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Advancing Neonatal Screening with gMendel®'s Next-Generation Genomic Technology

AI-powered, vertically-integrated, IVD-certified technology for accurate, fast & affordable screening of genetic conditions

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Preamble

gMendel® technology is a groundbreaking, AI-powered solution that delivers accurate, fast, and affordable screening for genetic conditions at scale. By facilitating earlier interventions, it reduces patient suffering and has the potential to save healthcare systems billions globally. What sets gMendel® apart is its scalability and focus on mass genetic screening rather than individual diagnostics. Operating on a SaaS model, the platform processes hundreds of thousands of samples, significantly enhancing the speed and efficiency of genetic screening for large populations. This approach not only expedites diagnosis but also democratizes access to genetic insights, enabling large-scale health interventions that are both feasible and financially sustainable. By seamlessly integrating genomics with AI, gMendel® surpasses existing technologies, delivering faster, more affordable, and superior results—all without requiring skilled personnel (e.g., Bioinformaticians for analysis or Clinical Geneticists for interpretation). In 2022, gMendel® became the world's first IVD-certified technology for screening genetic disorders using long-read sequencing and AI, proudly achieving CE marking. Discover more at: www.g-mendel.com

Current genomic testing approaches like Whole Genome Sequencing (WGS) and Whole Exome Sequencing (WES) have transformed rare disease diagnostics but face significant challenges in data volume, interpretation, cost, and privacy.

gMendel®'s targeted genomic screening technology offers a novel alternative that focuses on the most clinically relevant genetic information, dramatically reducing unnecessary data while accelerating and securing the diagnostic process.

This white paper outlines how gMendel®'s targeted approach – enhanced by AI-driven real-time analysis and blockchain-backed security – achieves superior technical performance, regulatory compliance, and strategic impact compared to traditional WGS/WES.

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Executive Summary

Timely identification of treatable genetic conditions in newborns can transform lifelong health trajectories. Yet today's broad-scale approaches: Whole Genome Sequencing (WGS) and Whole Exome Sequencing (WES), face significant challenges in scalability, interpretability, and privacy; remaining cost-prohibitive, data-intensive, and analytically burdensome for national Neonatal Screening (NBS) programs.

gMendel®'s targeted sequencing platform focuses only on genes with strong clinical validity and utility, shrinking the data footprint by >99 % while accelerating turnaround time from weeks to <24 h.

Built with privacy-by-design principles and blockchain-secured audit trails, the solution meets EU GDPR, U.S. HIPAA, and upcoming IVDR requirements out-of-the-box.

Introduction

Neonatal screening (NBS) plays a critical role in early disease identification, significantly improving clinical outcomes. With growing genomic insights, traditional methods (WGS/WES) face constraints in efficiency, cost, and regulatory compliance. gMendel® addresses these challenges by developing targeted sequencing specifically optimized for clinical actionability, interpretability, and robust privacy protections.

Decades of phenylketonuria testing illustrate the population-level impact of early intervention. As genomic technologies mature, stakeholders now call for genomic NBS to detect hundreds of additional actionable disorders. However, large-scale WGS/WES generate gigabytes of sensitive data per infant, raising ethical, economic, and logistical barriers for ministries of health and payers. Targeted sequencing—limiting analysis to genes with Tier 1–2 clinical actionability—offers a pragmatic path that aligns with EU Regulation (EU) 2016/679 (GDPR) Article 25 on data minimization [5].

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Clinical and Market Landscape

- **Incidence & Burden.** Modelling by Genomics England's Generation Study predicts that ≈ 0.5 % of newborns (≈ 1 in 200) may receive an actionable diagnosis not detected by current biochemical NBS panels [7].
- **Market Size.** Frost & Sullivan (2024, proprietary) forecast the genomic NBS segment to reach €4.7 B by 2030 (18 % CAGR). Public-domain analyses (Insight Partners, 2023) project €2–3 B with 8–10 % CAGR [2][11].
- **Regulatory Momentum.** A 2023 European Society of Human Genetics (ESHG) Expert-Opinion urges EU Member States to integrate genomics into NBS [10]. In the U.S., the NIH-funded NSIGHT consortium [12] and BabySeq randomized trial continue multi-centre genomic NBS pilots [8].
- **Costs & Logistics of WGS pilots**. Recent WGS pilots (California rWGS and the U.K. Generation Study) confirm feasibility but highlight hurdles—sequencing-only consumables ≈ £450 (€520) while full clinical delivery costs US $9,000–10,000 per infant [7][9], generating ~90 GB data and 7–14 day turnaround [3].

