medical product. Over 150 million people worldwide are estimated to have an allergy to one or more foods, with reactions ranging from rashes and hives to fatal anaphylaxis [1]. As a cure for food allergies does not exist, people with food allergies must avoid consuming food allergens in order to prevent a reaction from occurring [1]. One way to avoid the consumption of food allergens is to detect the presence of food allergens in foods prior to consumption. Our design team wrote and distributed a survey to determine whether there was a market interested in such a food intake tracking device, and what their concerns and priorities were for a hypothetical wearable device. Additionally, from a survey of current products available to track the potential intake of food allergens, lateral flow immunochromatic assays were determined to be the most suited for implementation in a wearable food intake tracking device. However, we found that current methods would be considered too cumbersome for the average person, and in order to achieve market penetration and product adherence, the design must be simplified and easy to use. Modifications to the standard assay for translation to a wearable device include decreasing the size of the device and integrating the different materials in the standard kit for increased speed and portability, as well as incorporating electronic elements to automate the process, visualize the data, and wirelessly communicate the results. Our device will be similar to a wide-body retractable pen, with an approximate size of a pregnancy test. In order to market the proposed health product as a medical device, a Pre-Market Approval (PMA) must be submitted the United States Food & Drug Administration (FDA) because although the technology is safe and well-known, the intended use and product classification are not substantially equivalent to FDA-approved devices using similar technologies. Additionally, sufficient testing to show that the device is both safe and effective must be done. The value proposition associated with the development of the proposed device are that its use can be expanded to be useful to anyone interested in testing food for a particular ingredient and it has the potential to collect significant amounts of data related to consumer food intake.

References:

[1] AB SCIEX, "Allergen Testing", AB CIEX. [Online]. Available: http://www.absciex.com/applications/food-and-beverage-testing/allergen-testing?country=Canada [Accessed Dec. 2014].

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1 Introduction

According to the Food Allergy Research & Education, researchers have estimated that over 15 million Americans and 1 in 13 children have food allergies [1]. This results in over 300,000 trips to emergency rooms and approximately $25 billion per year in costs to the healthcare system [1]. In the Food Allergen Labeling and Consumer Protection Act, the following eight foods and their protein derivatives are considered major food allergens: milk, egg, fish (e.g. bass, flounder, or cod), crustacean shellfish (e.g. crab, lobster, or shrimp), tree nuts (e.g. almonds, pecans, or walnuts), wheat, peanuts, and soybeans [2]. There is currently no cure for food allergies, and thus people affected must strictly avoid foods which they are allergic to or suffer allergic reactions which can result in serious health consequences. However, despite mandatory labeling of food products with allergens, 37.9% of reported food allergy incidences are due to undeclared food allergens [3]. AB SCIEX notes that:

> One of the biggest reasons for a food recalls presently is the detection of unclaimed allergens. [...] Side-effects from the consumption of a food allergen can range from rashes and hives to loss of consciousness or severe (and potentially fatal) anaphylaxis. Food producers and regulators continuously strive for specific and sensitive methods to detect allergens at trace levels, to ensure consumer safety, meet regulations, and avoid expensive product recalls. [4]

As such, we propose the design of a wearable device which can be used to test food samples for the presence of food allergens and track instances of potential food allergen intake. In addition, this technology can be extended to be useful for those who have multiple allergies and even to those who have no food allergies, but would want to avoid certain ingredients within foods.

2 Market Identification

To ensure that our design will be accepted and used by consumers, we created and distributed a survey to identify a target market and to understand the needs and wants of that market. Based on the results of the survey, the target market for the proposed device includes people with food allergies, intolerance and sensitivities.

2.1 Survey Design & Results

asd Our design team wrote and distributed a survey (See Appendix A) in order to gather information regarding the needs and interests of the target market. The survey asked over a hundred participants for input on the foods that they avoided, reasons for food avoidance, food consumption habits, interest in a device to track their intake of specific foods, etc. In addition, we asked the respondents that if a hypothetical device existed to test for food allergens, what specific features would they like to see in the device. To increase the statistical power of the survey and avoid isolating potential populations that would be interested in tracking food allergen intake, the survey was distributed to people with and without allergies.

Some of the results of the survey are illustrated in Appendix B and included below:

- 67% of respondents were allergic to at least one type of food, and 72% of these respondents indicated that they would be interested in testing food for allergens
- While a majority of those with food allergies were interested in such a device, 1 in 3 respondents who had no food allergies also indicated interested in the device
- Milk was the most common food allergy amongst our respondents, followed by peanuts and tree nuts

- While there was no clear maximum that respondents would be willing to pay for the device, 77% of respondents indicated that the maximum cost per test should be below $2 per test

From comments posted on online forums and to the survey itself, we noticed that some parents of children with food allergies would purposely avoid certain foods due to their children's allergies. In addition, we received some comments suggesting that this device would be useful in schools to assist young children in avoiding food allergens. According to the survey, the top three priorities among respondents for a hypothetical food allergen intake tracking device were accuracy, ease of use, and cost (Appendix B). These were our focus points for the device design.

2.2 **C**urrent Solutions

Current products available and in development for the detection of food components mainly fall into one of the following three technical categories: lateral flow immunochromatic assays, microwell immunosorbent assays, and spectroscopy.

2.2.1 Lateral Flow Immunochromatic Assays

In food allergen testing products that use lateral flow immunochromatography, the food sample travels through a porous nitrocellulose strip [5]. Antibodies are embedded at various regions on the strip, which react with allergen proteins in the food sample to produce a colourimetric indicator of allergen presence [5]. The user is required to prepare the food sample by swabbing the food to be tested and mixing it with an extraction buffer prior to using the test strip [6]. The entire process takes approximately 5 to 10 minutes and the use of antibodies makes this technique relatively specific. Current products in the market that use this technology include the Reveal 3-D line of food allergen test kits by Neogen [7], Lateral Flow Test Kits by bioavid Diagnostics [8], and Food Allergen Lateral Flow Kits by MIoBS [9]. Other uses for this technology in the medical field include virus detection and pregnancy testing, where the presence of certain residues are detected in urine [10].

2.2.2 Microwell Immunosorbent Assays

These technologies use ELISA, or enzyme-linked immunosorbent assay, which uses antibodies and a colour change to identify the presence of a substance. Unlike lateral flow strips in section 2.2.1, this technology relies on a multi-step protocol to immobilize the substance of interest and a secondary antibody or substrate which facilitates the colour change. A colourimetric equipment to measure such change allows microwell immunosorbent assays to be more sensitive, and capable of accurately yielding the concentration of a test substance in solution, given a standard curve to compare against. This entire process takes anywhere between 30 to 75 minutes, depending on the type of test and sensitivity required [11]. As such, they are inadequate for use in the general population. Pre-existing technologies in the food industry which use this technology include Neogen's BioKit and Alert series [11] and Crystal Chem's ELISA kits [12]. In the medical device field, microwell immunosorbent assays are used for in vitro diagnosis of diseases in medical labs [13] and measuring serum antibody levels [14].

2.2.3 Spectroscopy

Spectroscopy-based technologies operate by deconstructing the spectrum of light reflected from a food sample and characterizing it using a database of known spectrums for different foods. Light is emitted onto a sample of food and the the light reflected is collected and translated into a digital signal that can be sent wirelessly to a server for analysis and interpretation. After the signal has

been interpreted, the server sends the user a breakdown of the components of the food sample, which would encompass food allergens. This type of technology, specifically the QTRAP® 5500 System by AB SCIEX, has been used by the FDA for food contaminant testing but is currently too expensive and cumbersome for personal use [15]. As a result, there are several products in development, including the Tellspec by Tellspec Inc. [16] and the SCiO by Consumer Physics [17], aiming to scale the technology down to a portable device for everyday use using near infrared light (NIR). Some drawbacks to this technology are that it relies on having a comprehensive database of reference spectrums to compare against and the sensitivity of food allergen detection may be lost during the miniaturization process [18].

2.3 Technology Selection

Although the products introduced above can be used for food allergen testing, there is currently no product available which is portable, easy to use and can quickly detect allergens. Lateral flow immunochromatic assay is arguably the ideal technology among the three for use in a wearable device because its implementation is simple, the individual units are standalone, and the results are generated relatively quickly. See Appendix D for a comparison chart.

3 Device Design

This section will discuss the specific design specifications of the device.

3.1 Design Strategy

One important aspect of designing such devices for use in the consumer market is adherence. Adherence is vital to ensuring that a product is successful in the long term and not deemed an unnecessary gadget. As such, our design philosophy centered around creating a device that would be easy to use. From our research of current solutions, we found that current methods would be considered too cumbersome for the average person, and would make them feel like a chemist at the dinner table. Thus, consumers would be reluctant to use such technologies, and thus the adherence would be quite low. To tackle this issue, we considered items which consumers are familiar with, such as utensils (e.g. spoons, forks, thermometers), stationery (e.g. pens, pencils, highlighters), and even other devices/tools which involve the swabbing or dipping of items (e.g. pregnancy tests and cotton swabs). Furthermore, we had a strong focus on automation, since many of the current methods require a multi-step procedure involving several iterations of mixing of reagents and incubating. This automation would make the entire process seamless for the user, and thus increase product adherence.

