



4 μL sample Advances in Allergy Testing

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A HYCOR BIOMEDICAL
WHITE PAPER

“The 4 μL sample volume utilized on the NOVEOS system offers many key advantages for the clinical laboratory when compared to other high throughput systems”.^x

– Dr Boer Ph.D.

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Improving Lives

Easy access to allergy testing by using small sample volumes and disruptive technology is opening new opportunities for laboratories and benefits clinic, physicians, patients and parents.

TECHNOLOGY IS ADVANCING

In the past three decades, the world has seen staggering technological changes. In 1990, just 9 % of households had personal computers, the World Wide Web was just beginning, and cellular phones were bulky, limited, and rare. Thanks to plummeting prices, most consumers today own (large!) HD TVs and small cellular phones that contain more horsepower than the contemporary mainframe computers of the 1990's.



During that same time, fluorescence-based assays entered the allergy market requiring anywhere from 40 -70 μL of serum to conduct their tests. These 'state-of-the-art' technologies were essentially blood hogs for testing, requiring a significant volume from a single serum collection tube to conduct as few as 20 tests in each panel or mix(!).

Clinicians soon recognized that yesterday's allergy technologies demonstrated performance that was representative of very early serology-based testing: mediocre imprecision, limited agreement with allergy skin tests and known levels of interferences present in typical patient samples.

SOMETIMES SMALLER IS BETTER

The proven performance of 5 μL or less: Over the past 30 years, large manufacturers have introduced advanced technologies that have dramatically improved immunochemical testing for the clinical laboratory. The use of low sample volumes in assays has become commonplace in the clinical laboratory when testing for macromolecules at high concentration in a patient sample. For example, the first tests for human chorionic gonadotropin (hCG), a hormone produced by uterine cells surrounding an implanted embryo, utilized only 5 μL per test since the concentration of hCG in serum was elevated even early in the pregnancy. Similarly, many infectious disease and



autoimmune tests that measure the levels of IgG in the blood (a highly represented macromolecule), utilized 5 μL of serum in the dilutions for the assayⁱⁱ. Another example is testing for C-reactive protein (CRP) which requires a similar 5 μL in 495 μL dilution for cardiovascular disease risk. These tests on the Roche Elecsys, Abbott Architect, Siemens Centaur/Atellica/IMMULITE 2000 and other platforms routinely obtained highly accurate results for precision, specificity, and sensitivity despite the smaller sample size. **NOVEOS** by HYCOR Biomedical, continues in this tradition where smaller can clearly be better were its 4 μL sample size has routinely demonstrated superior performance in testing required for CE mark, FDA clearance and China's National Medical Product Administration (NMPA) approval. The system routinely meets or exceeds the current standards for precision, limit of detection and method comparison. The **NOVEOS** fluidics system has become the new standard in ensuring that analytical volumes are delivered accurately for each test; advanced liquid level detection systems safeguard volume delivery and monitor all aspects of the reaction chemistry.

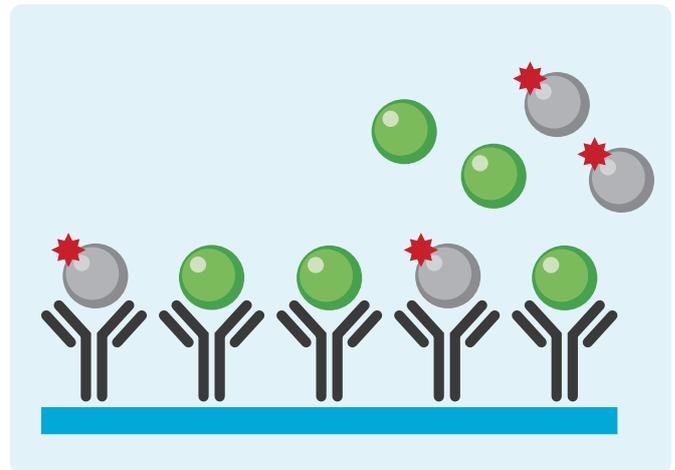
Repeatability and within-laboratory precision:

One of the regular questions that is asked is the level of accuracy and performance one can expect with the 4 μL sample volume. This question was directly evaluated in a bi-center study at Philipps-University Marburg (Site-1) and Charité Medical University Berlin (Site-2), respectively. The repeatability (within run) for house dust mite (HDM), Cat Dander, Peanut and Timothy Grass samples yielded a CV of 3%–6% and 3%–8% at sites 1 and 2, respectively. The total imprecision (within laboratory) for these same allergens was 3%–9% and 5%–12% for each respective site. Other analytical results for the **NOVEOS** allergen sIgE testing for these allergens were comparable at the two sites where the instrument exhibited excellent linearity, a limit of detection less than

0.1 kU/L and minimal impact to patient results by endogenous interfering substances (bilirubin, hemolysis, lipemia).

