

A Case Study on the Adoption of navify[®] Algorithm Suite by Medizinische Hochschule Hannover

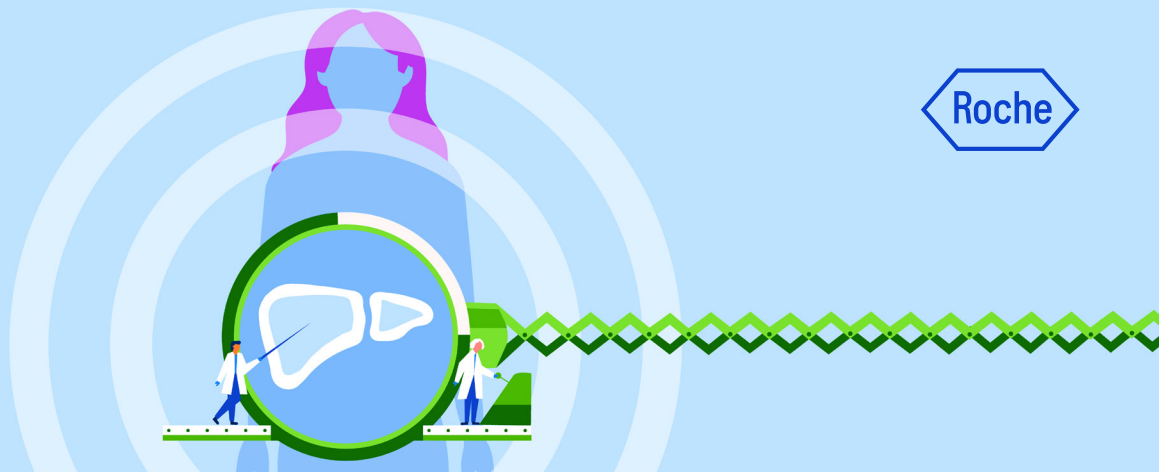
navify[®] Algorithm Suite, a digital platform offered by Roche Information Solutions, provides Medizinische Hochschule Hannover with efficient implementation of the GAAD algorithm for HCC.

Synopsis

Medizinische Hochschule Hannover is a University Hospital in Hannover, Germany that serves nearly 60,000 inpatients annually. The University Hospital is dedicated to providing patients with optimum diagnosis and treatment including novel digital solutions. One such solution is offered by navify[®] Algorithm Suite, a digital cloud-based platform that facilitates capturing the clinical benefits of the GAAD algorithm for hepatocellular carcinoma (HCC) by direct integration into the clinical workflow of existing laboratory systems. In a semi-structured interview, the lab director Prof. Dr. R. Lichtinghagen stated that navify[®] Algorithm Suite reduces manual actions required by 90%, from 10 steps for risk score calculation before using Roche solutions (i.e., navify[®] AlgoSuite Suite, GAAD) to just 1 step after implementation, hereby also reducing potential for manual error. Further, time savings of ~2 hours daily and ~8 hours weekly can be accrued, as reported by the lab director. Such time savings lead to estimated cost savings of ~€12,000 per year (estimation based on the average salary at the public rate in Germany, i.e., 58k€ for a lab technician, as listed publicly¹).² The successful implementation of navify[®] Algorithm Suite at Medizinische Hochschule Hannover bodes well for enabling local digital transformation in HCC patient management on a larger scale, with a continually expanding certified algorithm library.

1. Tabulated salary information for German public institutions listed on site: <https://www.oeffentlichen-dienst.de/entgelttabelle/tvoed-b-vka.html>. Average rate calculated for lab technicians at E6 to E8 salary level.

2. Disclaimer: Individual lab results may vary, and testimonials are not claimed to represent typical results. All testimonials are provided by real participants, and may not reflect the typical purchaser's experience, and are not intended to represent or guarantee that anyone will achieve the same or similar results.



Unmet Need: Early and Efficient Detection of HCC

Medizinische Hochschule Hannover, an established University Hospital in Hannover, Germany, is committed to utilizing the combined GAAD and **navify**[®] Algorithm Suite digital solution to capture the clinical benefits of the GAAD solution for hepatocellular carcinoma (HCC). The GAAD algorithm, an in-vitro diagnostic multivariate index algorithm, analyzes sex and age in combination with the results of two other Roche assays: Elecsys AFP and Elecsys PIVKA-II.³ The CE-marked GAAD algorithm helps physicians diagnose early stage hepatocellular carcinoma (HCC). **navify**[®] Algorithm Suite, a novel digital platform introduced by Roche in 2022, aims at enabling and supporting the integration of clinical algorithms such as GAAD into the technical IT workflow of laboratories or hospitals.⁴ Prior to the adoption of **navify**[®] Algorithm Suite to support the GAAD algorithm, Medizinische Hochschule Hannover tested an alternative digital solution for HCC that commanded greater resources with fewer performance benefits and no easy integration into the existing clinical workflow. As indicated by the laboratory director at Medizinische Hochschule Hannover during an interview.