Our source of inspiration comes from a conceptual design called A-Check, designed by Park Jung Eun [19]. The design simply requires the user to touch the food sample of interest with the tip of the device and look for a colour change. Our design borrows that simple concept to create a device in which consumers would want to use everyday.

3.2 User Design Specifications

From our market research, we concluded that the three most important features for consumers are accuracy, ease of use, and cost. As such, we integrated these features into our design philosophy.

3.2.1 Housing and architecture

Our device will be similar to a wide-body retractable pen, resembling a pregnancy test in size (illustrated in Appendix E). To keep costs low, the entire device will be built out of plastic. There are

three main compartments in the device: an extraction buffer cartridge, a buffer cap and a lateral flow strip. The disposable buffer cap is attached to the tip of the device and contains a swab to collect specimens for testing and a cap for the mixing of reagents. The tip will be sealed at the end using a retractable lid, similar to the design used by retractable markers. The swab can be extended out of the body using a spring mechanism, similar to those used in retractable pens, through a rod located in the main body. The extraction buffer and lateral flow strip compartments are contained in the body of the device and contain a simple mechanical connector to interface with the tip cap. Inside the device will be channels running the length of the device in which the user will load the test strip and buffer cartridge. Following this design, the user will retain the overall device while replacing the buffer cap and test strip between tests and replacing the buffer cartridge after 5 tests.

3.2.2 User Protocol

To create a device that is easy to use, we wanted the instructions to be actions which users are already familiar with. Our device will work in the following way:

1. If the buffer solution has run out, open the top of the device, pull out the empty cartridge and replace it with a new one.
2. Insert the test strip of interest into the device.
3. Snap on a new cap to the tip of the device.
4. Extend the swab tip and swab the food of interest for testing.
5. Retract the swab and press the TEST button located on the device to dispense extraction buffer into the cap.
6. Shake the device to mix well for 10 seconds.
7. Wait for the results, delivered either on the device via indicator lights, an on-device screen, or via a smartphone app.
8. Snap off the used cap from the tip and remove the used test strip for disposal.

3.3 Physical Mechanism

3.3.1 Lateral Flow Strip Dispensation

The lateral flow strip is going to be dropped in a channel that runs all the way to the buffer cap. The hole that connects the buffer cap to the channel is sufficiently narrow (less than 1 mm in width) such that surface tension of the buffer is stronger than the capillary action through the channel strip. Furthermore, since the strip is going to come in contact with the liquid first, any backflow would be absorbed by the strip itself which is sealed in a plastic backing. This will prevent any cross contamination between samples taken.

3.3.2 Buffer Dispensation

The buffer is dispensed through a micropump, which pumps the buffer solution into the cap. The micropump will pump pulses of fluid such that it will prevent back flow of the buffer through the channel and thus preventing contamination between each successive use. The buffer will be available for dispensing with each test use through cartridges that will be loaded into the device. Each cartridge will have the capacity to be dispense buffer for up to five uses. The buffer will be interfaced with the device via a blunt-tipped needle on the device and an elastomeric self-sealing septa cap on the buffer cartridge.

3.3.3 Swab Dispensation

The cotton swab will be part of the buffer cap which will be fed to its own channel in the device. A spring loaded button will be used to extend and retract the cotton swab. When the button is pressed, the tip of the cotton swab extends out of the tip of the buffer cap and comes in contact with the sample. The user then presses the button again to retract the swab and seal the tip as well. The buffer then is dispensed and immerses the swab in order to prepare the sample for absorption in the lateral flow strip.

3.3.4 Buffer cap

The buffer cap is a plastic component that looks similar to a pen cap with access holes for the cotton swab, the buffer channel as well as the lateral flow strip channel. The cotton swab extends and retracts through the opening at the tip of the cap. After the sample has been collected, a closing mechanism similar to a retractable marker closes the opening and allows the cap to be filled with buffer solution. The channels of the device connect directly to openings of the cap and they are sufficiently narrow to prevent backflow of the buffer.

3.4 Electronic Components

A micropump will be used in the device to precisely deliver a set amount of buffer solution to the buffer cap at the device tip. In addition, a user-accessible test button will allow the user to start the automation process. Two photoresistors (e.g. CDS photocell) will be used to detect the presence of dyed microspheres in the capture lines in the lateral flow strip test. The signal collected from the detector is processed and amplified in the device. These electronic components will be processed by an onboard chip, which controls all automation aspects, and can process the test data and display it via an indicator light, on-device screen, or via wireless bluetooth technology to a smartphone companion app. Furthermore, if the user uses a smartphone companion app, the data can be time stamped and GPS-tagged. By uploading the data collected to servers, a personalized diary can be created and further used to give demographic data about where food allergy reactions took place and what people are allergic to.

3.5 Internal Design

3.5.1 Buffer chamber

The buffer chamber of the cap will be made of HDPE, which is a suitable material that has the necessary strength characteristics needed for this component of the design. The cap will be manufactured through blow molding, and it will be hemispherical in shape with a diameter of 2 cm.

3.5.2 Lateral Flow Strip Design

The presence of allergen in the food sample shall be tested through a lateral flow immunochromatic assay. The test will qualitatively determine the presence of food allergen through a direct (double antibody sandwich) reaction scheme, working in the same way as pregnancy tests [20]. The test strip shall be composed of four main regions: the sample application pad, the reagent pad, the test pad, and the absorption pad.

The sample application pad comes in contact with the sample that has been prepared (mixed with the buffer) and then travels by capillary action to the reagent pad where it comes in contact with the dye conjugated antibodies [20]. As the sample continues to travel along the test strip, it comes in

contact with the secondary antibodies at the test and control lines [20]. For a positive test, the antigen present binds to the antibody present in the test line, whereas the unbound antibodies bind to the control line [20]. This causes both lines in the strip to change colour. In the case of a negative test, the dye conjugated antibodies only bind to the control line, since there is no allergen present that can bind to the test line [20]. The rest of the sample flows through to the absorption pad where it is trapped.

The materials of the test strip are selected in a manner that allows for the minimization of cost, increase in speed of the test, and optimization of test accuracy. Since the allergens that are typically tested are proteins, the choice of material for the membrane through which the sample travels is nitrocellulose paper [20]. In order to allow for a faster testing time of the sample, nitrocellulose paper with a high porosity will be chosen [20]. However, this will need to be tested in order to allow for the time limiting step of the reaction kinetics in the test and control lines to occur. A faster test facilitated by a greater flow rate could cause the sensitivity of the test will be lowered [20]. The sample application pad shall be made of CF4, which is an absorbent cotton linter material typically used for lateral-flow assays [21].

There are three antibodies that are going to be used in the lateral flow test: the detector reagent, test reagent, and control reagent antibodies. In the detector reagent, the antibodies are conjugated to blue latex microspheres that are present on the reagent pad section of the strip [20]. The detector reagent antibodies bind to the 1st epitope of the allergen of the food sample [21]. As the food sample travels to the test reagent, it comes in contact antibodies that target the allergen and binds to its 2nd epitope [21]. The control reagent is comprised of species-specific anti-immunoglobulin against detector reagent antibodies [21]. Furthermore, a membrane backing will be added to the strip to provide strength to the strip and prevent tearing [20]. The membrane shall be added through a process called direct casting.

3.6 Storage of the device:

While some lateral flow strips require refrigeration, proper manufacturing and packaging techniques can eliminate the need for strip refrigeration [22],[23]. As such, no special storage requirements are needed for our device and accessories.

3.7 Cost analysis

From our device survey, a majority of the respondents were willing to pay a higher price for the initial cost of the device, but indicated the desire for a low per-test cost (see Appendix B). While current one-time-use commercial tests have costs in the range of $12-$20 per test, our analysis of currently available technologies have demonstrated that it is possible to create tests at an extremely low cost [20]. The main drawback is a high initial capital investment, which can be recuperated from sales of the device and high-volume sales of test strips.

The device shall have a main and disposable component. The disposable components consist of the extraction buffer cartridge, the lateral flow strip, and the buffer cap (containing the cotton swab). The total cost of the disposable components is projected to be $1.49 (see Appendix F). This is in agreement with the results obtained from the survey where the majority of survey participants indicated a preference in a price of less than $1.99 per test (see Appendix B). The main device itself consists of the housing, circuitry (including photoresistors), Bluetooth transceiver and micropump. A breakdown of the costs of the device can be seen in Appendix F. The total cost of the device is $28.35.

This is in agreement with survey results where 64% of participants preferred a device cost over $25 (See Appendix B).

The cost of the test strip is based on the machinery and equipment required to produce it. The initial equipment needed includes: a microcentrifuge, incubator, vacuum oven, analytical balance, and machine for spraying antibodies/antigens on membranes.

3.8 Design Limitation

We acknowledge that, like any device, there are certain limitations of this design. Should the user not swab a region with the food allergen of interest, or if the allergen is hidden deep within the plate, the device will be unable to detect the presence of the allergen. As such, there is a dependence on the user to perform due diligence to ensure that all potential regions are tested.

4 Regulatory Strategy

The initial purpose of our device is to function as an unregulated health device, used to assist people in identifying potential allergens in food. It will be initially marketed for use by people who would want to avoid certain foods. As of now, lateral flow immunochromatic assays for food allergen testing, such as the Reveal 3-D test strips by Neogen, are analytical means by the FDA to establish thresholds for food allergens [24].