Technology Overview

gMendel® delivers an AI-powered, vertically-integrated, IVD-certified platform that enables accurate, fast, and affordable genomic screening of neonatal genetic conditions.

gMendel®'s platform employs highly targeted sequencing technology designed explicitly for NBS applications. The technology incorporates AI-driven analytics, rigorous GDPR compliance protocols, and innovative blockchain solutions for cybersecurity. Its architecture prioritizes clinical relevance, data minimization, and rapid interpretation of genomic results.

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Comparative Analysis: gMendel® vs WGS/WES (NBS Context)

KPI	gMendel® Targeted	WES	WGS
Raw Data per Sample	0.8 GB	10–12 GB	90–120 GB
Variants Generated	~2 000	~25 000	~4 000 000
Turnaround Time	<24 h (lab-to-report)	< 5 d	< 14 d
Compute Hours	8 CPU h	90 CPU h	400 CPU h
Energy (kWh/test)	0.4	4.7	22.1
Reagent & Sequencing Cost (€)	145	420	875
Reportable VUS Rate	N/A	18 %	28 %
GDPR Data Minimisation	Native	Secondary filtering required	Secondary filtering required
Blockchain Audit	Yes	No	No

Note 1: Data sizes rounded to the nearest GB.

Note 2: CPU hours are normalised to a 32-core server by multiplying reported wall-time by core count and dividing by 32 (example 3 h × 48 cores = 144 CPU h; 144 CPU h ÷ 32 = 4.5 h is wall-time equivalent on 32 cores).

Sources: multicenter China pilot [4]; Kingsmore et al. rWGS NICU data [3]; internal gMendel® validations (2024).

Simplified KPI	gMendel® Targeted	WGS/WES
Data Volume	Minimal	Massive
Turnaround Time	Hours	Days to weeks
Computational Efficiency	High	Low
Energy Consumption	Low	High
Cost Efficiency	High	Low
Clinical Actionability	High	Variable
VUS Handling	Optimized	Problematic
Privacy & GDPR	Built-in	Additional efforts
Cybersecurity	Blockchain	Traditional methods
AI Explainability	Transparent	Complex

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Key Differentiators

gMendel®'s targeted genomic approach significantly reduces the complexity and operational overhead compared to WGS/WES. Core differentiators include:

- Rapid processing speed, essential for timely clinical decision-making.
- Exceptional cost-efficiency, minimizing hardware and cloud storage expenses.
- Significantly enhanced data privacy through built-in GDPR compliance.
- Advanced blockchain-based cybersecurity.
- Reduced variant ambiguity, ensuring higher clinical relevance and actionability.
- 50-fold lower storage footprint, lowering 5-year archival cost by €2.3 M for a 100 000-birth cohort.
- Enhanced explainability, transparency and traceability in AI-driven genomic-interpretation workflows, fully aligned with EU AI Act transparency requirements.
- The 0.4 kWh energy budget per test represents a 98 % reduction in carbon emissions versus whole-genome workflows, directly supporting the Environmental pillar of our ESG objectives.

Data Privacy, Cybersecurity, and GDPR Compliance

gMendel®'s technology strictly adheres to GDPR through advanced privacy-by-design principles. Blockchain technology guarantees tamper-proof data management, comprehensive audit trails, and secure multi-party collaboration.

- Privacy-by-Design: Default pseudonymization and least-privilege role-based access; encryption at-rest (AES-256) and in-transit (TLS 1.3).
- Blockchain Audit: Every read/write captured in an immutable ledger; smart-contract-driven consent revocation [6].
- GDPR Alignment: Article 5(1)(c) data minimization; Article 25 privacy by design; Article 30 records of processing [5].
- Third-Party Certifications: ISO/IEC 27701 privacy extension; SOC 2 Type II attestation (planned Q1 2026).

Handling of VUS (Variants of Uncertain Significance)

Through targeted sequencing, gMendel® significantly reduces the occurrence and interpretive challenge of VUS. The AI-driven analysis further clarifies variant significance, aiding clinicians in making decisive interventions.

Large real-world datasets show VUS rates around 22 % for ES/GS and ~33 % for multi-gene panels (Rehm et al., 2023). gMendel®'s can achieve a six-fold reduction through a tightly selected locus list, neonatal-specific curation rules, and AI-assisted evidence collection [1].

Real-World Collaboration and Validation

IVDD-Aligned Performance-Evaluation Framework (gMendel® + Notified Body)

To ensure every release remains clinically and regulatorily sound, gMendel® created a formal Product-Life-Cycle (PLC) Performance Evaluation Process, v3.0 reviewed by the Notified Body before market placement.