Customer: Medizinische Hochschule Hannover (MHH), a University Hospital

Certified Centrum for Liver Cancer

MHH physicians contribute to Liver Cancer guidelines for patient management

The early and accurate detection of HCC, comprising ~90% of cases of liver cancer, is crucial for patient management and prompt treatment to prolong survival. HCC results in >830,000 deaths annually.^{5,6} While hepatitis B and hepatitis C infection are considered the primary risk factors for HCC, non-alcoholic steatohepatitis (NASH) associated with metabolic syndrome or diabetes mellitus is increasingly implicated in HCC development in Europe and North America. Although current guidelines recommend the routine surveillance of patients at risk with ultrasonography, this approach has shown limited success for diagnosis of early-stage HCC. Notably, 25% of all HCC cases present with potentially actionable genetic mutations, but relevant molecular information is derived from invasive tissue or liquid biopsies.⁷ Multiple serum biomarkers associated with HCC, such as alpha-fetoprotein

3. GAAD Method Sheet: Available on <https://diagnostics.roche.com/global/en/products/params/elecsys-gaad.html>

4. <https://diagnostics.roche.com/global/en/news-listing/2023/roche-introduces-navify-algorithm-suite-a-digital-library-of-m.html>

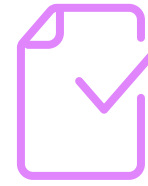
5. Baecker A, Liu X, La Vecchia C, Zhang ZF. Worldwide incidence of hepatocellular carcinoma cases attributable to major risk factors. Eur J Cancer Prev. 2018;27(3): 205-212

6. IARC, WHO. Cancer today. Available from: <https://gco.iarc.fr/today/data/factsheets/cancers/11-Liver-fact-sheet.pdf> (Accessed April 2023)

7. Llovet JM, Kelley RK, Villanueva A, et al. Hepatocellular carcinoma. Nat Rev Dis Primers 2021;7(1):6.

(AFP), protein-induced by vitamin K absence-II (PIVKA-II) and Lens culinaris agglutinin-reactive fraction of AFP (AFP-L3), have been proposed to improve detection.⁸ However, the use of these biomarkers alone does not provide adequate specificity or sensitivity and their inclusion in guidelines has been inconsistent.^{9,10,11}

The **navify**[®] algorithm, GAAD, combining gender (sex) and age with two biomarkers (Elecsys AFP and Elecsys PIVKA-II) has demonstrated good clinical performance for the detection of early-stage HCC, especially in conjunction with ultrasonography.^{12,13} GAAD calculates a risk factor score from 0–10, which is the likelihood of the patient developing HCC. A score below 2.57 indicates a negative result, while a score above 2.57 indicates a positive result and increased risk of HCC.



GAAD meets customer requirements for a CE-IVD certified digital solution that aids in diagnosis of HCC and is directly integrated into the clinical workflow with **navify**[®] Algorithm Suite.

Digital Solution: **navify**[®] Algorithm Suite

navify[®] Algorithm Suite supports the integration of medical algorithms such as GAAD for HCC into the customer IT environment and handles communication and transfer of data between customer IT systems and cloud-hosted medical algorithms. **navify**[®] Algorithm Suite enables workflow integration, so that physicians can order GAAD in the same fashion as they would order biomarkers through their standard ordering interface.

navify[®] Algorithm Suite is a secure, standalone cloud-based software intended to host digital clinical decision support (CDS) solutions based on medical algorithms or formulae, and to provide management, infrastructure, and functional services to such algorithms. The algorithms hosted by the digital platform are separate, individual products, which may be used independently. Today, **navify**[®] Algorithm Suite provides user access to algorithms for oncology medicine. An expansion of the clinical algorithm menu is planned shortly in cardiology and infectious disease patient management. In the future, **navify**[®] Algorithm Suite may also include information such as references to generic literature, medical guidelines, or study data.