4.1 Future Steps as a Medical Device

In the future, we would like market our device as a medical device. The intended use of our lateral flow immunochromatic in vitro diagnostic strip test for the qualitative detection of a specific of allergen to aid in the detection of cross contaminations or the presence of food allergen in food samples in conjunction with food labelling. Our proposed device will be classified as class II, due to this intended use and the risks. Negative results do not preclude food allergy reactions and anaphylaxis and should not be used as the sole basis for decision of food consumption. Our device is intended for people with food sensitivities and food allergies. Other specific groups in the general public that may be more interested in the device include public health and school boards.

The risk of the our device depends on the sensitivity of our lateral flow immunochromatic assay. Specifically, sensitivity is related to the flow rate and reaction kinetics [23]. However, there is a tradeoff between accuracy and speed of the test. The proportion of microspheres to antibody also affects the sensitivity in the final product. There is also an usage variability from user to user, which would affect the sensitivity and risk of the device. The function of the control line is an internal quality control within the device. This line ensures the functionality of the lateral flow technology, which reduces the chance a false result.

Currently, there is no FDA-approved medical device that tests for specific food molecules within food samples. We will be submitting our application to the Office of In Vitro Diagnostic and Radiological Health (OIVD). In Vitro Diagnostics (IVD) includes medical devices "that can detect diseases, conditions or infections..." in order to cure, mitigate, treat, or prevent diseases in man or other animals [25], [26], [27]. These tests can be used in laboratory, professional, and home settings [26]. For example, genetic, hematology, and microbial in vitro tests are submitted into OIVD. These tests use specimens from body to detect therapeutic response or disease screening. In our case, our device detects an allergen in food, with a purpose to prevent an adverse immune response due to food allergy. Our device is an in vitro diagnostic because our device is non-invasive, does not require an

invasive sampling procedure that prevents significant risk, does not by design introduce energy into a subject, and is not used as a diagnostic procedure without confirmation of the diagnosis by another medically established diagnostic product [27]. The regulatory decision tree (21 CFR part 812) for IVD investigational studies in the guidance documents for in vitro diagnostic tests supported our claim (Appendix G).

There are FDA-approved devices that use identical lateral flow immunoassay technology. For example, pregnancy strips are in vitro diagnostic tests for home use that use identical lateral flow immunoassay technology [30]. Pregnancy tests detect early pregnancy prior to the appearance of signs, so that the user can take immediate action [31]. They are marketed as over-the-counter products, with a risk classification of class II. Another marketed urine test detects Buprenorphine in human urine using lateral flow immunochromatography [29]. Molecules in the blood or cerebrospinal fluid (CSF) can also be detected using lateral flow immunochromatic assays [28].

4.2 Regulatory Pathway

We cannot submit a 510(k) premarket notification of intent to market the device. This is because substantial equivalence cannot be proved due to a lack of a device that has the same intended use AND has the same technological characteristics. We showed several lateral flow immunoassay tests that have a variety of intended uses, but none match our intended use as a qualitative detection of a food allergen (See Appendix H).

We will submit a premarket approval application (PMA) of intent to market the device. In our PMA application, we will indicate indications for use, device description, alternative practices (i.e. current solutions) and procedures, which have been discussed previously in our document. We will also provide a summary of non-clinical studies with reproducibility testing using the antibodies at different sites with different antibody lots. Our non-clinical tests will be performed by comparing our device to current FDA-approved means of detecting major food allergens, such as Neogen's Reveal 3-D line of test strips[34]. From this, we can get a measure of sensitivity and specificity of our device, compared to current FDA approaches. Risk/benefit analysis, safety and effectiveness (i.e. accuracy of the test) will be concluded from the non-clinical studies. Clinical studies will not performed because our specimen matrix is food samples, which do not require patient specimens. In addition, the guidance document for IVD does not strictly mandate a well-planned clinical study of the device in the target population defined by intended uses if the IVD uses novel technology or has a new intended use [kesha]. This type of testing and these requirements are supported by previously PMA-approved lateral flow tests or immunoassay tests that are considered IVD tests [32] [33].

4.3 Standards

Standards will be performed using recognized consensus standards for IVD tests. Specific standards and voluntary standards along with their respective recognition numbers are listed in Appendix I.

5 Conclusion

We propose an automated device to test for the presence of food allergens in food for the general population. From our market survey, this device would be valuable to those who want to avoid certain foods or those with food allergies, including adults, children, and potentially schools and

cafeterias who want a quick and easy way to test for allergens. In its current form, antibodies will be used to detect the presence of allergens. However, this concept can be extended using other technologies to quantitatively determine the level of allergens in the food. Furthermore, by measuring multiple allergens at once, we are able to paint a picture (albeit not complete) of what the person is eating, and this can be used to monitor diet, or in a big data format, to see what people are eating, their preferences, where they shop for food, where they eat, etc.. Another big data extension is that this data can track which places have high occurrences of allergen contamination (like online restaurant rating websites), create personal logs (of what people have previously eaten), and track allergens/food that people like to test, which would be useful for food agencies and restaurants to tailor their meals for a certain demographic.

References

[1] Food Allergy Research & Education, "Facts and Statistics", Food Allergy Research & Education. [Online]. Available: http://www.foodallergy.org/facts-and-stats [Accessed Dec. 2014].

[2] US Food and Drug Administration, "Food Allergen Labeling and Consumer Protection Act of 2004 (Public Law 108-282, Title II)", US Food and Drug Administration. [Online]. Available: http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/Allergens/ucm106187.htm [Accessed Dec. 2014].

[3] Leavitt Partners Global Food Safety Solutions, "Using Diagnostic Tools for Validation and Verification of an Allergen Control Program", Neogen. [Online]. Available: http://www.neogen.com/techlibrary/pdf/WhitePapers/Allergen_0813.pdf [Accessed Dec. 2014].

[4] AB SCIEX, "Allergen Testing", AB CIEX. [Online]. Available: http://www.absciex.com/applications/food-and-beverage-testing/allergen-testing?country=Canada [Accessed Dec. 2014].

[5]: Neogen Corporation, "Lateral Flow Immunochromatic Assays", Neogen Corporation. [Online]. Available: http://www.neogen.com/FoodSafety/pdf/L_F_Diagram.pdf [Accessed Dec. 2014].

[6]: Neogen Corporation, "Reveal 3-D Peanut Procedure", Neogen Corporation. [Online]. Available: http://www.neogen.com/FoodSafety/pdf/procedures/901041L_Pro.pdf [Accessed Dec. 2014].

[7]: Neogen Corporation, "Reveal® Test Kits", Neogen Corporation. [Online]. Available: http://www.neogen.com/FoodSafety/R_Product_List.asp?Test_Kit_Cat=203 [Accessed Dec. 2014].

[8]: bioavid Diagnostics GmbH & Co KG, "bioavid Diagnostics", bioavid Diagnostics GmbH & Co KG.[Online]. Available: http://www.bioavid.de/index2.html [Accessed Dec. 2014].

[9]: Morinaga Institute of Biological Science, Inc., "Food Allergen Lateral Flow", Morinaga Institute of Biological Science, Inc.. [Online]. Available: http://www.miobs-e.com/product/food_safety/food_allergen_lateral_flow/index.html [Accessed Dec. 2014].

[10] G. Zhang, et. al., "Immunochromatographic Lateral Flow Strip Tests", Biosensors and Biodetection Methods in Molecular Biology, vol. 504, pp 169-183, 2009. [Online]. Available: http://link.springer.com/protocol/10.1007%2F978-1-60327-569-9_12 [Accessed Dec. 2014].

[11] Neogen Corporation, "Food Safety Food Allergen Testing", Neogen Corporation. [Online]. Available: http://www.neogen.com/FoodSafety/FS_FA_Index.html [Accessed Dec. 2014].

[12] Crystal Chem Inc., "Food Allergen ELISA Kits", Crystal Chem Inc.. [Online]. Available: http://www.crystalchem.com/food-allergen-elisa-kits.html [Accessed Dec. 2014].

[13] J. F. T. Griffin, et. al., "Immunoglobulin G1 Enzyme-Linked Immunosorbent Assay for Diagnosis of Johne's Disease in Red Deer (Cervus elaphus)", Clinical and Diagnostic

Laboratory Immunology, vol. 12, no. 12, Dec. 2005. [Online]. Available: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1317074/ [Accessed Dec. 2014].

[14] MedLinePlus, "ELISA/western blot tests for HIV", U.S. National Library of Medicine. [Online]. Available: http://www.nlm.nih.gov/medlineplus/ency/article/003538.htm [Accessed Dec. 2014].

[15]: AB SCIEX, "U.S. Food and Drug Administration Selects AB SCIEX to Provide Mass Spectrometry Systems for Food Contaminant Testing", AB SCIEX. [Online]. Available: http://www.absciex.com/company/news-room/press-releases/us-food-and-drug-administration-selects-ab-sciex-to-provide-mass-spectrometry-systems-for-food-contaminant-testing [Accessed Dec. 2014].

[16]: TellSpec Inc., "TellSpec", Tellspec Inc.. [Online]. Available: http://tellspec.com/ [Accessed Dec. 2014].

[17]: Consumer Physics Inc., "SCiO - Consumer Physics", Consumer Physics Inc. [Online]. Available: http://www.consumerphysics.com/myscio/ [Accessed Dec. 2014].