Reduced interference when using 5 μL or less:

Another key advantage of a small sample size is that it has a direct impact on reducing other interferences observed in many samples. Interference can lead to falsely elevated or falsely low analyte results depending on the site of the interference in the immunoassay reaction.



The magnitude of the effect depends on the concentration of the interfering substance, but not necessarily in a directly proportional way.

Most manufacturers utilize a reaction chemistry where patient sample makes up 15% - 25% of the reaction volume; for example, a typical assay with 40 μL of sample combined with 160 μL of reagent results in 20% of the reaction volume originating from the patient sample. Interfering substances can potentially be present at significant levels in these reaction volumes, thereby impacting results. Conversely, the **NOVEOS** system, with its 4 μL sample size added to 56 μL reaction volume utilizes only 7% of the total volume with lower potential impact by these interferences.

ADVANCING TECHNOLOGY IS OPENING NEW OPPORTUNITIES

The issue with insufficient sample: Across the world, people have their blood drawn over a billion times a year. Most of the time this includes a trip to the doctor’s office, sometimes with an additional trip to a blood collection clinic. Common collection methods of arterial sampling, venipuncture or fingerstick, while generally safe the procedure can be painful and upsetting to the patient. Additionally, the typical blood draw is not without complications especially for patients who are young, have arterial issues, and are overweight, impaired, or generally uncooperative.

QNS can be observed in up to 10% of all samples collected.

Small sample size tests allow for more testing to be done on a single sample while minimizing QNS episodes. More importantly, **NOVEOS’** 4 µL sample volume enables the use of new technologies in blood collection for testing that should improve access to universal allergy healthcare.

New collection devices: New sample draw technologies have entered the market, are nearly painless and make it possible for the non-medical professional (layperson) to collect their own blood, eliminating the need for a trained professional. These new technologies allow

Up to 40%

QNS is also a common issue among pediatric patients who account for approximately 40% of the allergy testing population.



One of the more common reasons for sample rejection or redraw is insufficient sample volume. Quantity not sufficient (QNS) puts a major burden on the physician, clinical lab, and the patient. Quite frankly, the sample redraw itself is a major issue at the clinical laboratory since many patients will not willingly subject themselves to another venipuncture episode.

QNS is also a common issue among pediatric patients who account for approximately 40% of the allergy testing population. Within this group,

patients to collect small volumes of serum or plasma in the convenience of their home, office or in the physician office rather than traveling to the phlebotomy laboratory. Just as importantly, the devices allow patients to easily send drawn samples to the laboratory via direct mail. This logistic improvement allows follow-up testing with fewer or no redraws and should have a positive effect on reducing costs. Less sample per test improves the experience of patients by less complication, and perhaps ensuring better compliance.

Serving a bigger market: New sample collection methods and remote collection of blood samples is an opportunity to gain better access to laboratory tests and thereby provide better healthcare.

From a laboratory point of view, being able to reach out to more people is an opportunity to explore new markets, reach more patients, and attract more tests. **NOVEOS** is an essential piece of this strategy since it uses 1/10th the sample volume of other leading allergy systems and requires significantly less dead volume for a test to be run; for example, **NOVEOS** can perform up to 20 tests from a 200 μ L sample whereas other systems cannot achieve even a single test result.