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8. Piratvisuth T, Tanwandee T, Thongsawat S, et al. Multimarker Panels for Detection of Early Stage Hepatocellular Carcinoma: A Prospective, Multicenter, Case-Control Study. *Hepatol Commun.* 2022;6(4): 679–691.
 9. Vogel A, Cervantes A, Chau I, et al. Hepatocellular carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2018;29 (4): 238–255.
 10. Marrero JA, Kulik LM, Sirlin CB, et al. Diagnosis, Staging, and Management of Hepatocellular Carcinoma: 2018 Practice Guidance by the American Association for the Study of Liver Diseases. *Hepatology.* 2018;68(2): 723–750
 11. Omata M, Cheng AL, Kokudo N, et al. Asia-Pacific clinical practice guidelines on the management of hepatocellular carcinoma: a 2017 update. *Hepatol Int.* 2017;11(4): 317–370.
 12. Chan HL, Vogel A, Berg T, De Toni EN, Kudo M, Trojan J, Malinowsky K, Findeisen P, Klein HG, Hegel JK, Schöning W. A comparative analysis of Elecsys GALAD and Elecsys GAAD score to detect early-stage hepatocellular carcinoma in an international cohort. Presented at EASL ILC. 2022 Jun;2022: 22–6.
 13. Chung-Feng Huang et al. The clinical utility of Elecsys GAAD score the diagnosis of hepatocellular carcinoma. Poster presented at: APASL Single Topic Conference on Hepatocellular Carcinoma; 2022 June 23–25; Taipei, Taiwan.

Benefits of navify® Algorithm Suite

The integration of navify® Algorithm Suite with laboratory systems such as LIS (laboratory information system) reduces manual steps through automation. The user no longer needs to take aliquots from the sample, assign them to a rack, analyze them separately and enter the results. The implementation of GAAD with navify® Algorithm Suite saves 3–4 minutes per case for ~40 cases per day per reports from the lab director in a semi-structured interview. The resulting saving of 2 hours user time daily approximates cost savings of €230 per week, €1,000 per month and €12,000 per year (estimated based on the average salary of the public rate in Germany, i.e., 58k€ of a lab technician, as listed publicly).¹⁴ In a semi-structured interview, the lab director Prof. Dr. R. Lichtinghagen stated that the clinical workflow is streamlined to reduce the number of required individual manual steps by 90% from 10 to just 1 step, decreasing potential for error by making manual steps redundant. Lab directors can invest the saved effort and time in creating additional value, for example by serving more patients.



Designed for optimal information security management, navify® Algorithm Suite complies with GDPR (General Data Protection Regulation) in Europe as well as HIPAA (Health Insurance Portability and Accountability) in the USA.

“The GAAD algorithm is like a digital parameter that runs in routine as a normal laboratory value – now we have no additional effort!”

Prof. Dr. R. Lichtinghagen

Adoption of navify® Algorithm Suite carries a relatively low resource burden and integration into the workflow can be achieved with only light efforts from customer IT admin, typically numbering hours throughout the integration journey. navify® Algorithm Suite is designed to provide multiple technical integration methods to support variability in the real world. These integration options are discussed with customers during the pre-sales phase and the optimum integration method is identified. A few planning meetings between the lab director, customer’s IT department and Roche personnel are needed for alignment and 2–4 hours of time as invested by the customer’s IT department can cover configuration and solution testing in the customer’s lab. The integration timeline is dependent on the complexity of the situation.

Key steps in the integration process are:

1. Develop integration scenario with customer IT: typically complete in ~24 hours
2. PIVKA-II validation (if required): ~2–3 days likely needed
3. Implementation: ~2–3 weeks expected duration
4. Go live and use navify® Algorithm Suite

14. Tabulated salary information for German public institutions listed on site: <https://www.oeffentlichen-dienst.de/entgelttabelle/tvoed-b-vka.html>. Average rate calculated for lab technicians at E6 to E8 salary level.

Solutions used pre-implementation of Roche products to calculate HCC risk score

Competitor table-based machine + GALAD algorithm + Competitor biomarker reagents.

Pre-implementation workflow

1. Identify sample in core lab
2. Take an aliquot manually
3. Create a “GALAD rack” for aliquots
4. Assign identifiers for each aliquot to the corresponding sample
5. Take the rack and walk over to table based analyzer
6. Run aliquots in sequence on analyzer (biomarker)
7. Write down parameter values for each aliquot
8. Go to LIS based office computer
9. Type in LIS noted parameter values for each patient
10. GALAD calculation is performed automatically as mathematical formula is embedded

Solutions used post-implementation of Roche products to calculate HCC risk score

cobas® instruments + **navify**® Algorithm Suite + **navify**® GAAD algorithm + Elecsys PIVKA-II and Elecsys AFP reagents.

Post-implementation workflow

One step – with **navify**® Algorithm Suite, GAAD is a digital biomarker that can be ordered in the LIS as laboratory routine by simply clicking a button.

*“Integration through the **navify**® Algorithm Suite increases data security and standardizes our IVDR-compliant processes.”*

Prof. Dr. R. Lichtinghagen

Conclusion

The **navify**[®] algorithm GAAD met the customer requirements for a CE-IVD certified solution that aids in the diagnosis for HCC and was integrated into the local digital systems and clinical workflow with relatively low effort from the customer. The successful implementation of **navify**[®] Algorithm Suite at Medizinische Hochschule Hannover bodes well for enabling local digital transformation in HCC patient management on a larger scale, with a continually expanding certified algorithm library.