[18]: Consumer Physics Inc., "FAQ", Consumer Physics Inc.. [Online]. Available: http://www.consumerphysics.com/myscio/faq.htm [Accessed Dec. 2014].

[19] J. E. Park, "A-Check: Testing Device For Food-Allergic People", Tuvie. [Online]. Available: http://www.tuvie.com/a-check-testing-device-for-food-allergic-people/ [Accessed Dec. 2014].

[20] Bangs Laboratories, Inc., "Lateral Flow Tests", Bangs Laboratories, Inc.. [Online]. Available: http://www.bangslabs.com/sites/default/files/imce/docs/TechNote%20303%20Web.pdf [Accessed Dec. 2014].

[21] GE Healthcare Life Sciences, "Sample pads for Immunoassays", GE Healthcare Life Sciences, [Online]. Available: http://www.gelifesciences.com/webapp/wcs/stores/servlet/catalog/en/GELifeSciences-us/products/AlternativeProductStructure_23129/ [Accessed Dec. 2014].

[22] R-Biopharm AG, "RIDA®QUICK Gliadin", R-Biopharm AG. [Online]. Available: http://www.r-biopharm.com/products/food-feed-analysis/allergens/gliadin-gluten/item/ridaquick-gliadin [Accessed Dec. 2014].

[23] Bangs Laboratories, Inc., "Immunochromatographic, Lateral Flow or Strip Tests Development Ideas", Pall Corporation. [Online]. Available: http://www.pall.com/main/oem-materials-and-devices/literature-library-details.page?id=4154 [Accessed Dec. 2014].

[24] The Threshold Working Group, "Approaches to Establish Thresholds for Major Food Allergens and for Gluten in Food", US Food and Drug Administration. [Online]. Available: http://www.fda.gov/downloads/Food/GuidanceRegulation/UCM316632.pdf [Accessed Dec. 2014].

[25] US Food and Drug Administration, "In Vitro Diagnostic Device Labeling Requirements", US Food and Drug Administration. [Online]. Available: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/DeviceLabeling/InVitroDiagnosticDeviceLabelingRequirements/ [Accessed Dec. 2014].

[26] US Food and Drug Administration, "In Vitro Diagnostics", US Food and Drug Administration. [Online]. Accessed: http://www.fda.gov/medicaldevices/productsandmedicalprocedures/invitrodiagnostics/ [Accessed Dec. 2014].

[27] US Food and Drug Administration, "Guidance for Industry and FDA Staff: In Vitro Diagnostic (IVD) Device Studies -Frequently Asked Questions", US Food and Drug Administration. [Online]. Available: http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM071230.pdf [Accessed Dec. 2014].

[28] US Food and Drug Administration, "510(k) substantial equivalence determination decision history", US Food and Drug Administration. [Online]. Available: http://www.accessdata.fda.gov/cdrh_docs/reviews/K112422.pdf [Accessed Dec. 2014].

[29] US Food and Drug Administration, "K13005 510(k) Summary", US Food and Drug Administration. [Online]. Available: http://www.accessdata.fda.gov/cdrh_docs/pdf13/K130055.pdf [Accessed Dec. 2014].

[30] US Food and Drug Administration, "IVD Over the counter (OTC) record K131931 and corresponding 510(K) Premarket Notification Information", US Food and Drug Administration. [Online]. Available: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfIVD/Detail.cfm?ID=3124 [Accessed Dec. 2014].

[31] US Food and Drug Administration, "Home use tests", US Food and Drug Administration. [Online]. Available: http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/HomeUseTests/ [Accessed Dec. 2014].

[32] OraSure Technologies, Inc., "Summary of Safety and Effectiveness Data", US Food and Drug Administration. [Online]. Available: http://www.fda.gov/downloads/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/PremarketApprovalsPMAs/UCM091919.pdf [Accessed Dec. 2014].

[33] Roche Diagnostic, "Summary of safety and effectiveness data (SSED)", US Food and Drug Administration. [Online]. Available: http://www.accessdata.fda.gov/cdrh_docs/pdf13/P130015b.pdf [Accessed Dec. 2014].

[34] The Threshold Working Group, "Approaches to Establish Thresholds for Major Food Allergens and for Gluten in Food", US Food and Drug Administration. [Online]. Available: http://www.fda.gov/downloads/Food/IngredientsPackagingLabeling/UCM192048.pdf [Accessed Dec. 2014].

Appendix A: Market Identification Survey

Food Consumption and Tracking

* Required

Do you avoid any foods in particular (aside from allergies)? Why?

Do you have any of the following food allergies, sensitivities, or intolerances?
This list is based on the US FDA's labeling requirements for food allergens.

- [ ] Milk (including lactose)
- [ ] Eggs
- [ ] Fish (e.g. bass, flounder, cod)
- [ ] Crustacean shellfish (e.g. crab, lobster, shrimp)
- [ ] Tree nuts (e.g. almonds, walnuts, pecans)
- [ ] Peanuts
- [ ] Wheat (i.e. gluten)
- [ ] Soybeans
- [ ] Other:

How often do you eat out? *

- ( ) Never
- ( ) Once a week
- ( ) Few Times a week
- ( ) Often
- ( ) Always

Do you find yourself ordering the same foods due to food avoidance? *

- ( ) Never
- ( ) Sometimes
- ( ) Often
- ( ) Always

Would you eat out more if you didn't have to avoid certain foods? *

- ○ Yes
- ○ No

How often do you purchase pre-packaged or pre-cooked foods?

- ○ Never
- ○ Sometimes
- ○ Often
- ○ Always

How often do you check labels and/or ingredients list before purchasing foods? *

- ○ Never
- ○ Sometimes
- ○ Often
- ○ Always

Would you like to test food for any of these allergies, sensitivities, or intolerances? *

- ○ Yes
- ○ No

Allergen Testing Device

Suppose a device existed which would test foods for a specific allergen or foodstuff.

How often would you use this device?

- ○ Every meal
- ○ Every time I eat out
- ○ When I think the food might contain an allergen
- ○ Rarely
- ○ Never

How would you like the information displayed? (select all that apply)

- ☐ Basic colour indicator
- ☐ On-device indicator light(s)
- ☐ On-device screen
- ☐ Smartphone companion app

On a scale from 1-10, rate these features in terms of importance.

1 = least important, 10 = most important

	1 (Least Important)	2	3	4	5 (Somewhat Important)	6	7	8	9	10 (Most Important)
Lightweight	○	○	○	○	○	○	○	○	○	○
Ease of Use	○	○	○	○	○	○	○	○	○	○
Cost per test	○	○	○	○	○	○	○	○	○	○
Speed	○	○	○	○	○	○	○	○	○	○
Accuracy (min. concentration of allergen required for a positive result)	○	○	○	○	○	○	○	○	○	○
Versatility (test for multiple allergens at once)	○	○	○	○	○	○	○	○	○	○
Durability	○	○	○	○	○	○	○	○	○	○
Reusability	○	○	○	○	○	○	○	○	○	○

What is the maximum you would be willing to pay for such a device?

- ○ $0.00 - $9.99
- ○ $10.00 - $24.99
- ○ $25.00 - $49.00
- ○ $50.00 - $99.99
- ○ $100.00+

What is the maximum would you be willing to pay per test?

- ○ $0.00 - $1.99
- ○ $2.00 - $4.99
- ○ $5.00 - $9.99
- ○ $10.00 - $24.99
- ○ $25.00 - $49.99
- ○ $50.00 - $99.99
- ○ $100.00+

Demographics Information

Please help us understand you better.

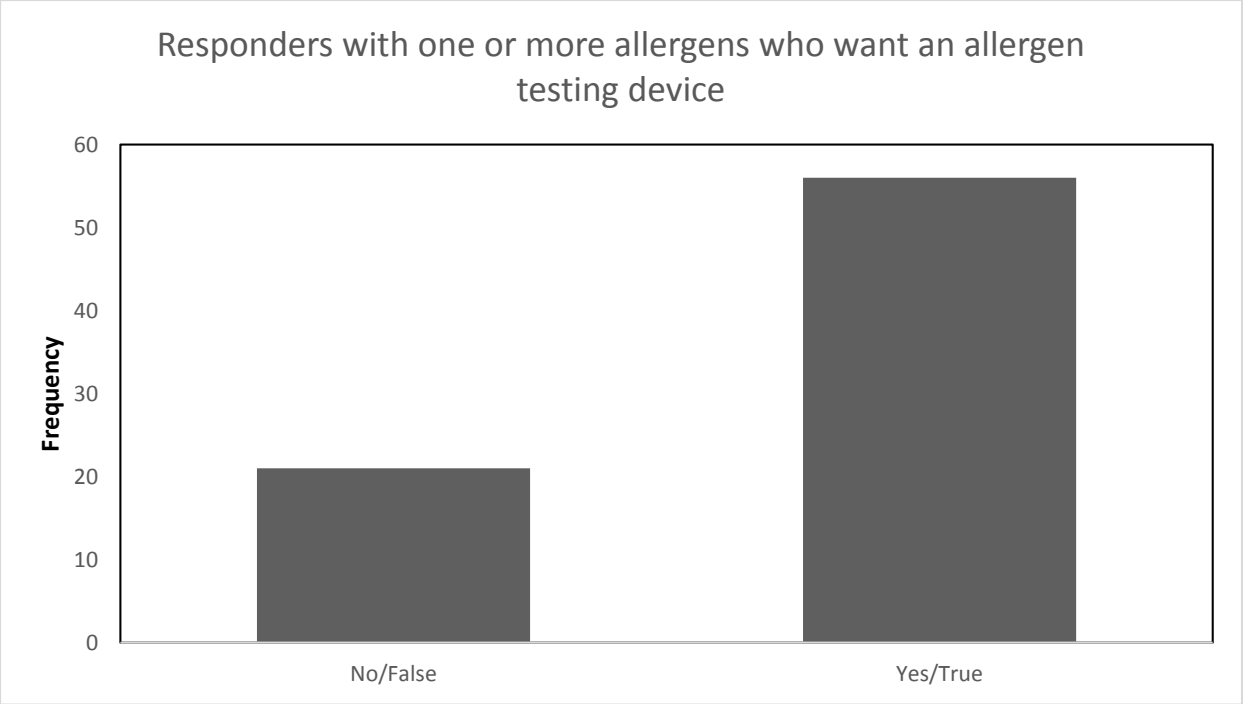
Age *

- Under 18
- 18-24 years old
- 25-34 years old
- 35-44 years old
- 45-54 years old
- 55-64 years old
- over 65
- Prefer not to answer