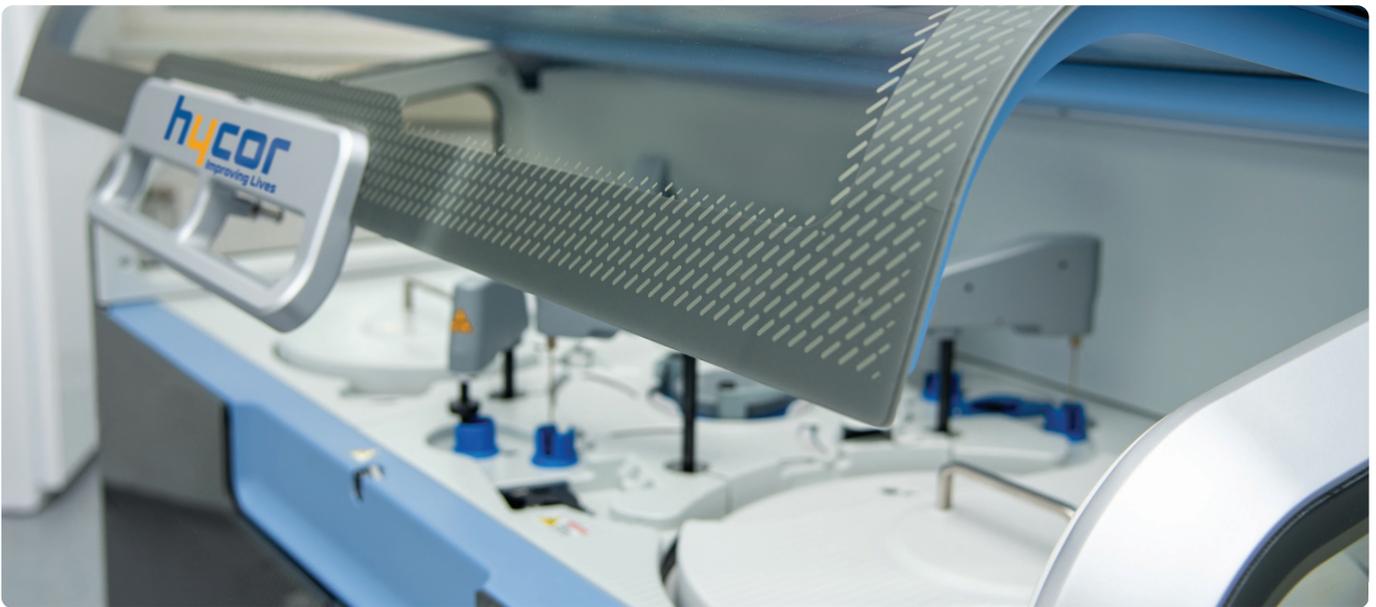
Doing more allergy tests with less sample benefits all patients and helps improve laboratory workflows, efficiency, and operating costs. The low sample requirements for the **NOVEOS** system and its minimal dead volume are key in reducing

costs, time and QNS frustration. This makes it a natural companion to these collection device technologies.

3 REASONS LABS SWITCH TO NOVEOS®

For the first time, **NOVEOS** combines proven microparticle technology with chemiluminescence to introduce a new standard in allergy testing. The **NOVEOS** system offers confidence that the allergy results are accurate and precise with limited impact from common sample-based interferences. This technology enables the use of a low sample volume that will become the industry standard for assays detecting IgE in serum and plasma.

The unique technology of the NOVEOS system and its small sample volume enables the use of new collection devices which opens the door to new opportunities for laboratory expansion.



ⁱ Betz D, Fane K. Human Chorionic Gonadotropin (HCG) [Updated 2020 Apr 27]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan

ⁱⁱ Neu N, Duchon J, Zachariah P. TORCH infections. Clin Perinatol. 2015 Mar;42(1):77-103, viii. doi: 10.1016/j.clp.2014.11.001. Epub 2014 Dec 20. PMID: 25677998.

ⁱⁱⁱ https://www.siemens-healthineers.com/cardiac/cardiac-assays/high-sensitivity-c-reactive-protein#TECHNICAL_SPECIFICATIONS

^{iv} <https://diagnostics.roche.com/>

^v <https://www.corelaboratory.abbott/us/en/offerings/brands/architect>

^{vi} <https://www.siemens-healthineers.com/laboratory-diagnostics/atellica-portfolio>

^{vii} Bauersachs D, Potapova E, Renz H, Benes SH, Matricardi PM, Skevaki C. Validation of the analytical performance of the NOVEOS™ System, a system which improves upon the third-generation in vitro allergy testing technology. Clin Chem Lab Med. 2020 Oct 25;58(11):1865-1874. doi: 10.1515/cclm-2020-0535. PMID: 32549134.

^{viii} Tate J, Ward G. Interferences in immunoassay. Clin Biochem Rev. 2004;25(2):105-120.

^{ix} Dankers, M., Fried E., Windle, M. Arterial Blood Gas Sampling, Medscape May 08, 2020

^x Doing more with less: Advancements in serum IgE testing by Eric Whitters, Ph.D. A Hycor Biomedical White paper. August 2021.



Pinpoint your TRUE allergy triggers with NOVEOS!

The New Standard in allergy testing, solving shortcomings of current technologies.

- 60 sample positions
- ~100 tests per hour after the first test result
- On-board reagent capacity of 10,500 tests
- Two configurations for your lab optimization:
 - Up to 1200 tests per run when connected directly to a deionized water source and waste drain
 - Up to 700 tests per run in stand-alone configuration
- Release result per patient or per run
- Accurate results with only 4µL per test
- Less intervention due to the small sample volume requirement
- Superb sensitivity due to microparticle approach
- Minimal biotin or cellulose-based CCD interference
- Flexible in staff allocation
- Improved workflow efficiency
- More allergy tests, saving time and reducing costs

Learn More! Schedule a Demo Online!

<https://www.hycorbiomedical.com/book-a-demo>

Improving the health, well-being and quality of life of individuals with allergic conditions.

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