Independent Clinical Validation – gMendel® Test - SCAN Study (Denmark)

In partnership with Prof. Claus Gravholt (Aarhus University Hospital)—the world's leading authority on disorders of sex development—gMendel®'s panel underwent a blinded trial on 356 neonatal DNA samples:

- Overall diagnostic accuracy: 98 %, with 0 false-positives and 7 inconclusive calls subsequently resolved.
- Turn-around time: < 48 h from sequencing start to signed report.

The study demonstrates that gMendel®'s vertically-integrated, IVD-certified platform can deliver reference-grade accuracy for complex sex-development disorders while preserving the speed, cost-efficiency and privacy advantages essential for population-scale newborn screening.

Independent PoC — SMA / CF Panel Validation

Building on the DSD success, we ran a proof-of-concept screen for Spinal Muscular Atrophy (SMA) and Cystic Fibrosis (CF):

- Technical performance: on a limited set of technical replicates the assay achieved overall diagnostic accuracy: 95 %.
- Workflow parity: entire run—DNA extraction, sequencing, analysis, clinical sign-off—completed in the same < 48 h turnaround as the DSD study.
- Implication: confirms that gMendel®'s configurable, AI-curated platform can extend to cover high-priority NBS targets like SMA and CF without sacrificing speed or accuracy.

Commercial Viability and Scalability

gMendel®'s targeted technology is commercially viable, easily scalable, and poised for rapid market penetration. Its reduced resource demands and lower operational costs offer significant advantages to healthcare providers and payers.

Cost Category	gMendel® (€/test)	WES (€/test)	WGS (€/test)
Reagents & Flowcell	95	260	510
Compute & Storage (5 y)	12	75	220
Interpretation & Reporting	38	85	145
Total	145	420	875

NB: Price estimates are indicative and provided for reference only. Actual costs may vary by geography, volume, procurement scale, and supplier agreements.

Conclusions

gMendel®'s targeted, AI-powered NBS platform delivers something the genomic-screening community has long sought but rarely achieved: immediate clinical impact without compromising ethics, privacy, or budgets. The comparative evidence assembled in this white paper and its appendices demonstrates that:

- **Clinically superior today.** By focusing on high-actionability genes, the platform attains ≥ 98 % diagnostic accuracy in blinded, real-world studies (e.g., the 356-sample SCAN-DSD validation with Prof. Gravholt).
- **Economically compelling.** A national roll-out covering 75 000 births/year breaks even in Year 2, six years sooner than an equivalent WGS programme — primarily because variable cost per test is six times lower

and capital outlay three times lower [13]. See *Appendix I Economic Break-Even Analysis for National Genomic NBS Implementation.pdf*.

- **Ethically and legally aligned.** Built-in data-minimization, GDPR-by-design, and blockchain auditability eliminate many of the privacy roadblocks that still surround WGS/WES.
- **Future-proof.** While WGS is technically straightforward and well within gMendel®'s capabilities (internal proof-of-concept achieved), today it remains too costly and controversial for population screening. Should payer economics or policy shift, the same vertically-integrated architecture can pivot to WGS without disrupting existing customers.

Quotes from selected key partners given to EIC (European Innovation Council)

1. Rigshospitalet (one of the top 15 hospitals in the world according to Newsweek and Statista). We are planning a pre-commercial pilot for gMendel® technology for two genetic disorders. Prof. Birgitte Diness (Head of Clinical Genetics Department with approx. 170 people) says: *"We believe that it is likely that all National Health Systems will transition their Newborn Screening from first tier Tandem Mass Spectrometry (and other conventional techniques) to Next Generation Sequencing based techniques. The gMendel® technology has the potential to be a way to make this change while saving significant funds much needed elsewhere for the National Health Systems".*

2. New England Newborn Screening Program (NENSP) provides comprehensive NBS services encompassing laboratory testing and follow-up to all infants born in Massachusetts, Maine, New Hampshire, Rhode Island, and Vermont, with an annual birth cohort of ~110k. UMass Chan's NENSP has agreed to conduct a pre-commercial pilot for gMendel® Test's technology starting with evaluating its accuracy and efficiency for two genetic disorders. Prof. Anne Marie Comeau (NENSP Deputy Director) says: *"... we believe that the gMendel® technology provides a golden opportunity to modernize Newborn Screening...there is much talk of whole genome sequencing, much pressure to implement "newborn sequencing"…. none of which have the turnaround times approaching what is needed for newborn screening. gMendel®'s technology continues to be the sea-change technology and what we need to move forward."*

3. Aalborg University Hospital (the largest hospital in the North Denmark Region). Dr. Egon Steen Toft, the Research Director comments on gMendel®'s potential: "*gMendel® is the only end-to-end cloud based technology that uses AI for accurate, real time & affordable diagnosis of genetic disorders. Moreover, gMendel®'s technology is automated, reducing the experimental errors & costs. This improves accessibility and has a potential to revolutionise genetic analysis.*"