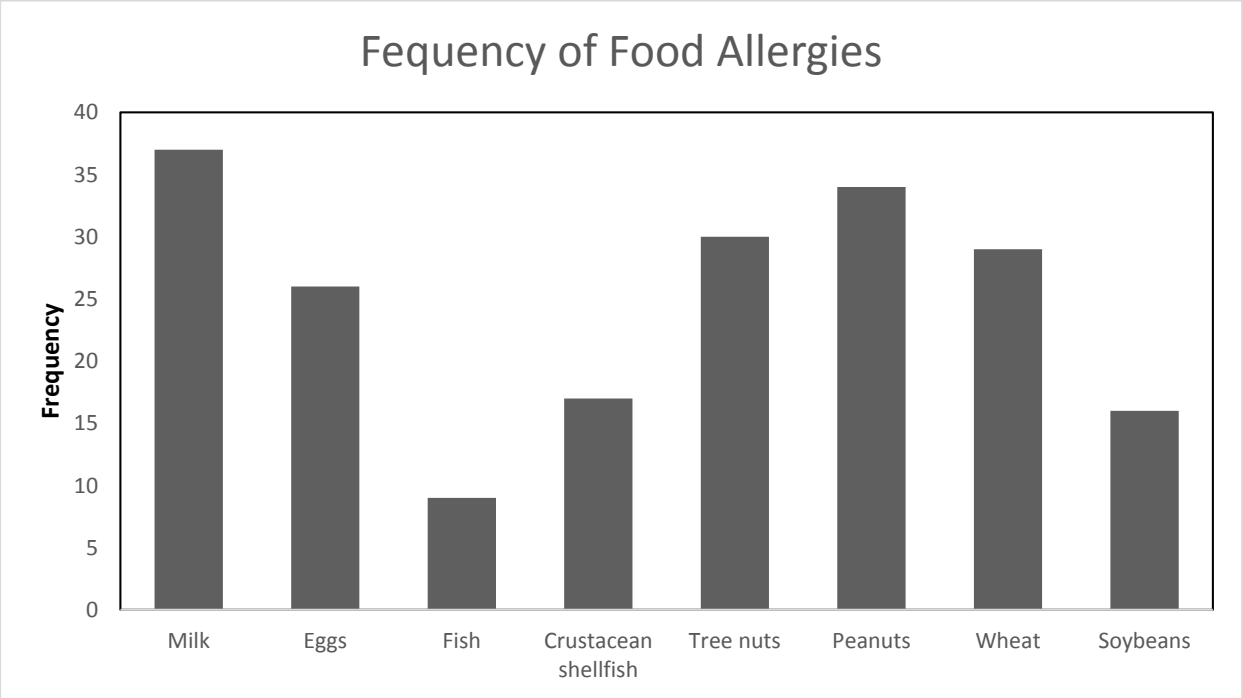
How many people live in your household? *

- 1
- 2
- 3-4
- 5+
- Prefer not to answer

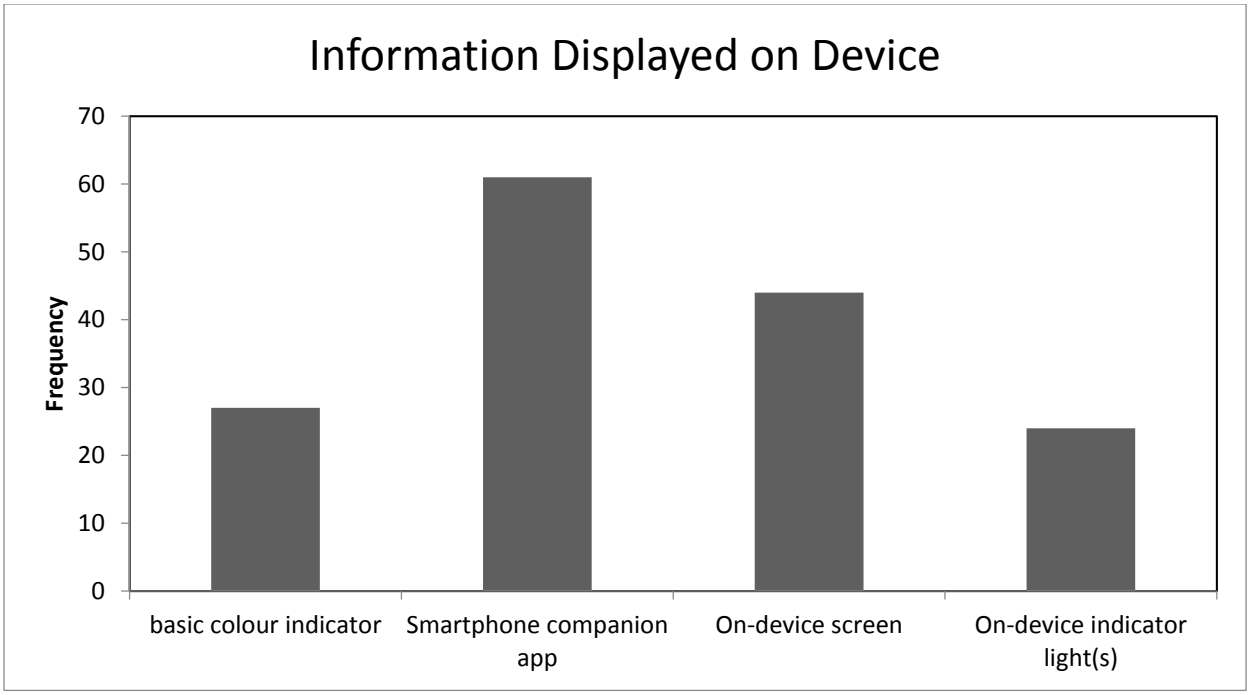
Appendix B: Survey Result



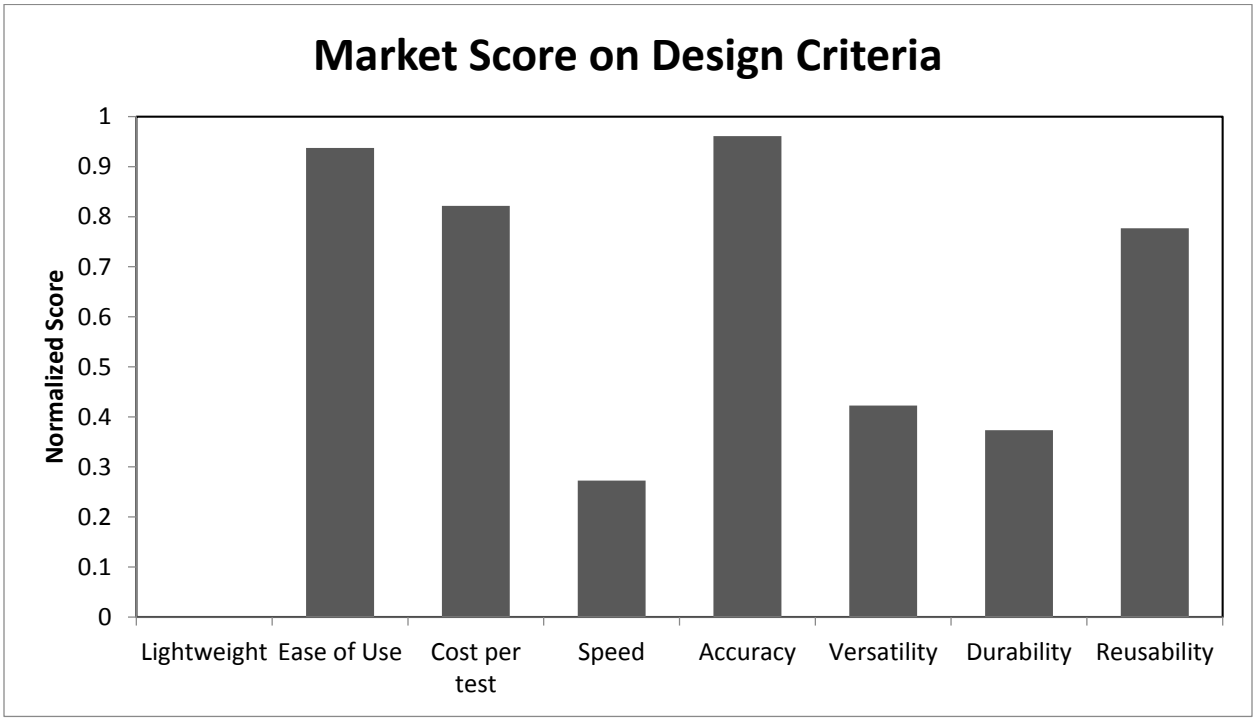
From this, we can see that 73% of respondents who have food allergies want a device to test for allergens.



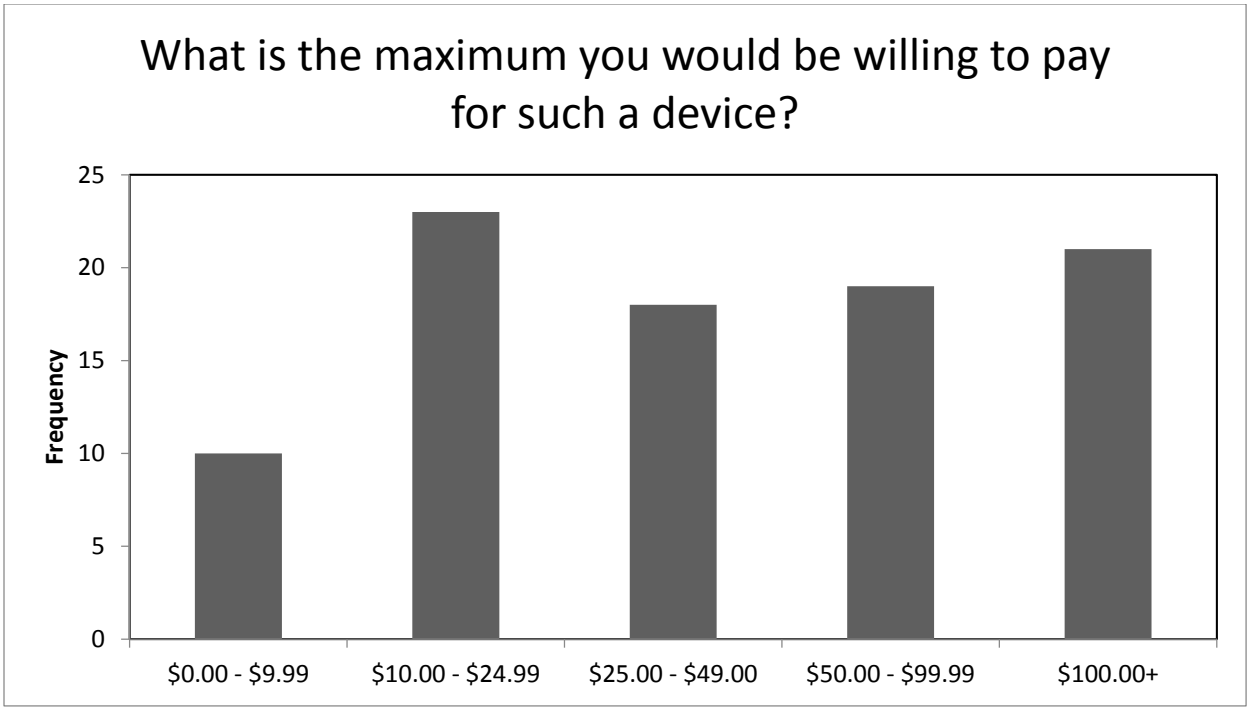
Our market has a high occurrence of milk, peanuts, and nut allergies.

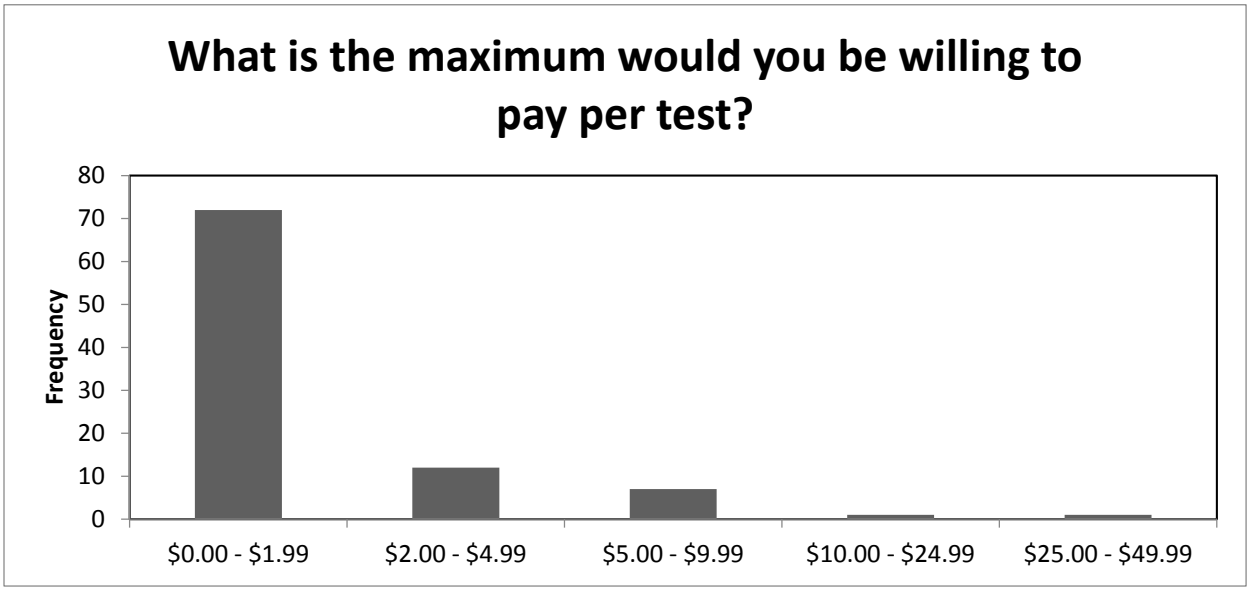


The smartphone companion app was the most popular choice for receiving the information from the device.



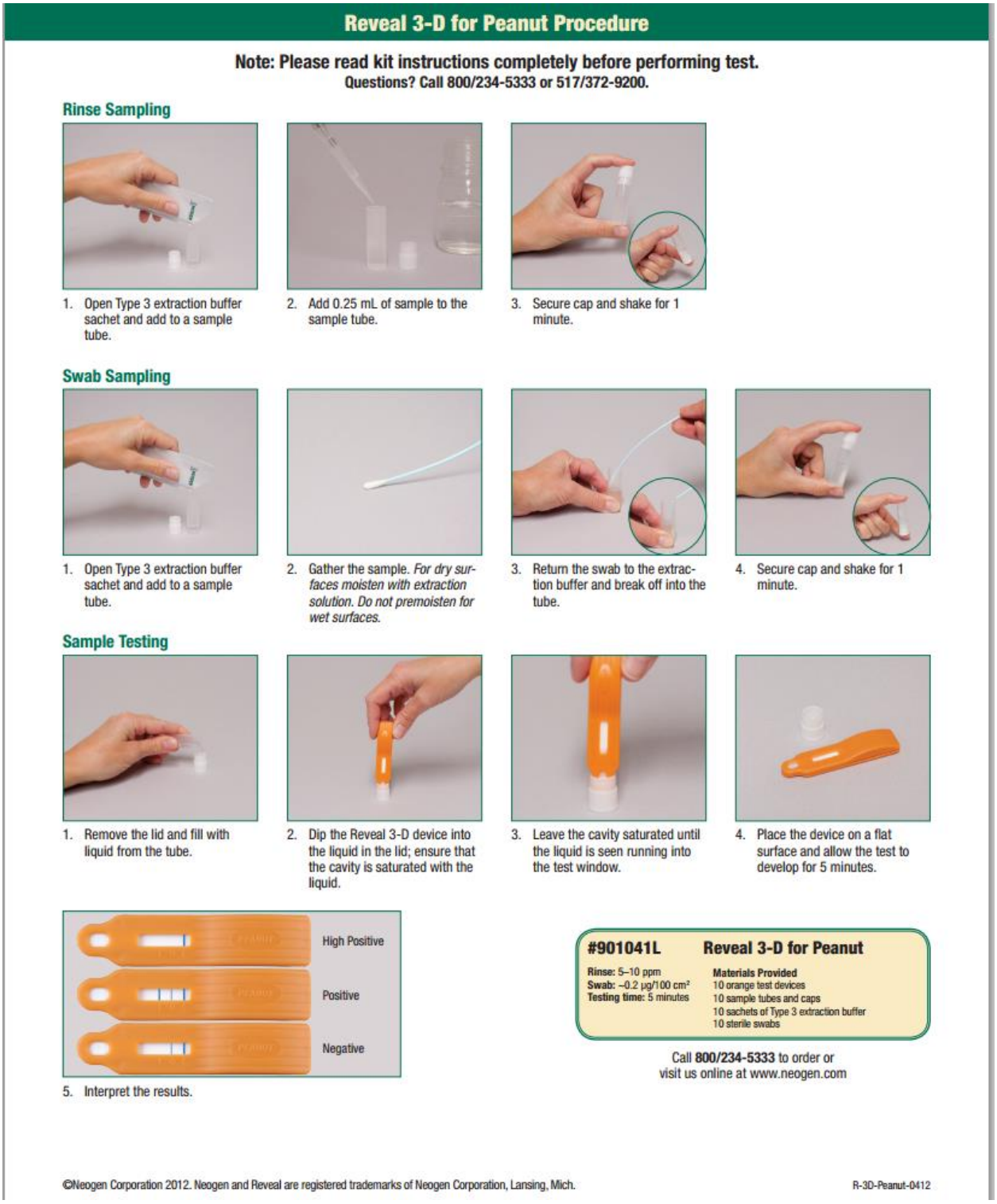
The top three choices for design criteria are: ease of use, accuracy, and cost per test.