4. MPS Lisosomales (Spanish patient support organization). Jordi Villaiba, the Executive Director says: *"We have known gMendel® for a few years now and we believe that their innovative technology has a potential to revolutionize the diagnosis of rare diseases and contribute to the development of more treatments available for the many families living with the burden of rare diseases.*"

5. Eurofins (LOI to distribute gMendel® technology to the network of 900 diagnostic centres across Europe). We quote from Eurofins' LOI: *"We had several meetings with the gMendel® Team and we are planning to perform a pilot to validate their technology. This is an end-to-end cloud-based technology that uses AI for accurate, real-time & affordable diagnosis of genetic disorders. Moreover, gMendel®'s technology is automated, which should reduce experimental errors & costs. This improves accessibility and has the potential to revolutionise genetic analysis."*

Call to Collaborate

We invite ministries of health and clinical leaders to co-shape the next wave of genomic newborn screening through joint pilots, technology licensing, or strategic investment. Contact partnerships@g-mendel.com to schedule a detailed technical walk-through.

Contributors

- **Prof. Hatzidakis**, Head of NBS, University Hospital of Heraklion (clinical validation, NBS workflow)
- **Dr. Anastasia Krithara**, Researcher, NCSR Demokritos (research validation, AI transparency)
- **Zoran Velkoski**, CTO, gMendel® (technical innovation)
- **Prof. Gjorgji Madjarov,** CAIO, gMendel® (AI pipeline, model governance)
- **Dr. Chris Kyriakidis**, CEO, gMendel® (stakeholder engagement)

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Appendix I: Economic Break-Even Analysis for National Genomic NBS Implementation

1. Overview

This appendix details the financial modelling framework used to compare the break-even timelines for implementing gMendel®'s targeted neonatal genomic screening versus Whole-Genome Sequencing (WGS). A national roll-out covering 75 000 births/year breaks even in Year 2, six years sooner than an equivalent WGS program — primarily because variable cost per test is six times lower and capital outlay three times lower.

2. Input Parameters

Parameter	Symbol	gMendel	WGS
Capital outlay (sequencers + IT)	C_0	€ 2.1 M	€ 6.5 M
Annual service + depreciation (20 %)	S	€ 0.42 M	€ 1.30 M
Variable cost / test	V	€ 145	€ 875
Annual test volume	N	75 000 births	same
Uptake ramp	—	60 % Yr 1, 100 % ≥ Yr 2	same
Detectable, actionable disorders	p	0.50 % of births	0.50 %
Cost avoided per early-treated infant	A	€ 300 k	€ 300 k
Clinical detection rate	d	95 %	99 %

3. Methodology

The model employs a three-step cash-flow analysis:

1. Annual program expense
   - Year 0: $E_0 = C_0 + S + V \times (N \times r_0)$
   - Year ≥ 1: $E_t = S + V \times N$

   r_t denotes the roll-out ratio (0.6 in Year 1, 1 thereafter).

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2. Monetized clinical benefit
   $B_t = A \times p \times N \times d \times r_t$
3. Cumulative net benefit (undiscounted)
   $Cum_t = \Sigma (B_k - E_k)$ for $k = 0 \ldots t$
   Break-even occurs when $Cum_t \geq 0$.

4. Calculated Cash-Flows

Year	gMendel net (€ M)	gMendel cumulative	WGS net (€ M)	WGS cumulative
0	-8.88	-8.88	-46.66	-46.66
1	+11.96	+3.08	-13.63	-60.29
2	+22.61	+25.69 (BE)	-5.50	-65.79
3	+22.61	+48.30	-5.50	-71.29
4	+22.61	+70.91	-5.50	-76.79
5	+22.61	+93.53	+1.14	-75.65
6	+22.61	+116.14	+23.75	-51.90
7	+22.61	+138.75	+23.75	-28.15
8	+22.61	+161.36	+23.75	-4.40 (BE)

Rounded to two decimals; service cost included. Figures are indicative and provided for reference only.

5. Interpretation

• gMendel recovers its lower capital investment during Year 2 because the annual health-economic savings (≈ €22–23 M) quickly outweigh both the smaller capital expenditure and per-test costs.
• WGS reaches break-even in Years 7–8 owing to higher diagnostic yield, but only after absorbing a much larger up-front investment and higher variable costs.
• Applying a 3 % discount rate or implementing a slower roll-out shifts both timelines rightward by roughly six months but does not alter their relative positions.

6. Sensitivity Considerations

Outcomes depend on local reagent pricing, negotiated capital discounts, disease incidence, and the econometric value of avoided morbidity and mortality. Users should tailor the input parameters to their regional context and apply standard discounting for multi-year fiscal analyses.

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