From these two graphs, we can see that the market does not have a strong preference to the price of the device, but has a strong preference to the maximum cost per test.

Appendix C: Current Solutions



Reveal 3-D for Peanut Procedure

Note: Please read kit instructions completely before performing test.
Questions? Call 800/234-5333 or 517/372-9200.

Rinse Sampling

1. Open Type 3 extraction buffer sachet and add to a sample tube.
2. Add 0.25 mL of sample to the sample tube.
3. Secure cap and shake for 1 minute.

Swab Sampling

1. Open Type 3 extraction buffer sachet and add to a sample tube.
2. Gather the sample. *For dry surfaces moisten with extraction solution. Do not premoisten for wet surfaces.*
3. Return the swab to the extraction buffer and break off into the tube.
4. Secure cap and shake for 1 minute.

Sample Testing

1. Remove the lid and fill with liquid from the tube.
2. Dip the Reveal 3-D device into the liquid in the lid; ensure that the cavity is saturated with the liquid.
3. Leave the cavity saturated until the liquid is seen running into the test window.
4. Place the device on a flat surface and allow the test to develop for 5 minutes.

5. Interpret the results.

#901041L **Reveal 3-D for Peanut**

Rinse: 5–10 ppm
Swab: ~0.2 µg/100 cm²
Testing time: 5 minutes

Materials Provided
10 orange test devices
10 sample tubes and caps
10 sachets of Type 3 extraction buffer
10 sterile swabs

Call **800/234-5333** to order or
visit us online at www.neogen.com

R-3D-Peanut-0412

Neogen Corporation, "Reveal 3-D Peanut Procedure", Neogen Corporation. [Online]. Available: http://www.neogen.com/FoodSafety/pdf/procedures/901041L_Pro.pdf [Accessed Dec. 2014].

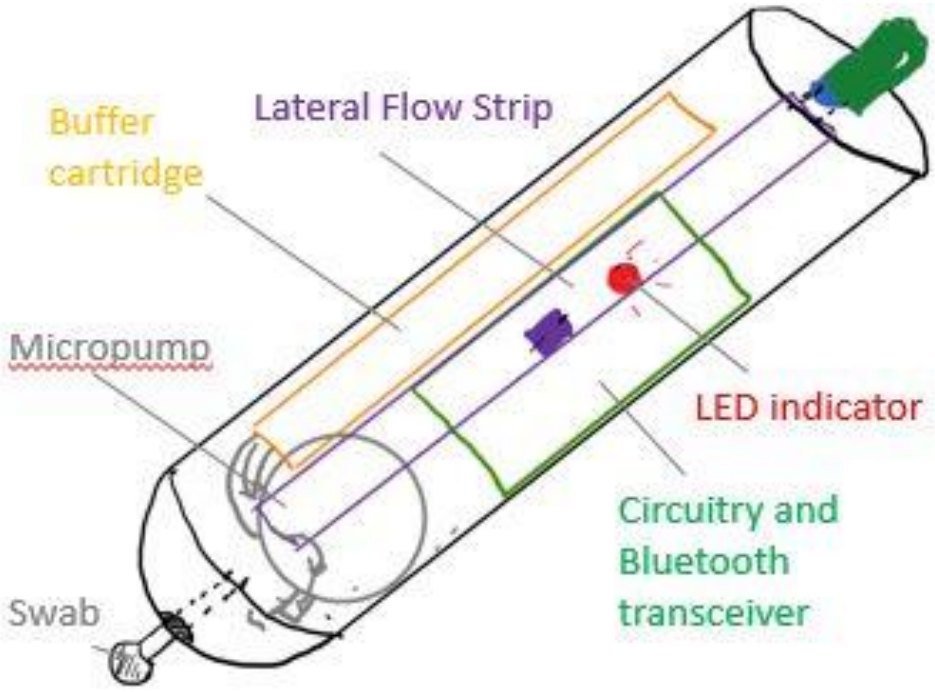
Consumer Physics SCiO

Consumer Physics Inc., "SCiO - Consumer Physics", Consumer Physics Inc. [Online]. Available: http://www.consumerphysics.com/myscio/ [Accessed Dec. 2014].

Appendix D: Technical Specifications Comparison

Factor	Optimal	Neogen Reveal 3D	Crystal Chem ELISA Kits	AB SCIEX QTRAP 5500	TellSpec
Technology		Lateral Flow Immunochromatic Assay	Microwell Immunosorbent Assay	Spectroscopy (LC/MS/MS)	Spectroscopy (NIR)
Accuracy	High	5 ppm	variable, as low as 0.256 ppm	High	Unknown - not designed for this purpose
Ease of Use	No special equipment required	Requires pipettes	Requires pipettes, several wash steps, and various reagents	Complex procedure	No special equipment required
Time Required for Test	Low	Low (10 mins)	High (30-75 mins)	High, depending on elution time during LC step	Low (mins)
Incubation Time	Low	Low (5 mins)	High (30 mins)	N/A	None
Display of Result	Simple Yes/No	Simple Yes/No	Compare versus standard curve	Requires analysis of results	Yes
Initial Cost	Medium	$0	$0	High	High ($349 initial cost and $69.99 per year access to database)
Cost per test	Low	approx. $16	Variable, depending on reagents used	Variable, depending on reagents used	None
Special Requirements	None	Refrigerated	Refrigerated	None	Access to the internet

Appendix E: Product Sketches



Appendix F: Cost Analysis

Device

Component	Dimensions	mass	cost of component	cost of component + safety margin/labour cost
Cap (HDPE blow molding)	hemisphere (2cm diameter)	2.03 g	$ 0.004	$0.008 [F1]
Lateral flow strip	N/A	N/A	N/A	$0.38 [20]
Housing	cylinder (diameter: 3 cm, length: 12 cm)	84.82 g	$ 0.19	$ 0.38 [F2]
Buffer solution per cartridge	N/A	N/A	N/A	$ 0.568 [F3]
Buffer cartridge (asuming 5 times the volume of the buffer cap)		10.12 g	$0.02	$0.04 [F1]
Bluetooth transceiver	4x2 cm	N/A	N/A	$4 [F4]
Micropump (curiejet piezoelectric micropump)	17.2x17.2x17.2 mm	N/A	N/A	$10 [F5]
Circuitry	(5cm x 2cm) rough estimate	N/A	N/A	$ 4.9 (rough estimate: pcb = $2, microcontroller = $2, photoresistors = $1, op

				amp = $.30, rest of circuitry = $1)
Disposable components total			$0.99	$1.49 (safety margin of 1.5)
Device total			$18.9	$28.35 (safety margin of 1.5)

Cost breakdown of lateral flow strip

Component	Cost per test ($)
Test Line Antibodies	0.01
Membranees	0.02
Control Antibodies	0.01
Absorbent Pad	0.001
Conjugate Antibodies	0.02
Sample Pad	0.002
Latex Microspheres	0.01
Membrane Backing	0.01
Desiccant	0.02
Pouch	0.08
Plastic Housing	0.20
Total	0.38

[F1] RecycleINme, "HDPE Blow molding - US Plastic prices", RecycleINme. [Online]. Available: http://www.recycleinme.com/scrapresources/DetailedPrice.aspx?psect=2&cat=US%20Plastic%20Prices&subcat=HDPE%20-%20Blow%20Molding [Accessed Dec. 2014].

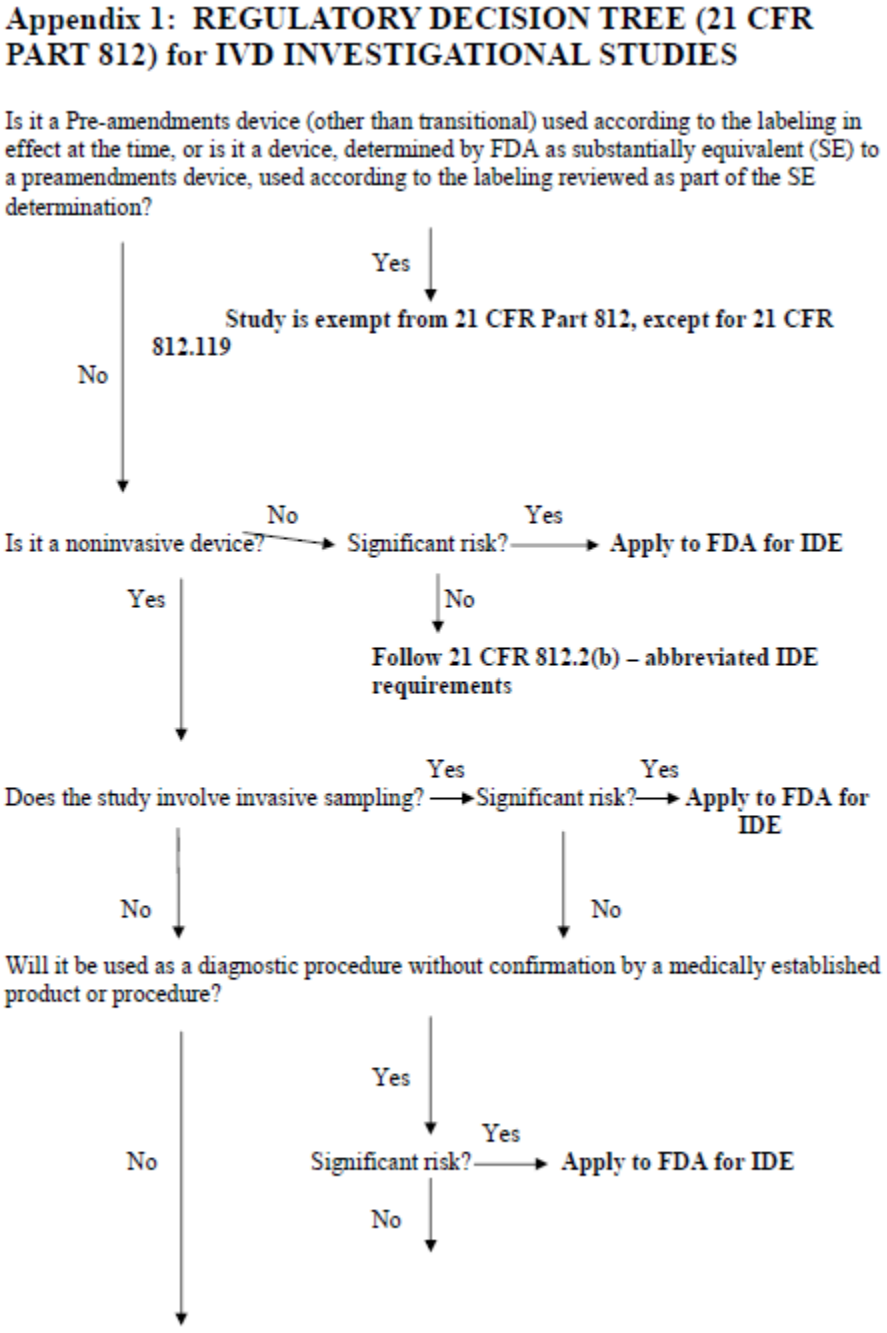
[F2] RecycleINme, "HDPE injection - US Plastic prices", RecycleINme. [Online]. Available: http://www.recycleinme.com/scrapresources/DetailedPrice.aspx?psect=2&cat=US%20Plastic%20Prices&subcat=HDPE%20-%20Injection [Accessed Dec. 2014].

[F5] Microjet technology, "CurieJet Printer ink diaphragm Micropump", Alibaba. [Online] Available: http://www.alibaba.com/product-detail/CurieJet-Printer-ink-diaphragm-Micropump_704293821.html [Accessed Dec. 2014].

[F4] Alibaba, "Bluetooth circuit board", Alibaba. [Online]. Available:http://www.alibaba.com/showroom/bluetooth-circuit-board.html [Accessed Dec. 2014].

[F3] Clonetech Takara, "Cell lysis buffer", Clonetech. [Online]. Available:http://www.clontech.com/US/Products/Protein_Expression_and_Purification/Reagents/Cell_Lysis_Buffers [Accessed Dec. 2014].

Appendix G: FDA Decision Tree



US Food and Drug Administration, "Guidance for Industry and FDA Staff: In Vitro Diagnostic (IVD) Device Studies -Frequently Asked Questions", US Food and Drug Administration. [Online]. Available: http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM071230.pdf [Accessed Dec. 2014].

Appendix H: FDA Similarities Table

Item	Proposed Device	Chemtrue hCG Pregnancy	Wondfo Buprenophine Urine Test	CrAg Lateral Flow assay	Notes
510(k) number	-----	K131931	K130055	K112422	
Product code	----	LCX	DJG	GMD	Product codes are different for each predicate because each predicate has different intended use. Our product code for our intended use does not exist.
Risk classification	class II	class II	class II	class II	All of these tests are non-invasive technologies.
Technology principle	Lateral flow immunochromatic assay	(same) Colloidal gold conjugate lateral-flow immunoassay	(same) Lateral flow chromatographic immunoassay	(same) dipstick sandwich lateral flow immunochromatographic assay	No significant difference in technology principle
Result Interpretation	LED and Phone (bluetooth connection)	Visually-read line intensity	Qualitative	Visually-read line intensity	No significant difference in result interpretation
Sensitivity	around 5 ppm	20 mlU/mL	10ng/mL	1.25ng,/mL	Sensitive enough to give a qualitative result.

Real time	5 to 10 minutes	read the results at 3 minutes	read at 5 minutes	read at 10 minutes	same
Quality control	built in internal control	built in internal control	built in internal control	built in internal control	same
Device format	Pen-style	Midstream	Dip card / test cup	Dipstick	same
Indication of Use	Over the counter	Over the counter	Over the counter	Prescription use only	no significant difference
Storage		4-30 degree Celsius	10 - 30 degree celsius	20-25 degree celsius	no significant difference (around room temperature)
Specimen matrix	food sample	human urine	human urine	cerebral spinal cord (CSF) and serum	
Intended Use	A qualitative immunoassay for determination of food allergens in food specimen	A rapid qualitative immunoassay for rapid determination of human chorionic gonadotropin (hCG) to aid in the early detection of pregnancy	assay for qualitative determination of Buprenorphine in human urine	immunochromatic graphic test system for qualitative detection of capsular polysaccharide antigens of Cryptococcus species complex in serum and CSF	**This means that we cannot establish substantial equivalence, even the technology is identical.**

Appendix I: Standards Table

Recognition number	Recognized Consensus standards and Voluntary standards
7-84: CEN 13640	Stability testing of in vitro diagnostic reagents [I1]
7-174: CLSI EP21-A	Estimation of total analytical error for clinical laboratory methods [I2]
7-233: CLSI EP17-A2	Evaluation of detection capability for clinical laboratory measurement procedures[I3]
7-113: CLSI I/LA23-A	Assessing the quality of immunoassay systems: radioimmunoassays, and enzyme, fluorescence and luminescence immunoassays[I4]
7-110: CLSI EP05-A2	Evaluation of precision performance of quantitative measurement methods [I5]
Material Testing	
ASTM D1004	Standard Test Method for Tear Resistance (Graves Tear) of Plastic Film and Sheeting[I6]
ASTM C272 / C272M - 12	Standard Test Method for Water Absorption of Core Materials for Sandwich Constructions[I9]
ASTM F639	Standard Specification for Polyethylene Plastics for Medical Applications[I7]
ASTM D3641 - 14	Standard Practice for Injection Molding Test Specimens of Thermoplastic Molding and Extrusion Materials[I8]
Quality Standards	
ISO 13485	Medical devices -- Quality management systems [I10]
IEC 60601-1	Medical electrical equipment - Part 1: General requirements for basic safety and essential performance [I11]

[I1] US Food and Drug Administration, "Recognized Consensus standards", US Food and Drug Administration. [Online]. Available: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/detail.cfm?standard__identification_no=12103 [Accessed Dec. 2014].

[I2] US Food and Drug Administration, "Recognized Consensus standards", US Food and Drug Administration. [Online]. Available: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/detail.cfm?standard__identification_no=31792 [Accessed Dec. 2014].

[I3] US Food and Drug Administration, "Recognized Consensus standards", US Food and Drug Administration. [Online]. Available: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/detail.cfm?standard__identification_no=30531[Accessed Dec. 2014].

[I4] US Food and Drug Administration, "Recognized Consensus standards", US Food and Drug Administration. [Online]. Available: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfstandards/detail.cfm?standard__identification_no=14932 [Accessed Dec. 2014].

[I5] US Food and Drug Administration, "Recognized Consensus standards", US Food and Drug Administration. [Online]. Available: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfstandards/detail.cfm?standard__identification_no=14909 [Accessed Dec. 2014].

[I6] ASTM International, "Standard test method for tear resistance (graves tear) of plastic film and sheeting", ASTM. [Online]: Available:http://www.astm.org/Standards/D1004.htm [Accessed Dec. 2014].

[I7] ASTM International, "Standard test method for tear resistance (graves tear) of plastic film and sheeting", ASTM. [Online]: Available:http://www.astm.org/Standards/F639.htm [Accessed Dec. 2014].

[I8] ASTM International, "Standard test method for tear resistance (graves tear) of plastic film and sheeting", ASTM. [Online]: Available:http://www.astm.org/Standards/D3641.htm [Accessed Dec. 2014].

[I9] ASTM International, "Standard test method for tear resistance (graves tear) of plastic film and sheeting", ASTM. [Online]: Available:http://www.astm.org/Standards/C272.htm [Accessed Dec. 2014].

[I10] ISO, "ISO 13285:2003", ISO. [Online]. Available: http://www.iso.org/iso/iso_catalogue/catalogue_tc/catalogue_detail.htm?csnumber=36786 [Accessed Dec. 2014].

[I11] ISO, "IEC 60601-1-11:2010", ISO. [Online]. Available: http://www.iso.org/iso/catalogue_detail.htm?csnumber=45605 [Accessed Dec. 2014].